South Carolina Alzheimer's Disease Research Center

2025 STATEWIDE AGING AND ALZHEIMER'S DISEASE RESEARCH SYMPOSIUM

October 9-10, 2025

Pastides Alumni Center

CLEMSON® UNIVERSITY INSTITUTE FOR ENGAGED AGING

UNIVERSITY OF South Carolina

MUSC Medical University of South Carolina

ACKNOWLEDGEMENT OF FUNDERS

The 2025 Statewide Aging and Alzheimer's Disease Research Symposium is supported through funding from the SC Department of Health & Human Services (USC Alzheimer's Disease Research Center Designation – Lead: Dr. Leonardo Bonilha, Public Health Lead: Dr. Daniela Friedman), the SmartState Center of Economic Excellence (SmartHOME Endowed Chair Dr. Sue Levkoff), and the National Institutes of Health, National Institute on Aging (K07AG088128 - Friedman, R13AG074603 – Friedman/Levkoff).

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ACKNOWLEDGEMENT OF PARTNERS

USC Brain Health

ALZHEIMER'S® ASSOCIATION

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ADDAM'S GAMECOCK GEAR

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ACKNOWLEDGEMENT OF PLANNING COMMITTEE

- Sayema Akter, PhD Student, Arnold School of Public Health
- Ally Hucek, PhD Student, Arnold School of Public Health
- Amanda Russell, MSW Student, College of Social Work
- Dr. Sue Levkoff, College of Social Work
- Quentin McCollum, College of Social Work
- Dr. Maggi Miller, Arnold School of Public Health
- Dr. Daniela Friedman, Arnold School of Public Health

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SHARE

Scholars in Health and Alzheimer's Research Engagement

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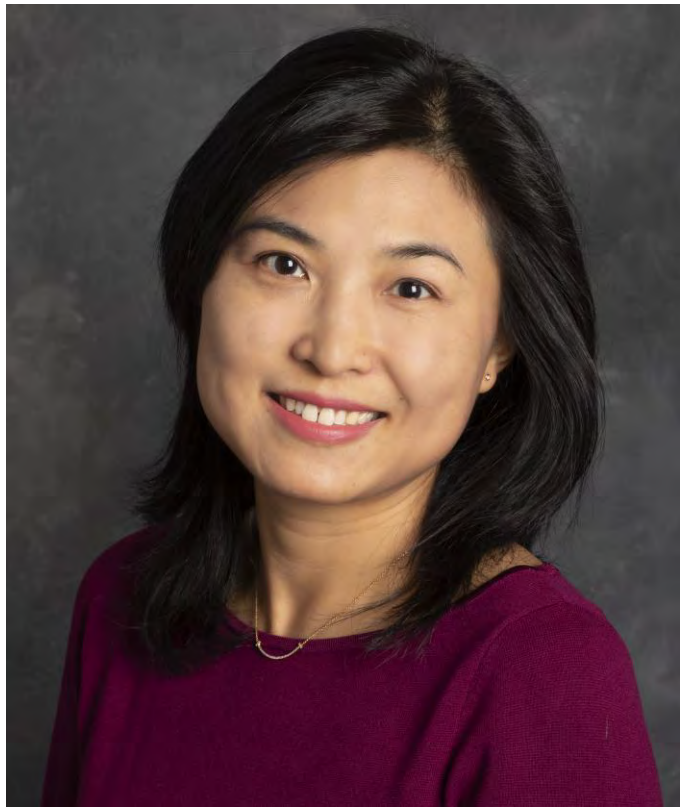
2025-2026 SHARE SCHOLARS



Dr. Chao Cai

Dr. Bryan Jenkins

Dr. Xueying Yang

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WELCOME FROM USC VICE PRESIDENT OF RESEARCH

Dr. Julius Fridriksson

UNIVERSITY OF South Carolina

SYMPOSIUM KEYNOTE: BRAIN HEALTH, LANGUAGE AND RECOVERY FROM NEUROLOGICAL INJURY

Dr. Leonardo Bonilha

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Language, Brain Health and Recovery from Neurological Injury

2025 Statewide Aging and Alzheimer's Disease Research Symposium
October 9-10, 2025
Pastides Alumni Center Ballroom

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South Carolina

Disclosures

- No conflicts of interest

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- PI/MPI - NIH
  - NIH/NIDCD R01 DC014021 (Language and aphasia)
  - NIH/NIDCD P50 DC014664 – Project 3 (Language and aphasia)
  - NIH/NIDCD R01 R01DC022458 (Aphasia)
  - P20GM155896 – Health Core (Translational research)
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- PI/MPI - Foundation
  - TDE (Brain Health)

Consulting

- Speakable LLC
- Allt.AI
- BrainWell


C-STAR
NIH
NIDCD
P50 DC014664 - Fridriksson
R01DC014021, R01DC022458, Bonilha
U01DC017521, U01DC022447 - Bonilha/Fridriksson

C-STAR

Julius Fridriksson

Chris Rorden

NIH
NIDCD

Sarah Newman-Norlund

Roger Newman-Norlund

Kelli Powell

Sara Sayers

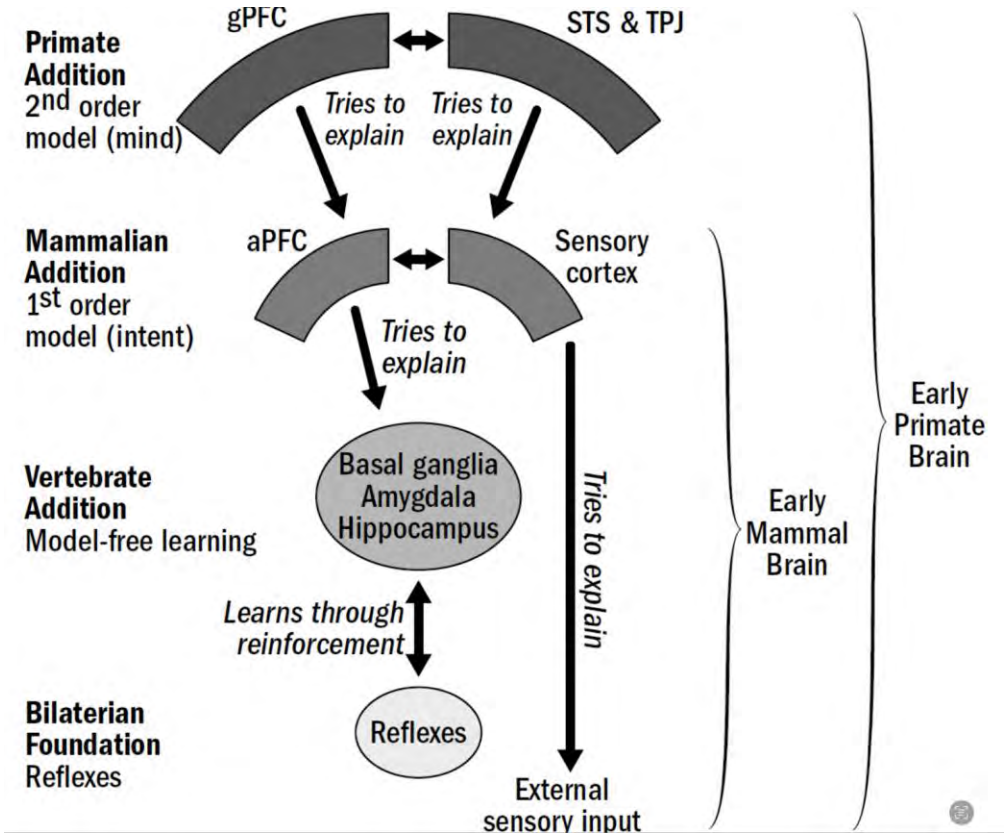
A B C @ USC

UNIVERSITY OF South Carolina

Outline

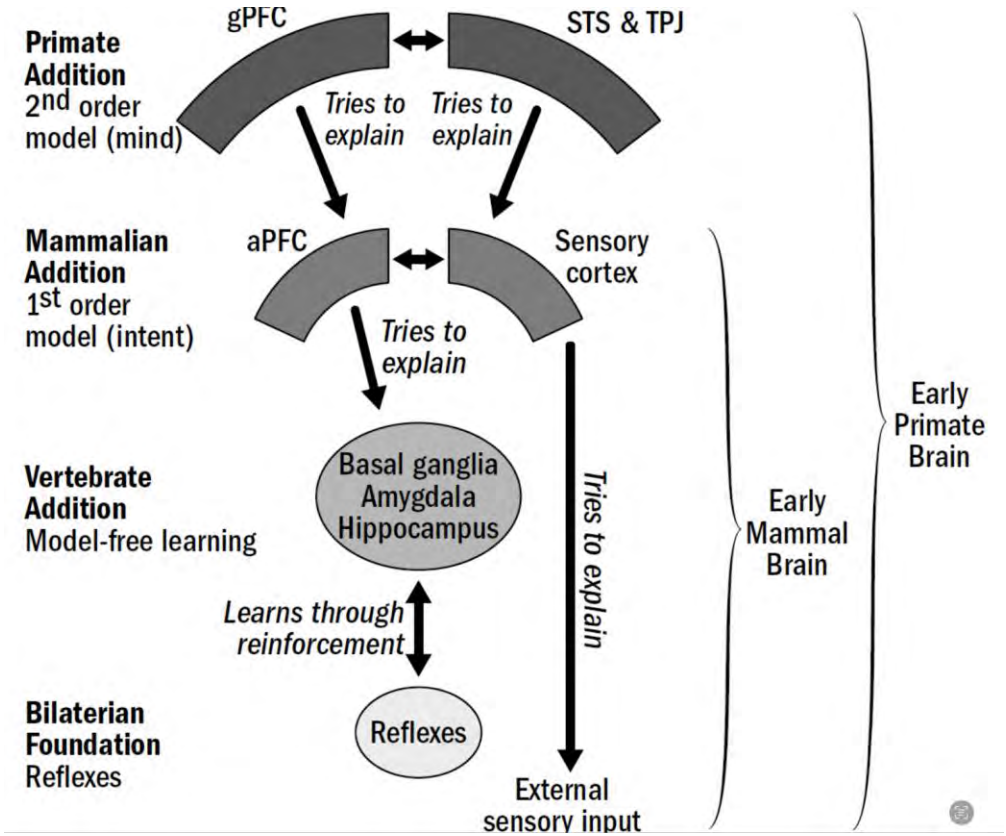
- Language
- Language Loss from Neurological Injury –Aphasia
- Research – Aphasia Severity and Recovery
- Brain Health

Language



Bennett, M. S. (2023). A brief history of intelligence: evolution, AI, and the five breakthroughs that made our brains. First edition

Language



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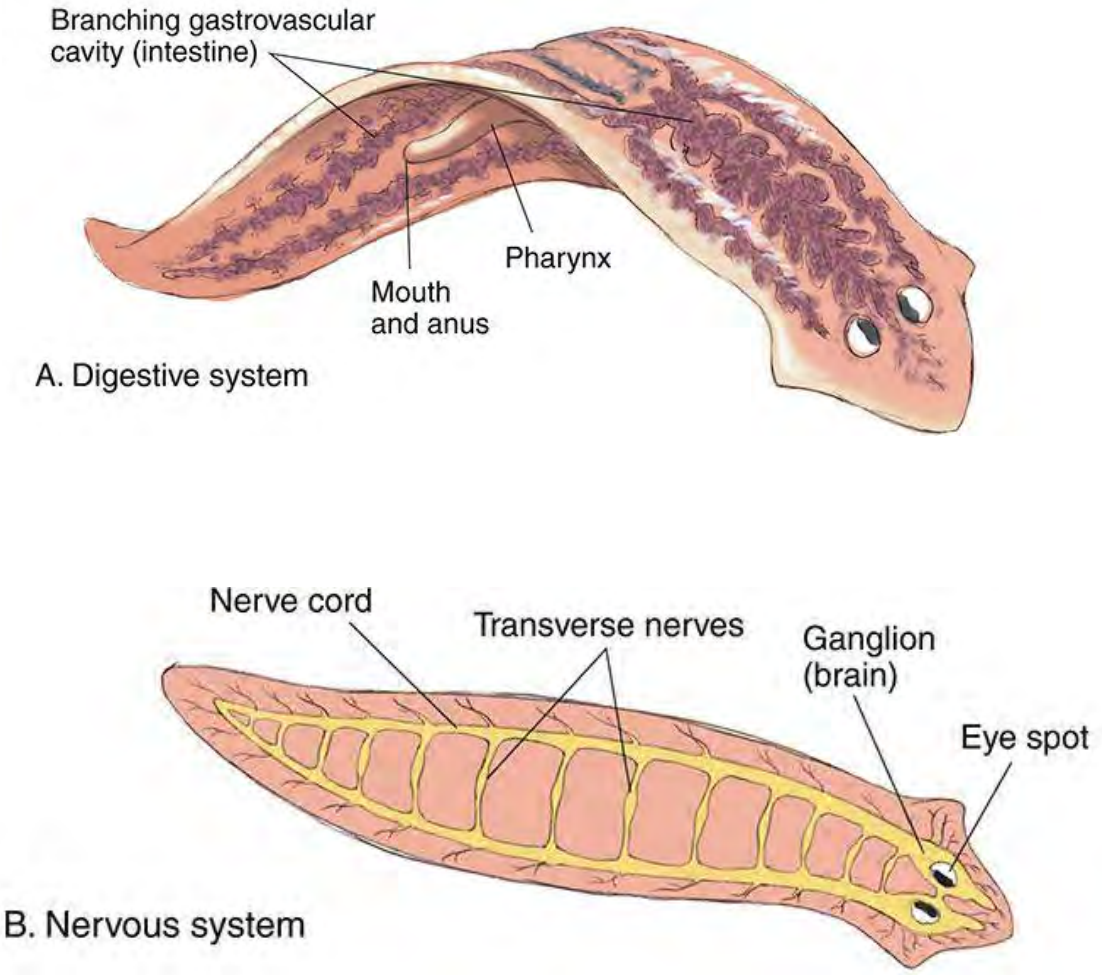
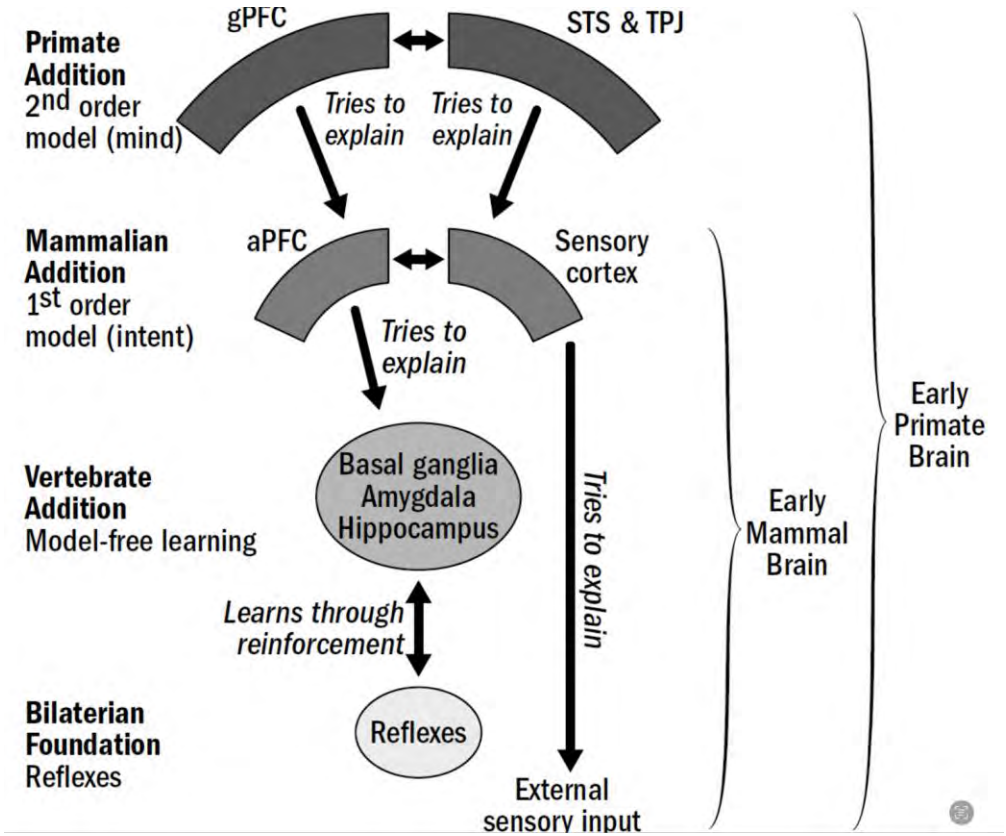


https://www.carlsonstockart.com/photo/flatworm-planaria-planarian-illustration/

Language



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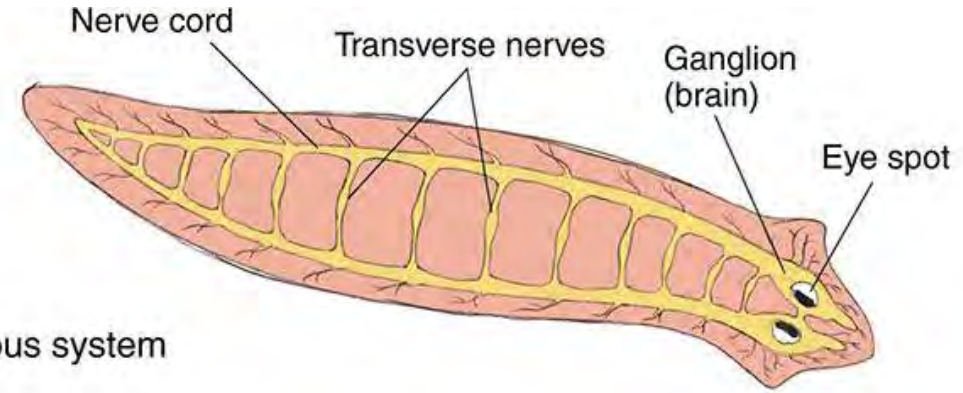

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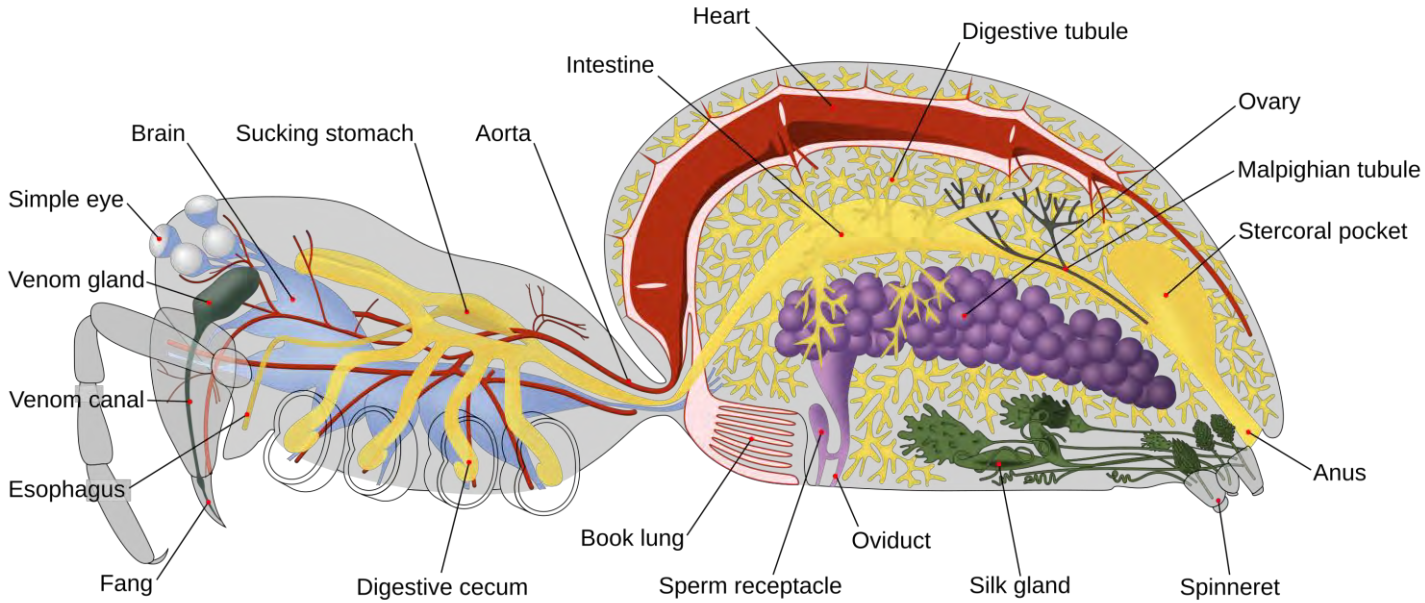

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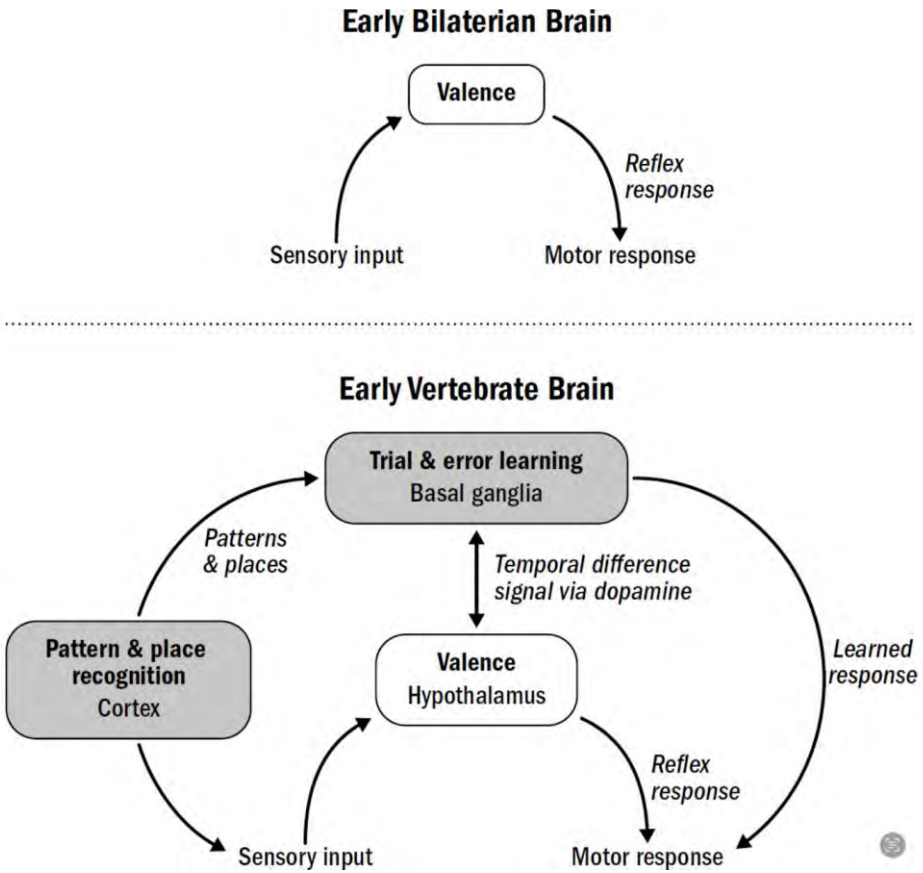

https://news.temple.edu/publications/temple-magazine/2012/spring/do-locomotion

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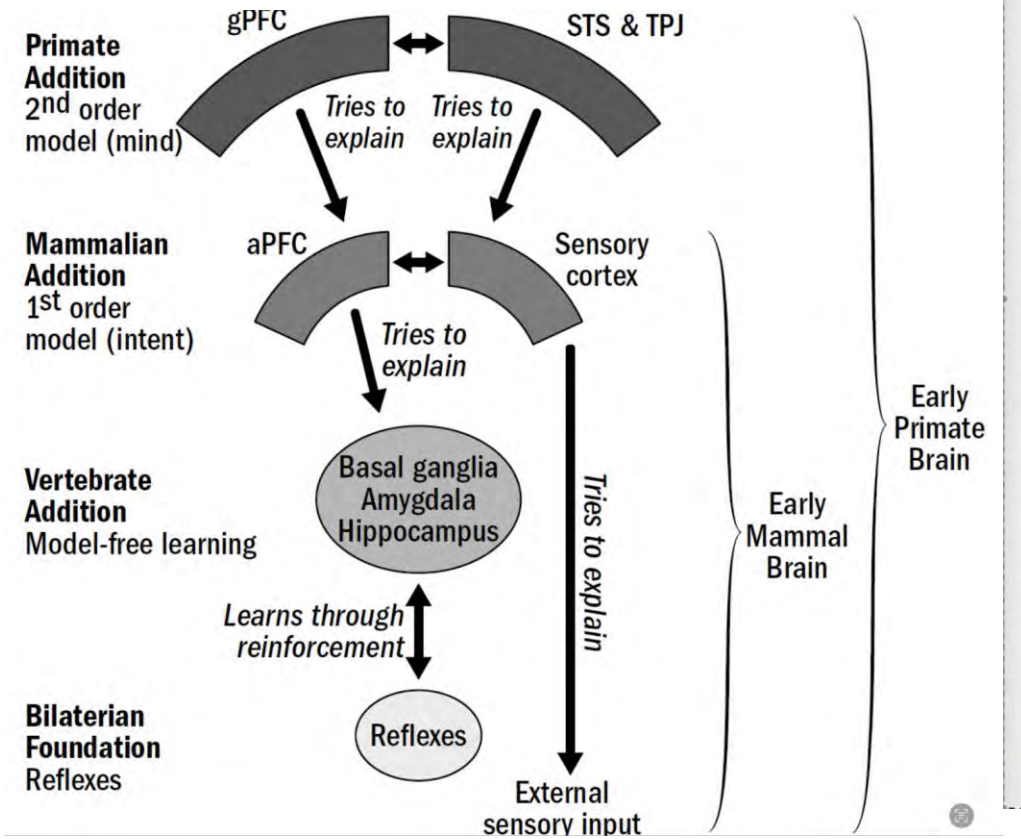

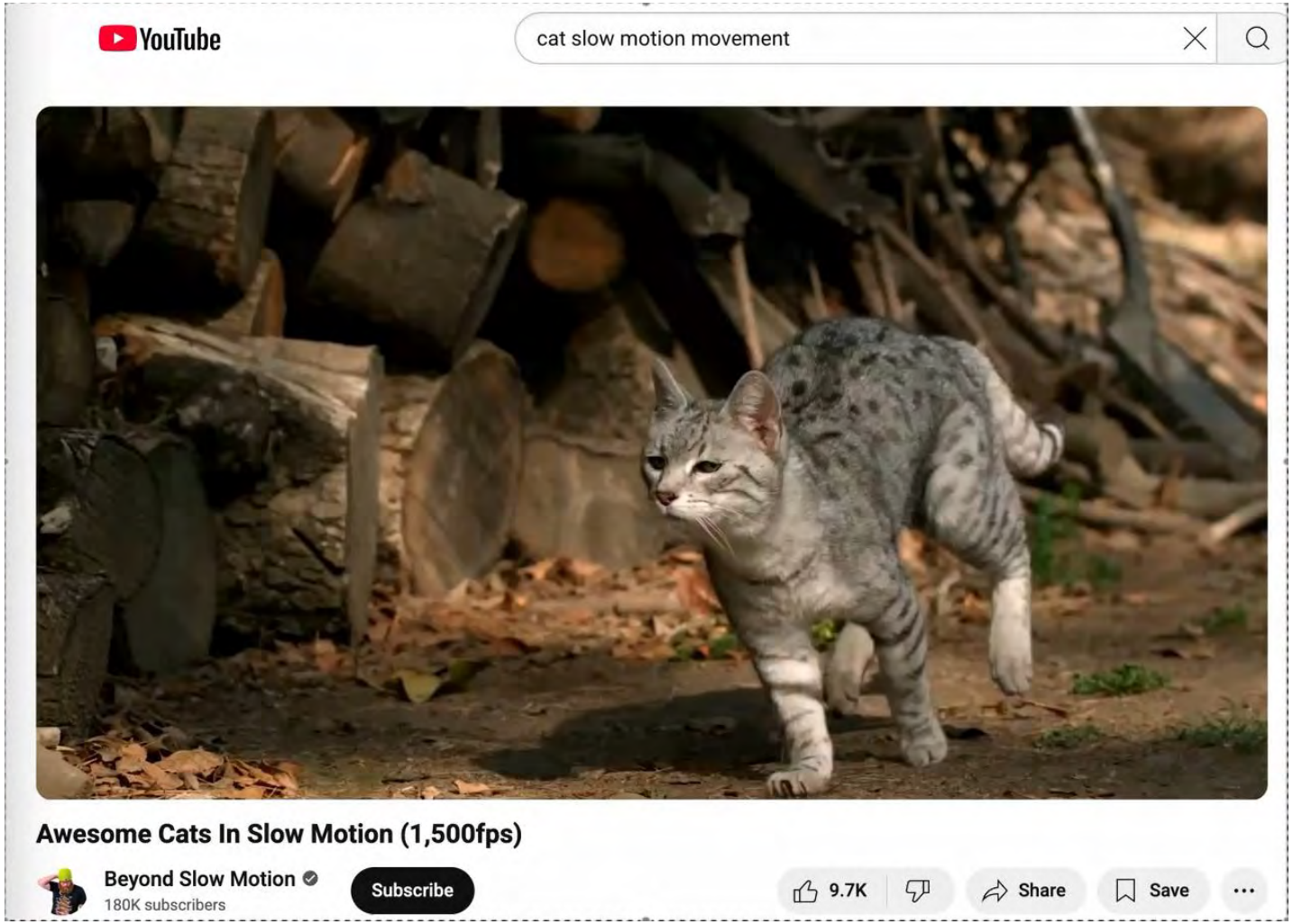

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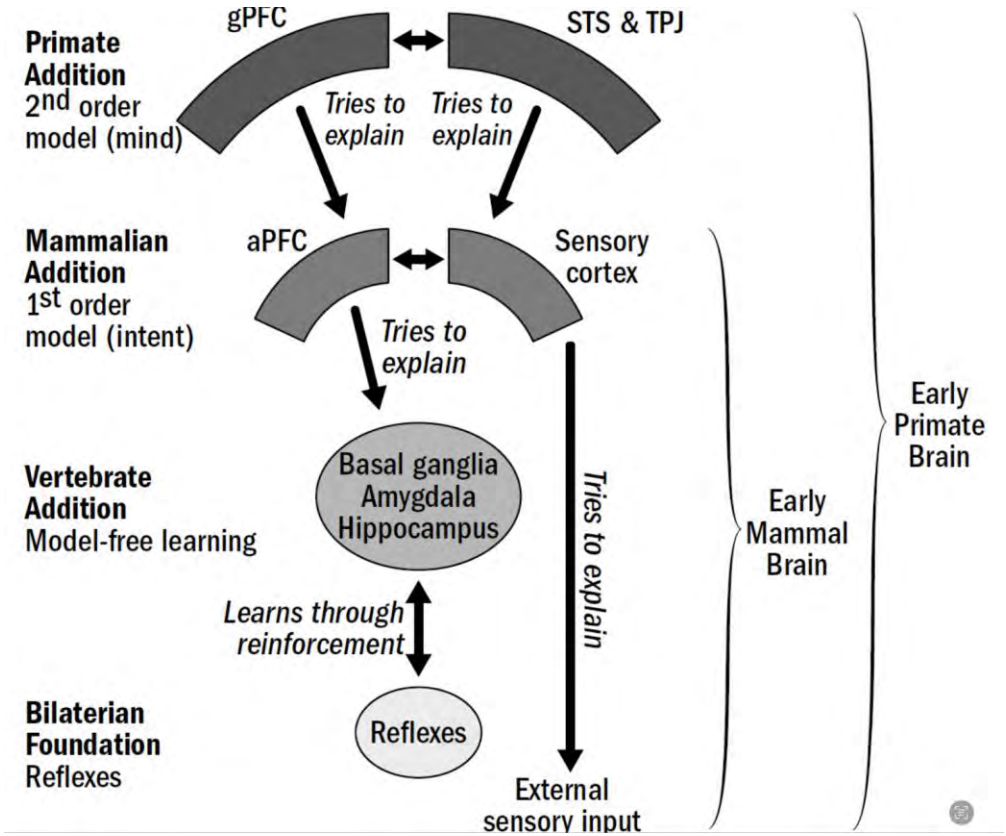

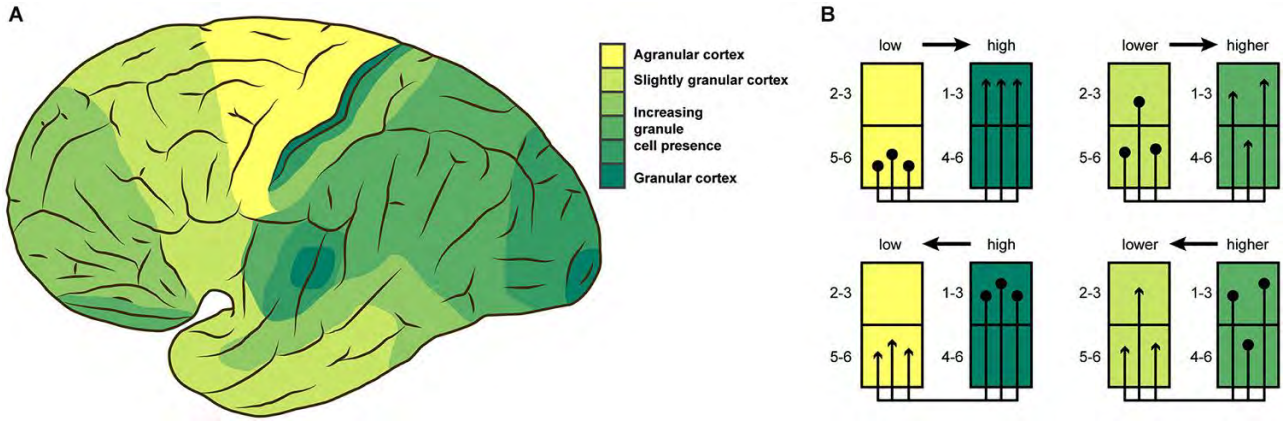

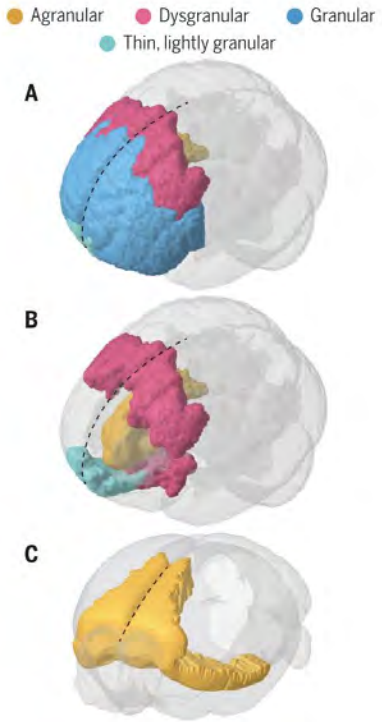

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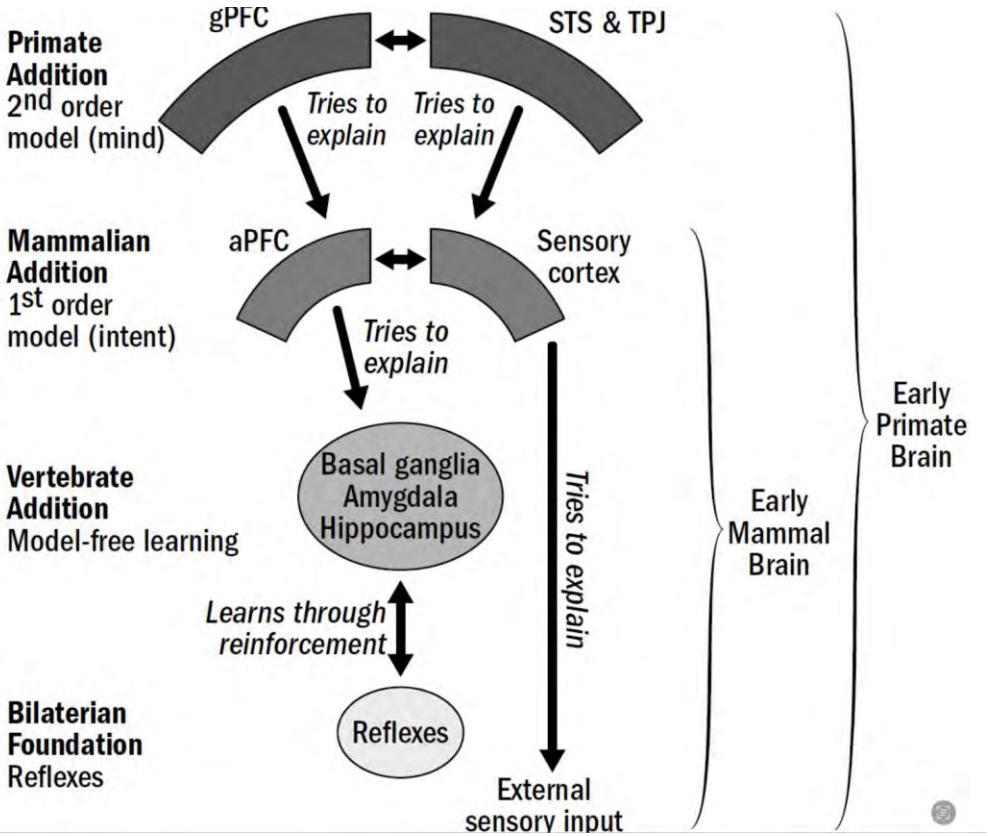
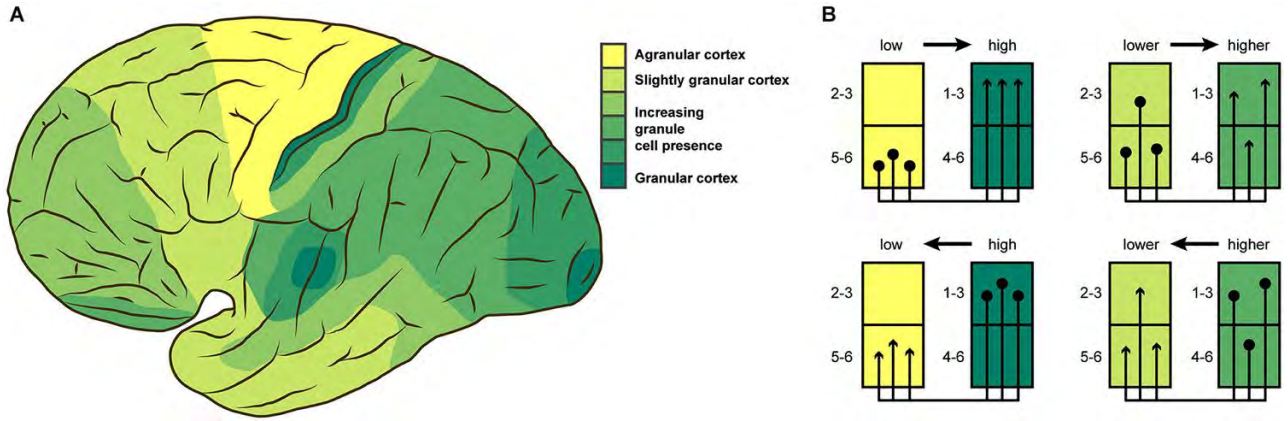
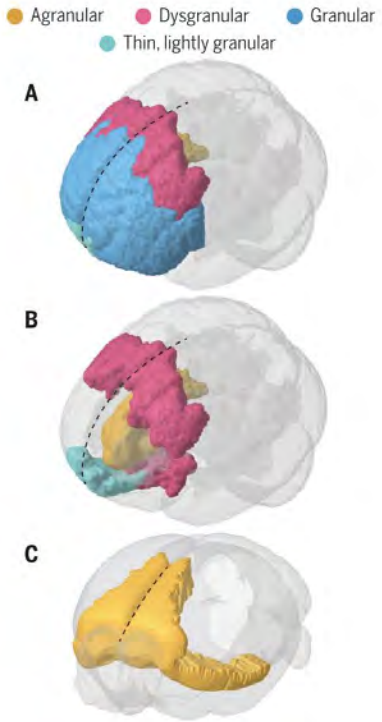






1- Steering

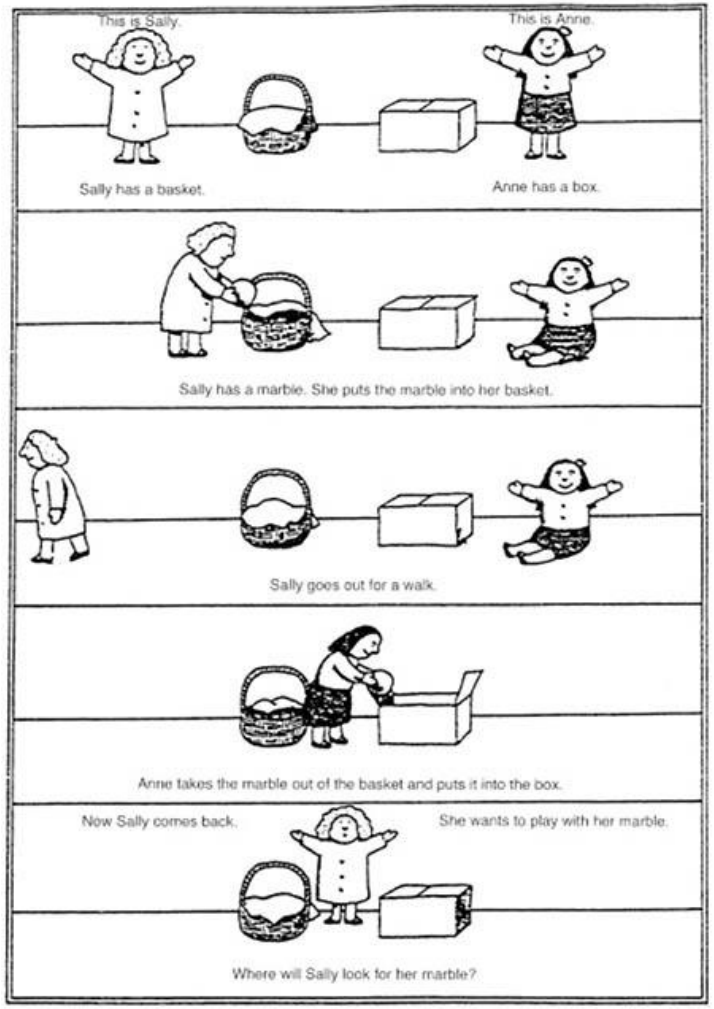
2- Reinforcement

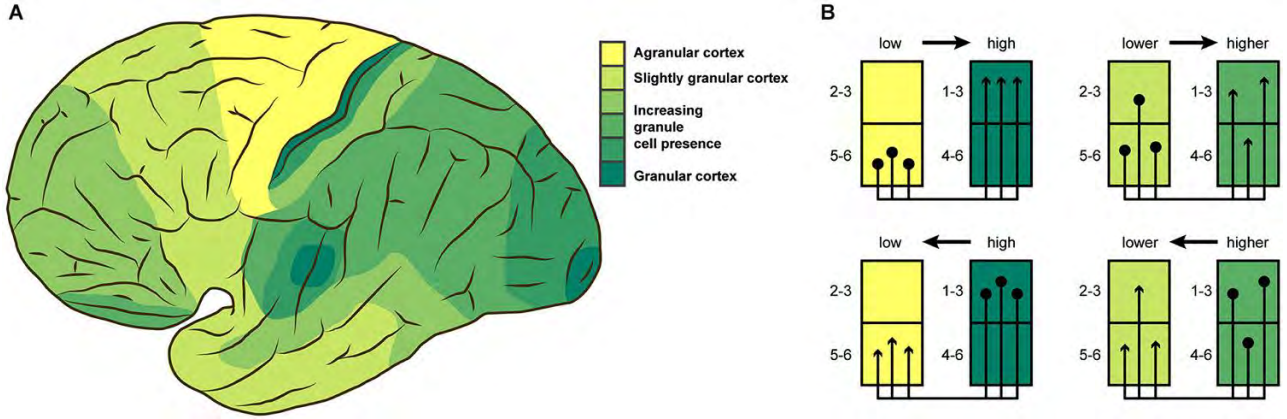
3- Simulation

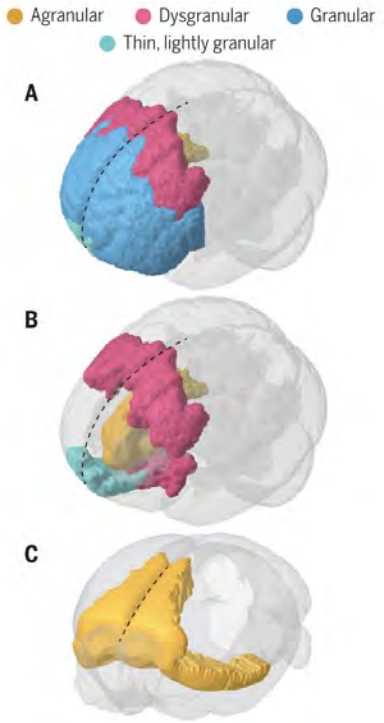
4- Mentalization

Bennett, M. S. (2023). A brief history of intelligence: evolution, AI, and the five breakthroughs that made our brains. First edition

Language







1- Steering

2- Reinforcement

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4- Mentalization

The original Sally–Anne cartoon used in the test by Baron-Cohen, Leslie and Frith (1985)

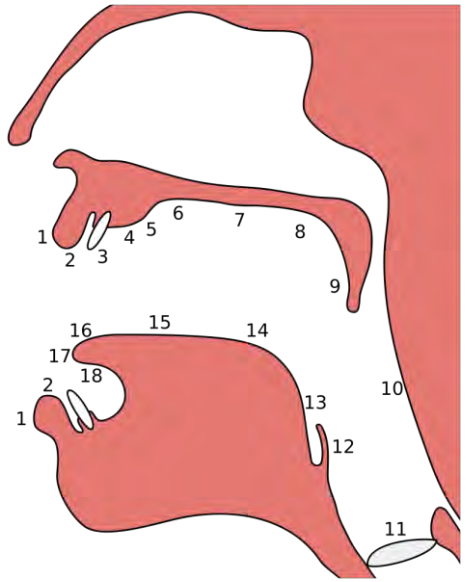
Aphasia

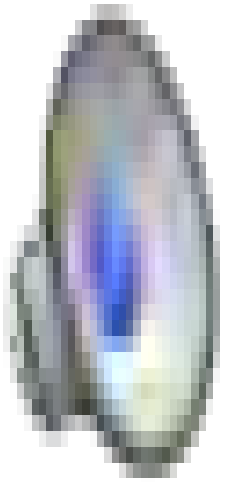
Aphasia

Dysarthria

Encephalopathy

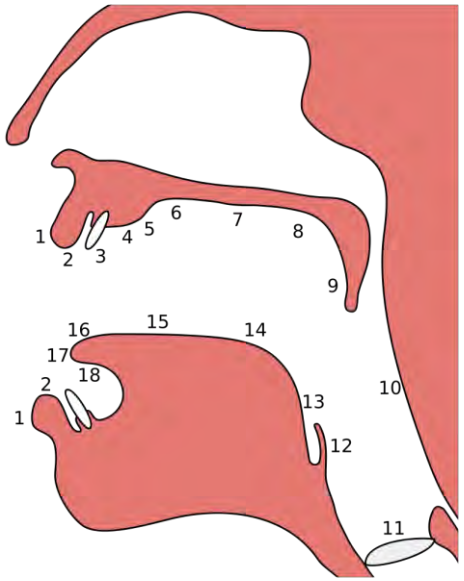
Aphasia

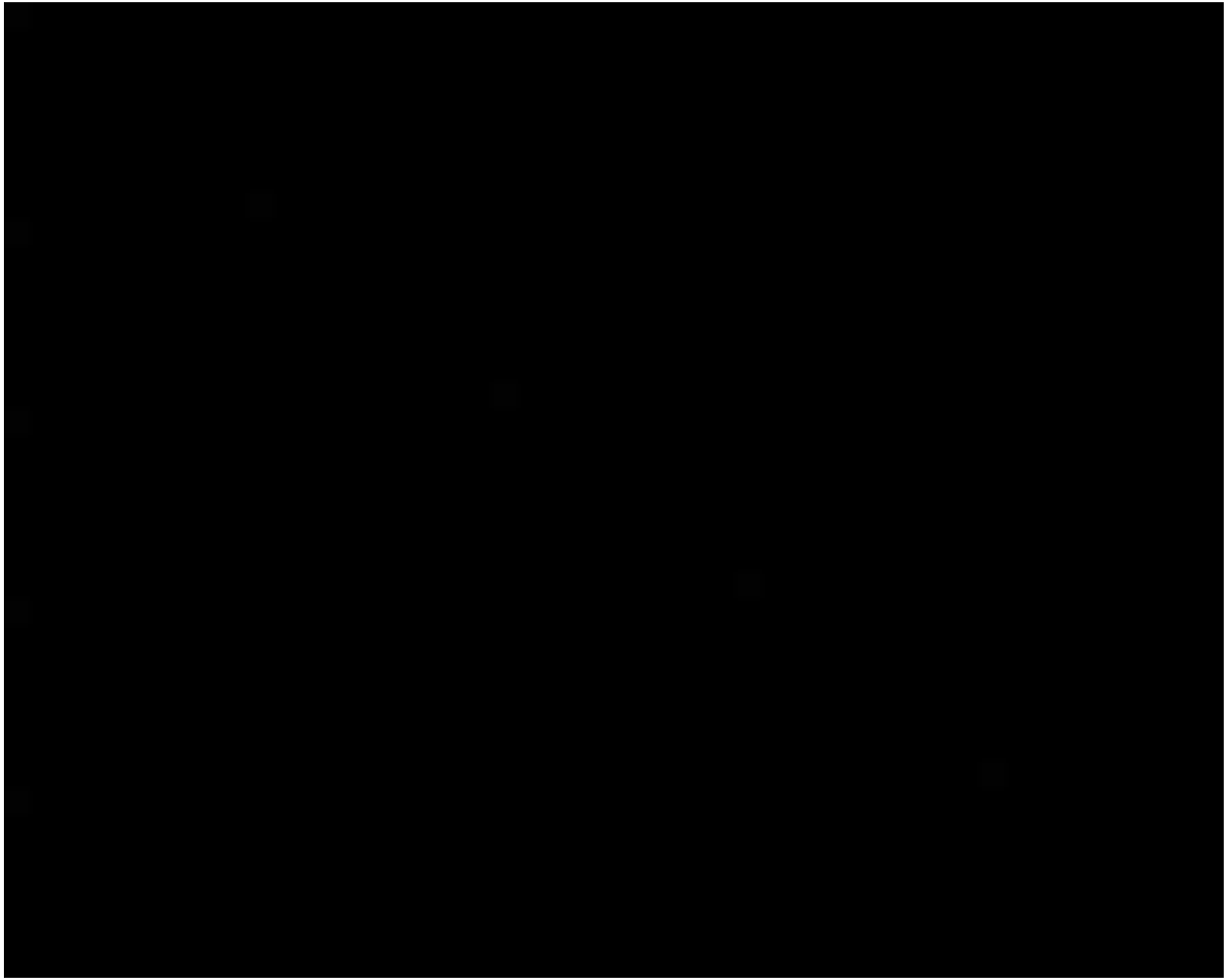




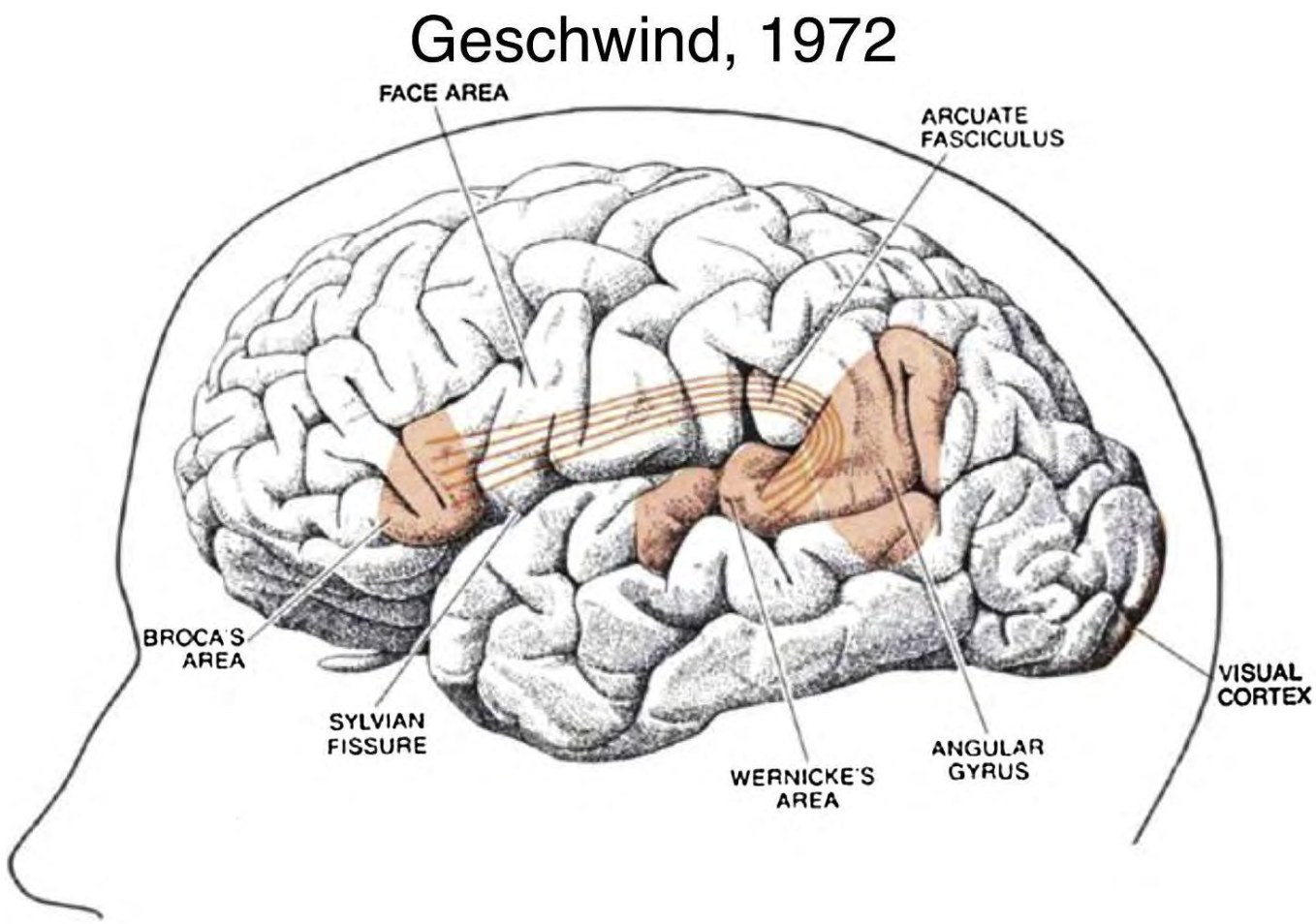
https://en.wikipedia.org/wiki/Place_of_articulation

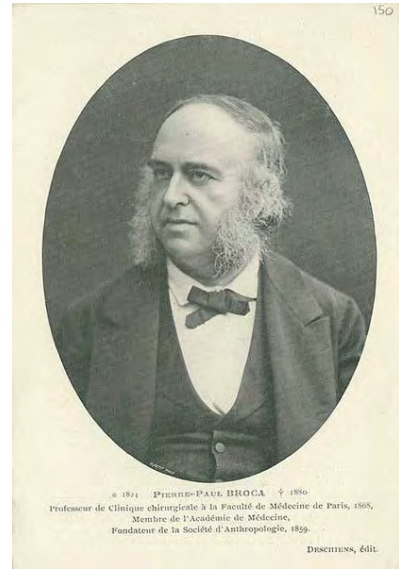
Aphasia

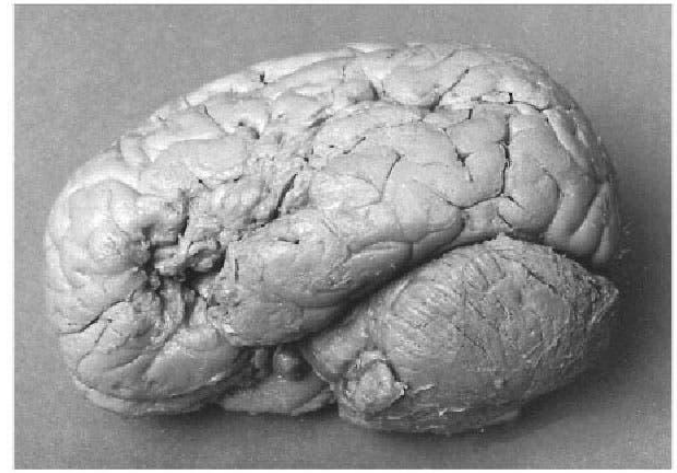
Aphasia	Dysarthria	Encephalopathy
Language test	Articulation test	Attention
Naming Repetition Comprehension	Bilabial Lingual Velar - pharyngeal	



Slide courtesy of Dr. Fridriksson

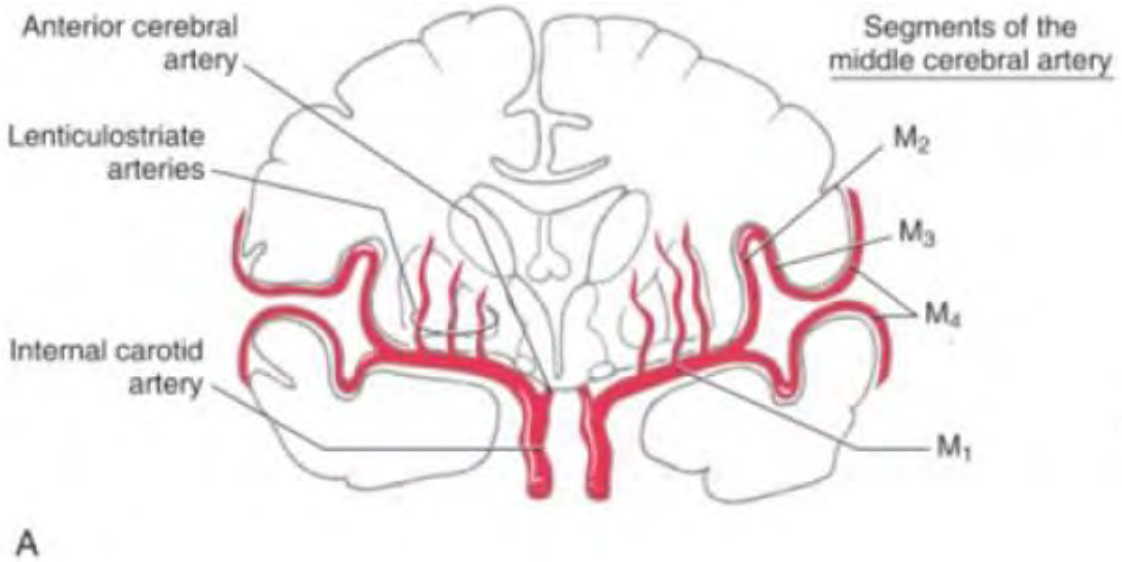


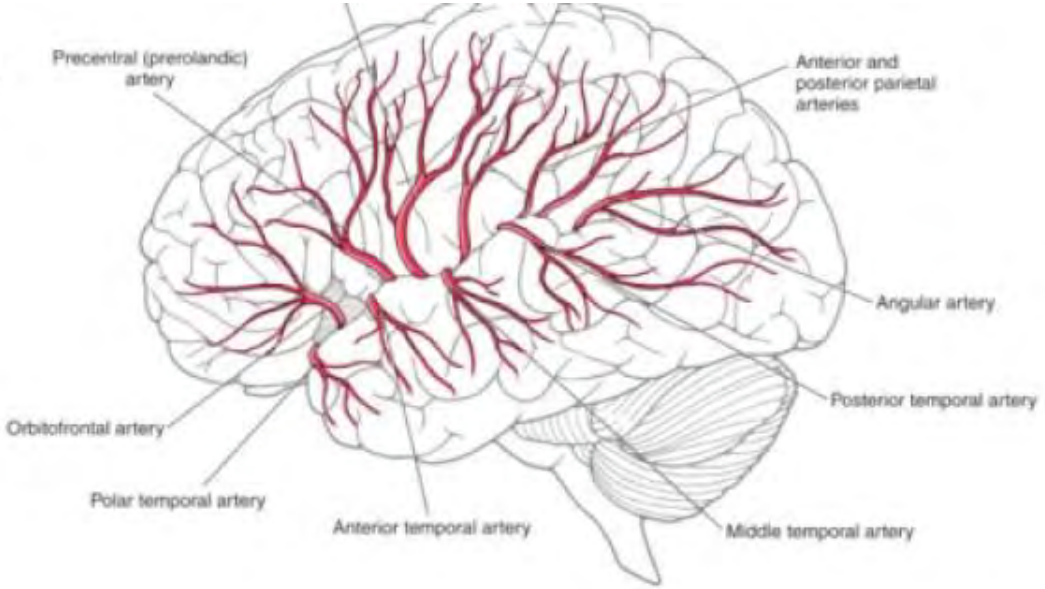


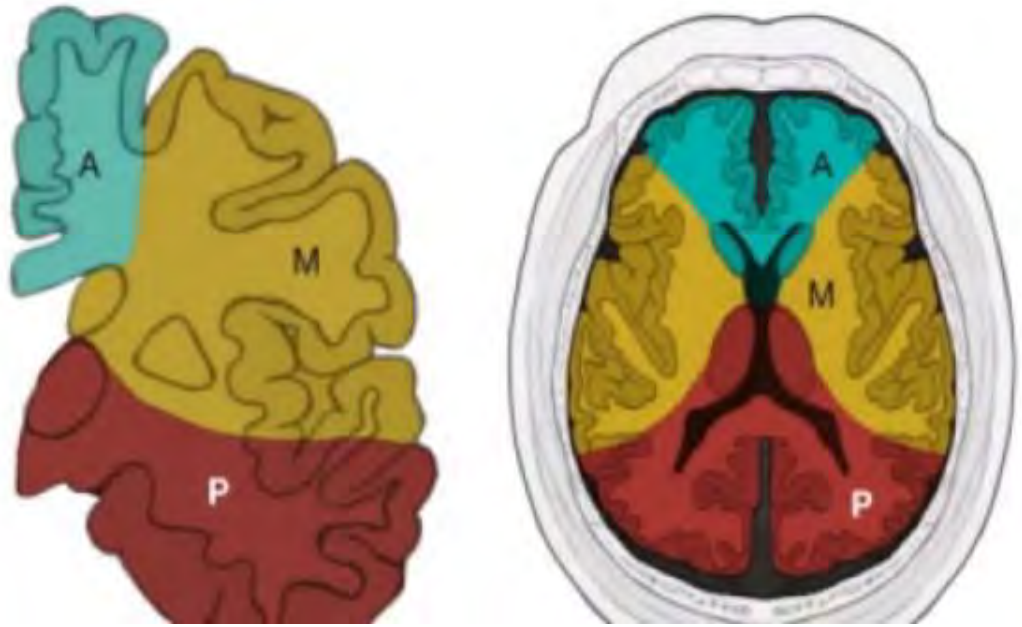


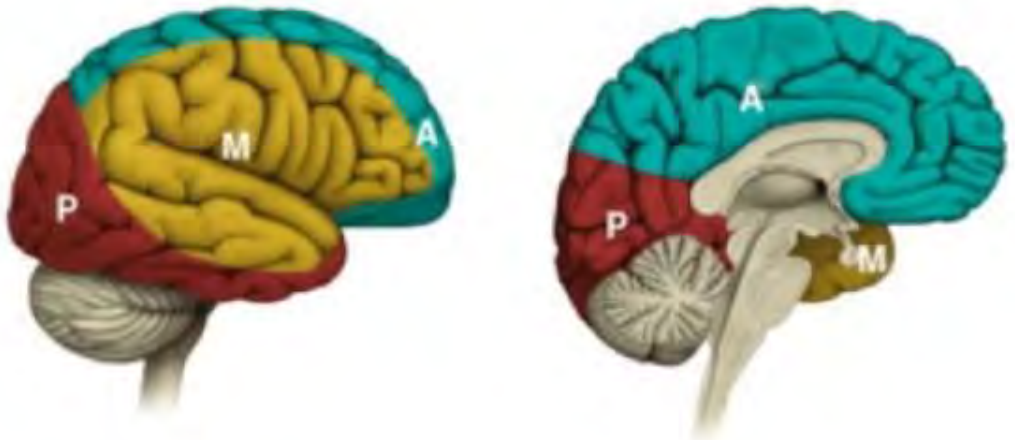
https://www.lindahall.org/about/news/scientist-of-the-day/paul-broca/

Tremblay et al. Brain and Language, 2016

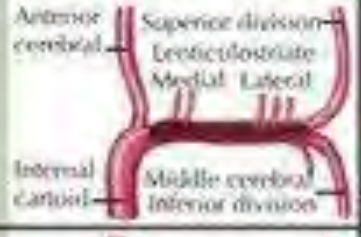
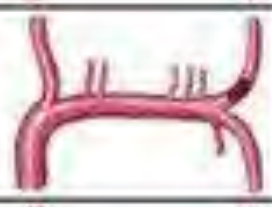


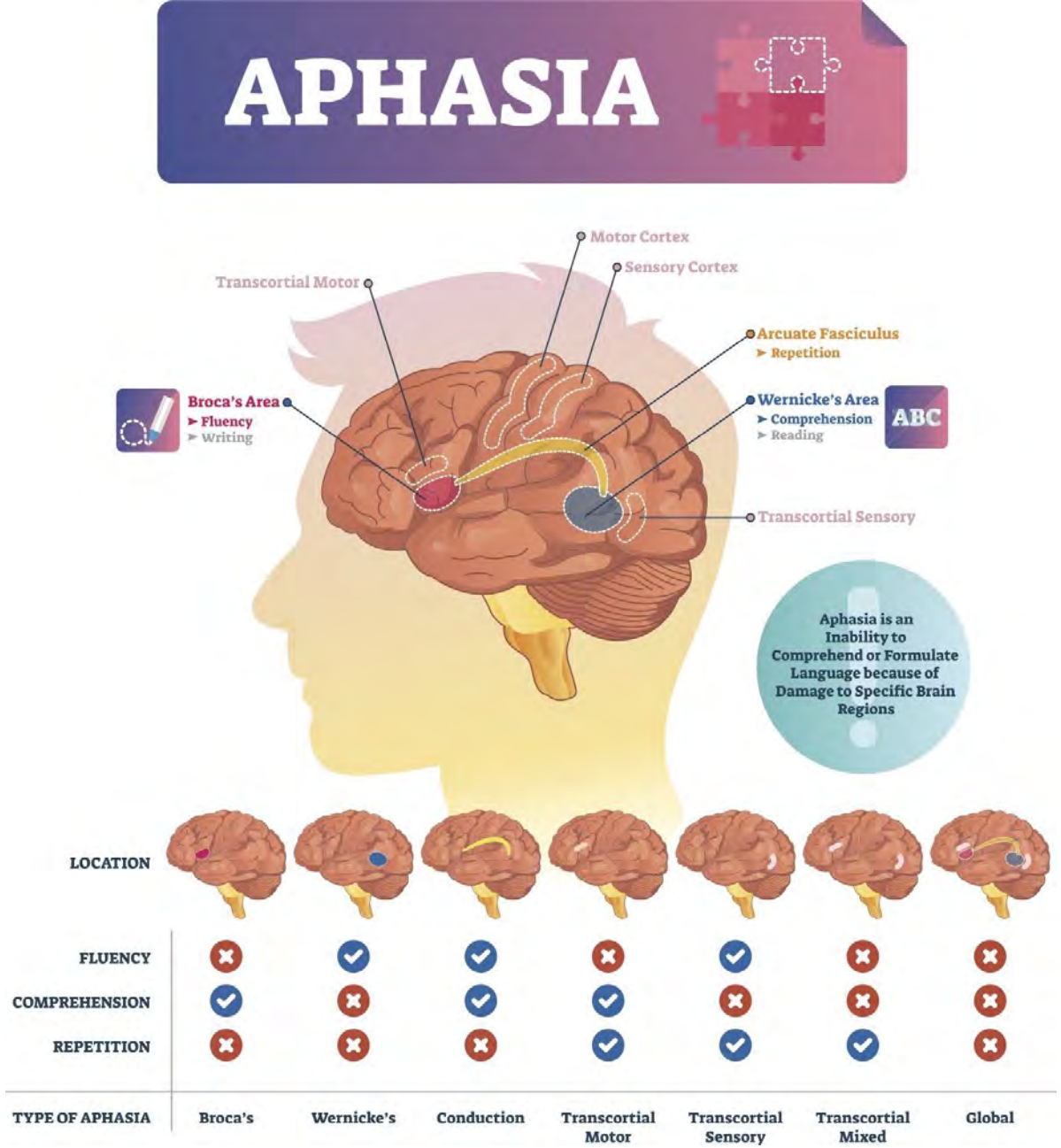




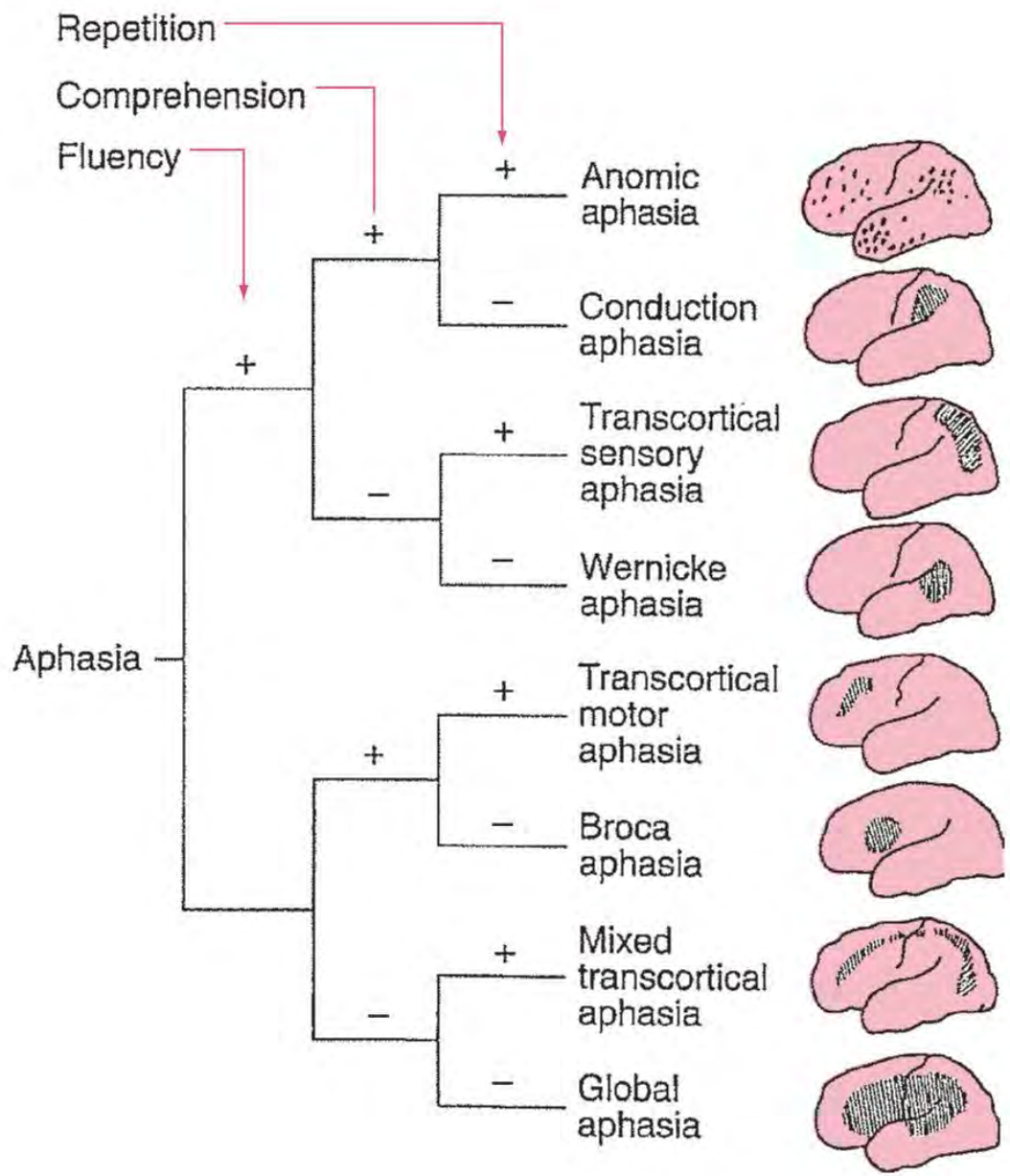


https://www.physio-pedia.com/Middle_Cerebral_Artery

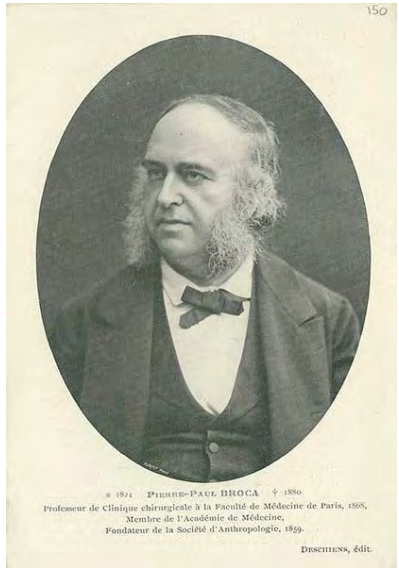
Lesion		Artery occluded	Infarct, surface	Infarct, coronal section	Clinical manifestations
Middle cerebral artery	Entire territory				Contralateral gaze palsy, hemiplegia, hemisensory loss, spatial neglect, hemianopsia Global aphasia (if on left side) May lead to decreased consciousness and even coma secondary to edema
	Deep				Contralateral hemiplegia, hemisensory loss Transcortical motor and/or sensory aphasia (if on left side)
	Parasylvian				Contralateral weakness and sensory loss of face and hand Conduction aphasia, apraxia, and Gerstmann syndrome (if on left side) Constructional dyspraxia (if on right side)
	Superior division				Contralateral hemiplegia, hemisensory loss, gaze palsy, spatial neglect Broca aphasia (if on left side)
	Inferior division				Contralateral hemianopsia or upper quadrantanopsia Wernicke aphasia (if on left side) Constructional dyspraxia (if on right side)
Anterior cerebral artery	Entire territory				Incontinence Contralateral hemiplegia Abulia Transcortical motor aphasia or motor and sensory aphasia Left limb dyspraxia
	Distal				Contralateral weakness of leg, hip, foot, and shoulder Sensory loss in foot Transcortical motor aphasia or motor and sensory aphasia Left limb dyspraxia

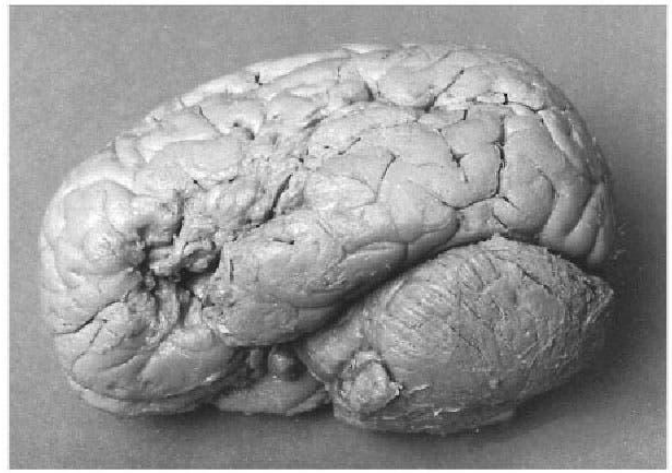


https://utswmed.org/medblog/aphasia-treatment-rehab/

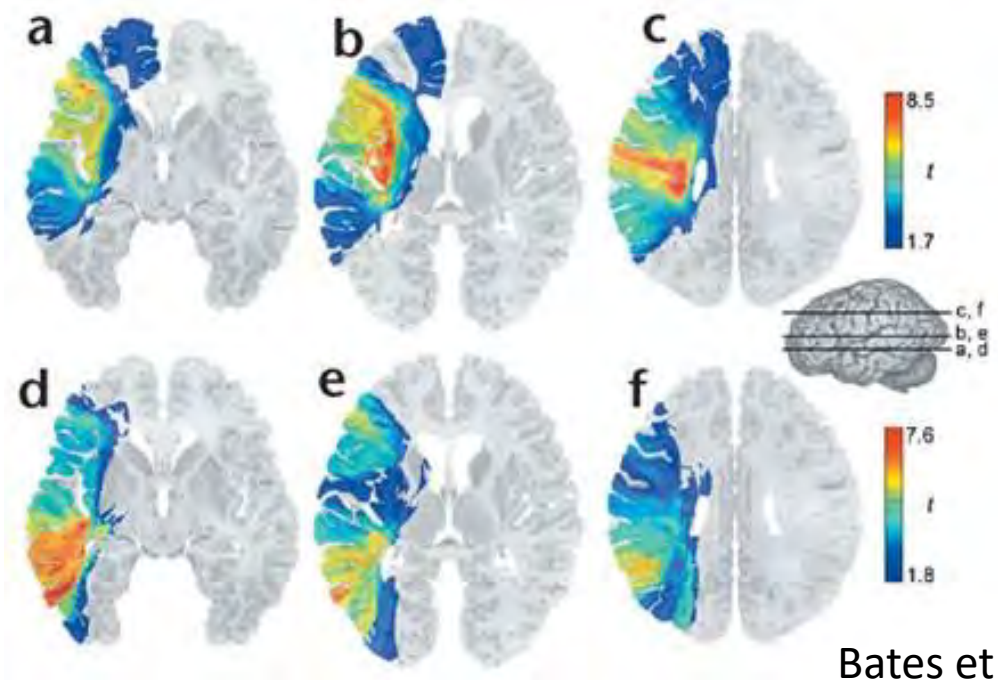


https://neupsykey.com/approach-to-the-patient-with-aphasia/

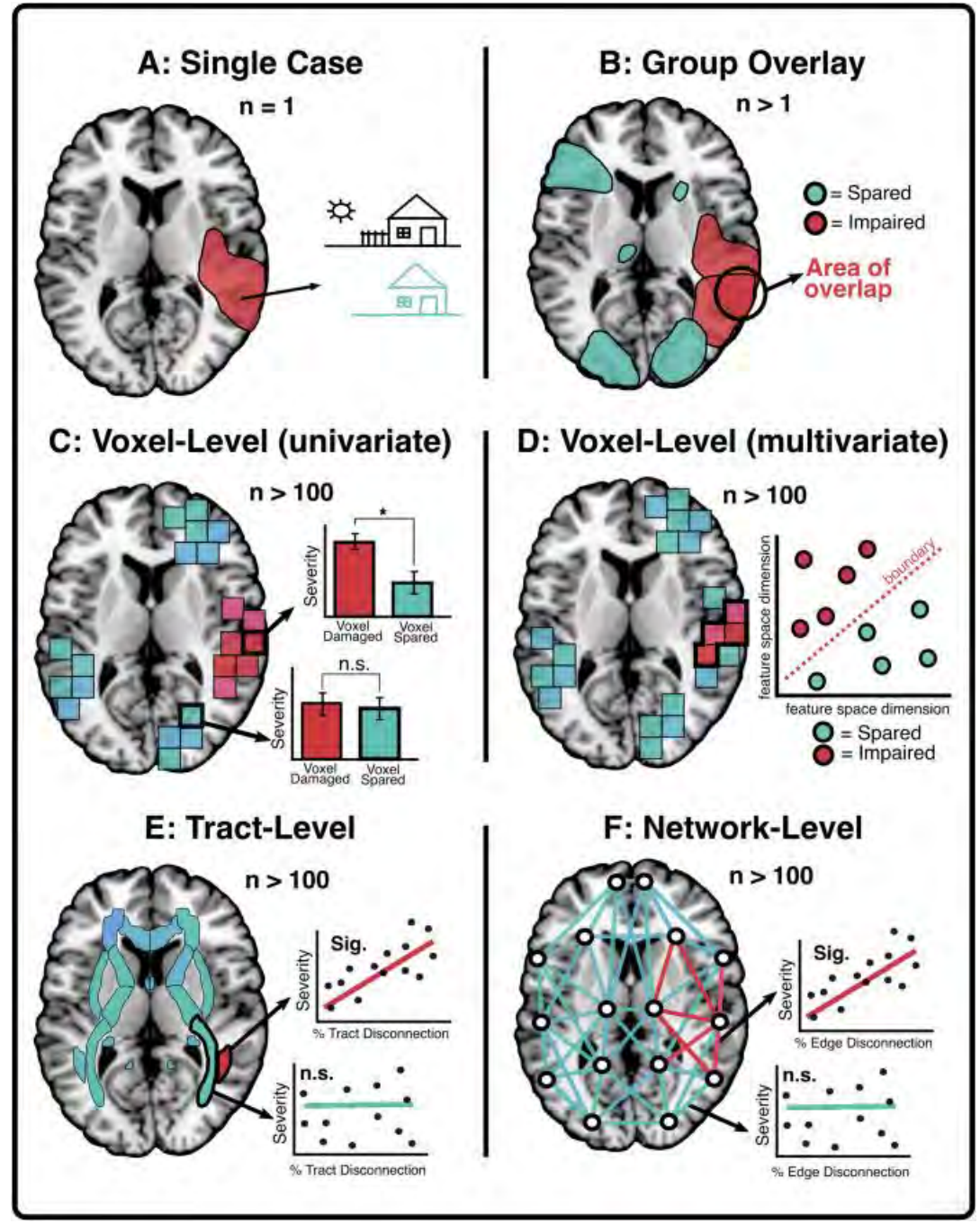




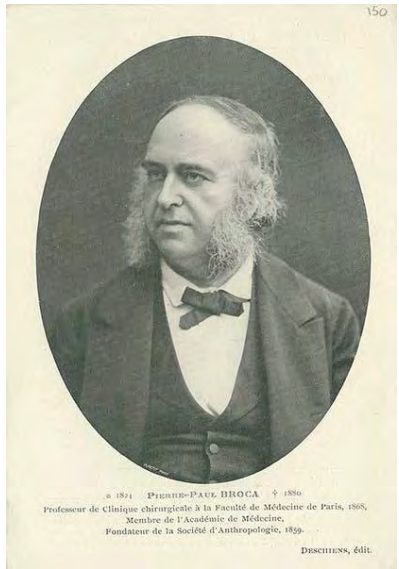
https://www.lindahall.org/about/news/scientist-of-the-day/paul-broca/

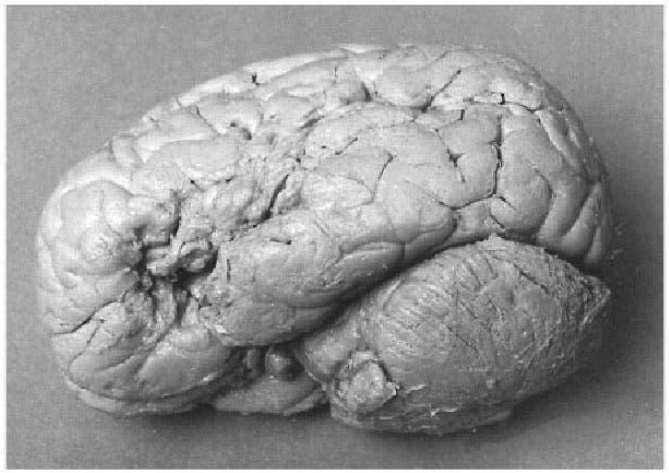


Bates et al. Nature 2003



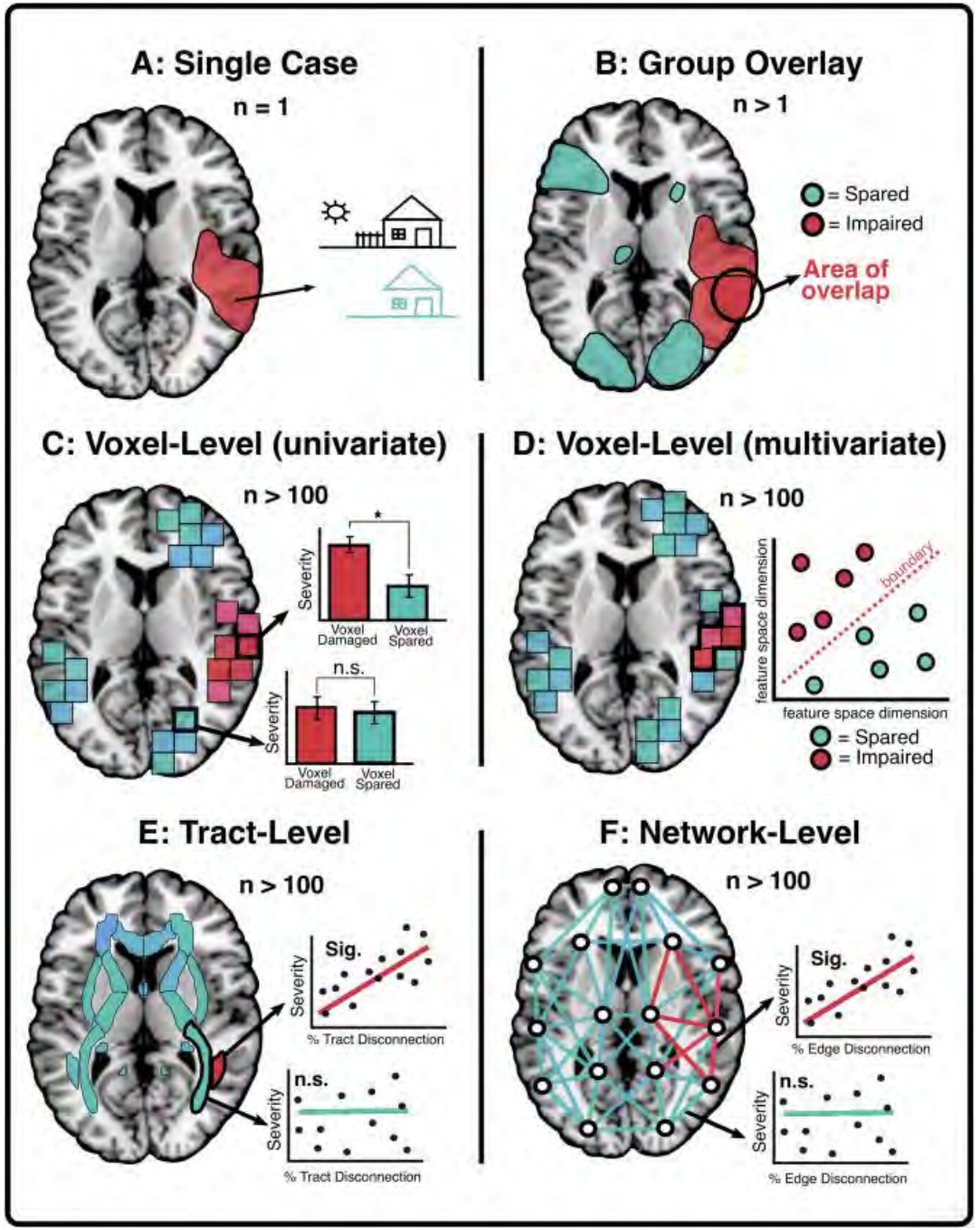
Moore et al. Cortex 2024



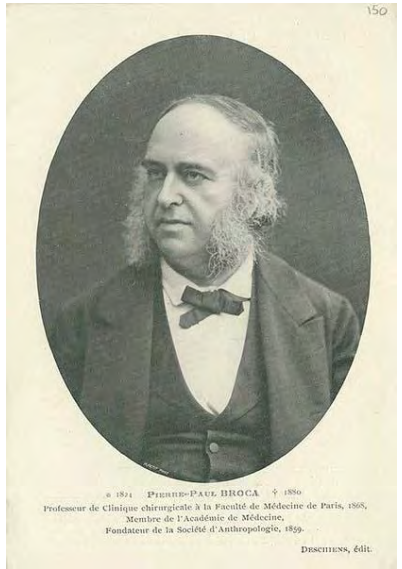


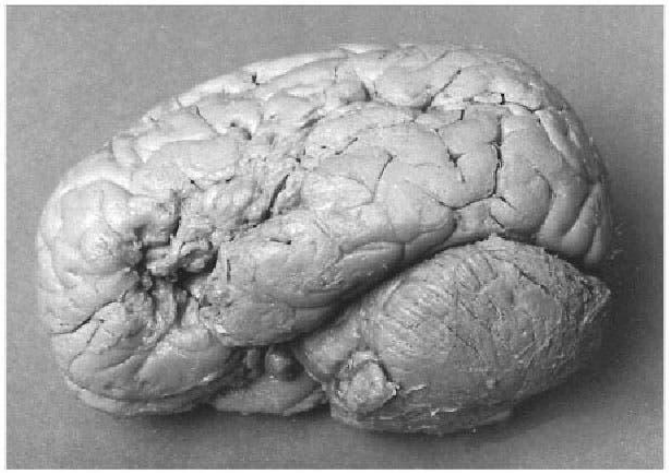
https://www.lindahall.org/about/news/scientist-of-the-day/paul-broca/

Chris Rorden



Moore et al. Cortex 2024





https://www.lindahall.org/about/news/scientist-of-the-day/paul-broca/

Julius Fridriksson

doi:10.1093/brain/awx363 BRAIN 2018: 141; 848–862 | 848

BRAIN
A JOURNAL OF NEUROLOGY

Anatomy of aphasia revisited

Julius Fridriksson,[1] Dirk-Bart den Ouden,[1] Argye E. Hillis,[2,3] Gregory Hickok,[4] Chris Rorden,[5] Alexandra Basilakos,[1] Grigori Yourganov[5] and Leonardo Bonilha[6]

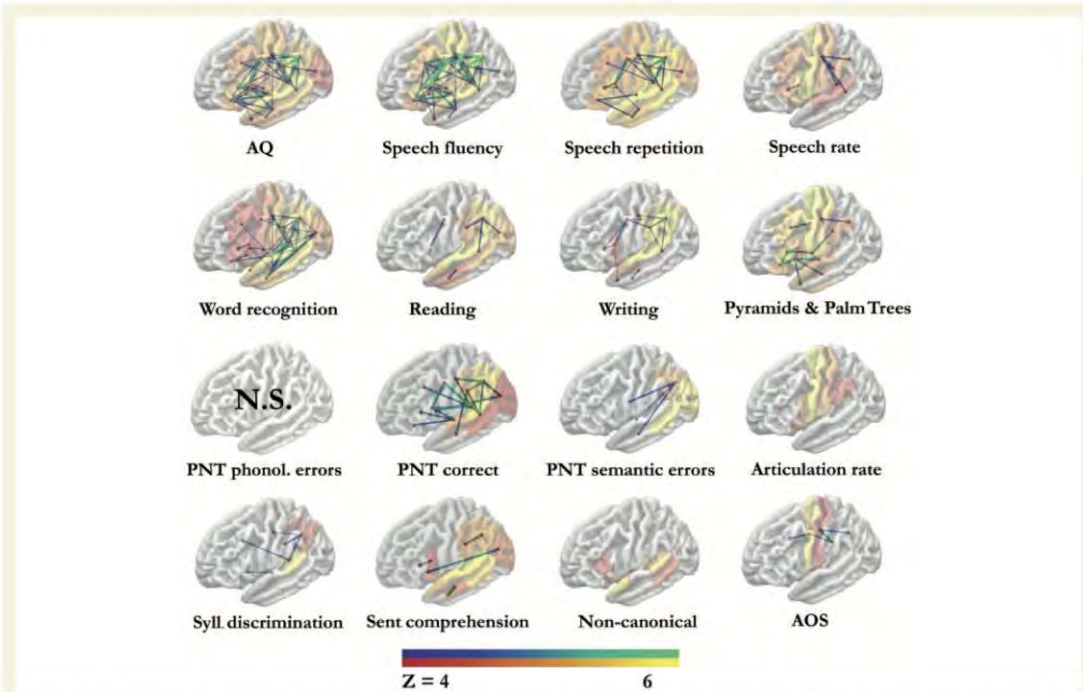


Figure 1 Univariate RLSM (red-yellow) and CLSM (blue-green) results for each of the speech and language tests. For CLSM, both colour intensity and link thickness denote how strongly damage to a given link predicts speech or language test performance. AQ = aphasia quotient; AOS = apraxia of speech; N.S. = non-significant.

Early factors that predict outcome

- Initial severity
  - Particularly at 2-4 weeks

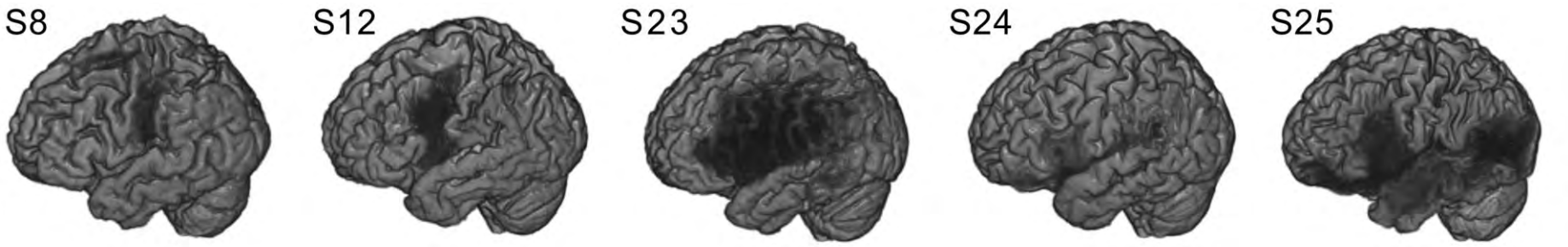
- Age not consistently found to influence recovery across studies

Stroke. 2009;40:3834-3840

Early factors that predict outcome

- Lesion alone does explain long-term changes [1, 2].

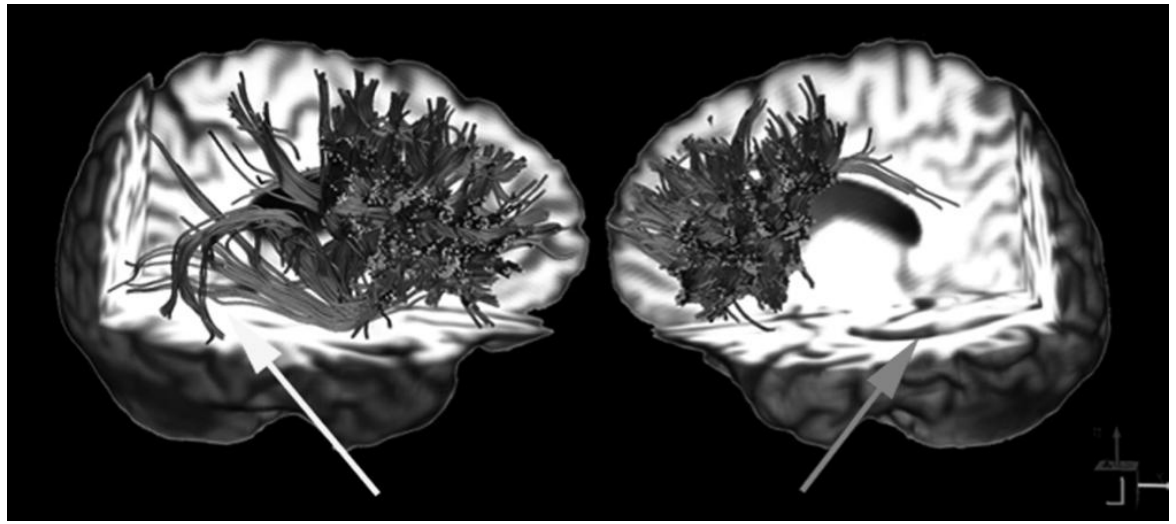
- 1. Hope TM, Leff AP, Prejawa S, Bruce R, Haigh Z, Lim L, Ramsden S, Oberhuber M, Ludersdorfer P, Crinion J. Right hemisphere structural adaptation and changing language skills years after left hemisphere stroke. Brain 2017;140:1718-1728
- 2. Naeser MA, Palumbo CL, Prete MN, Fitzpatrick PM, Mimura M, Samaraweera R, Albert ML. Visible changes in lesion borders on CT scan after five years poststroke, and long-term recovery in aphasia. Brain and language 1998;62:1-28



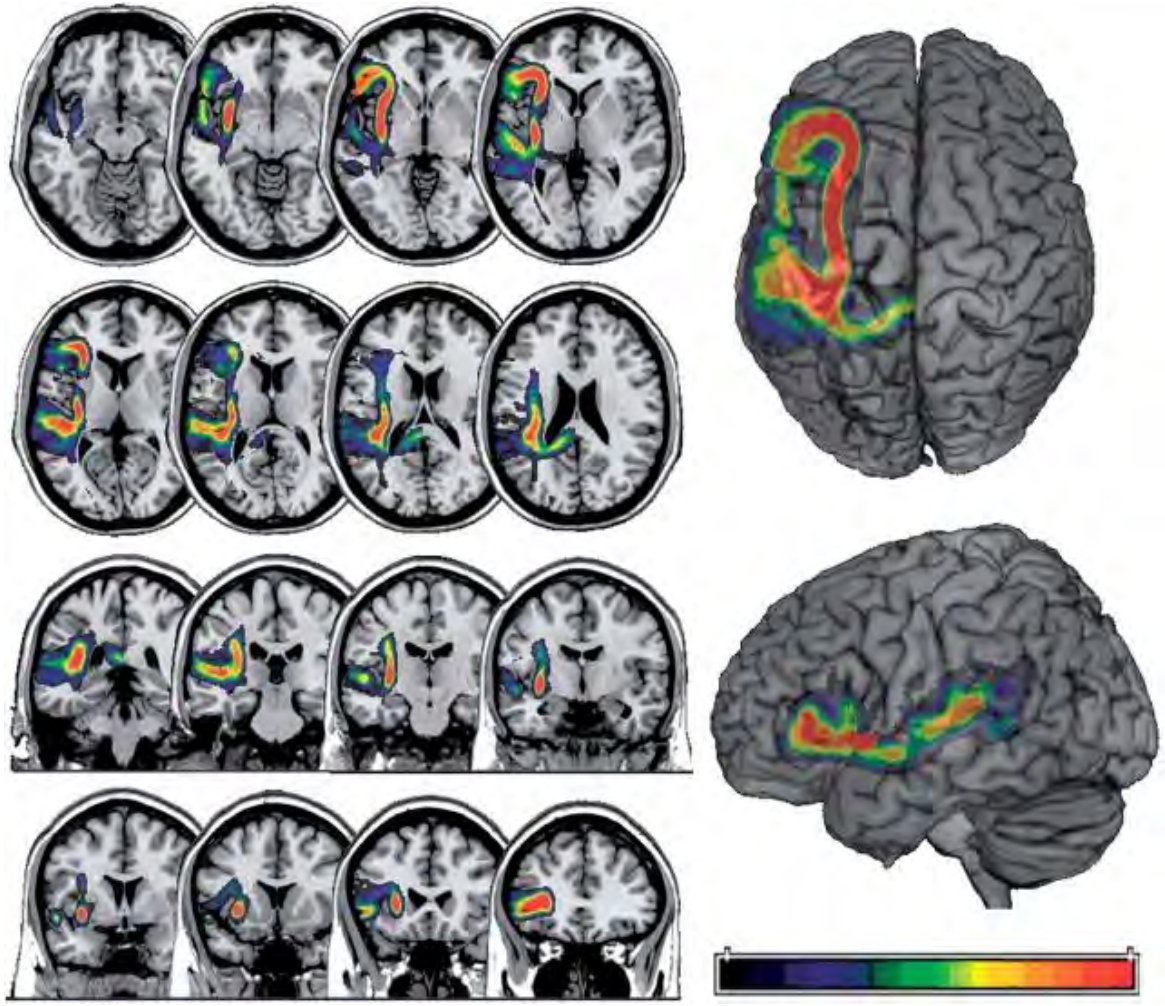
Correct naming:
91% [AQ=96], 90% [AQ=21], 4% [AQ=23], 5% [AQ=31], 5%[AQ=71]

Bonilha et al, Stroke, 2014

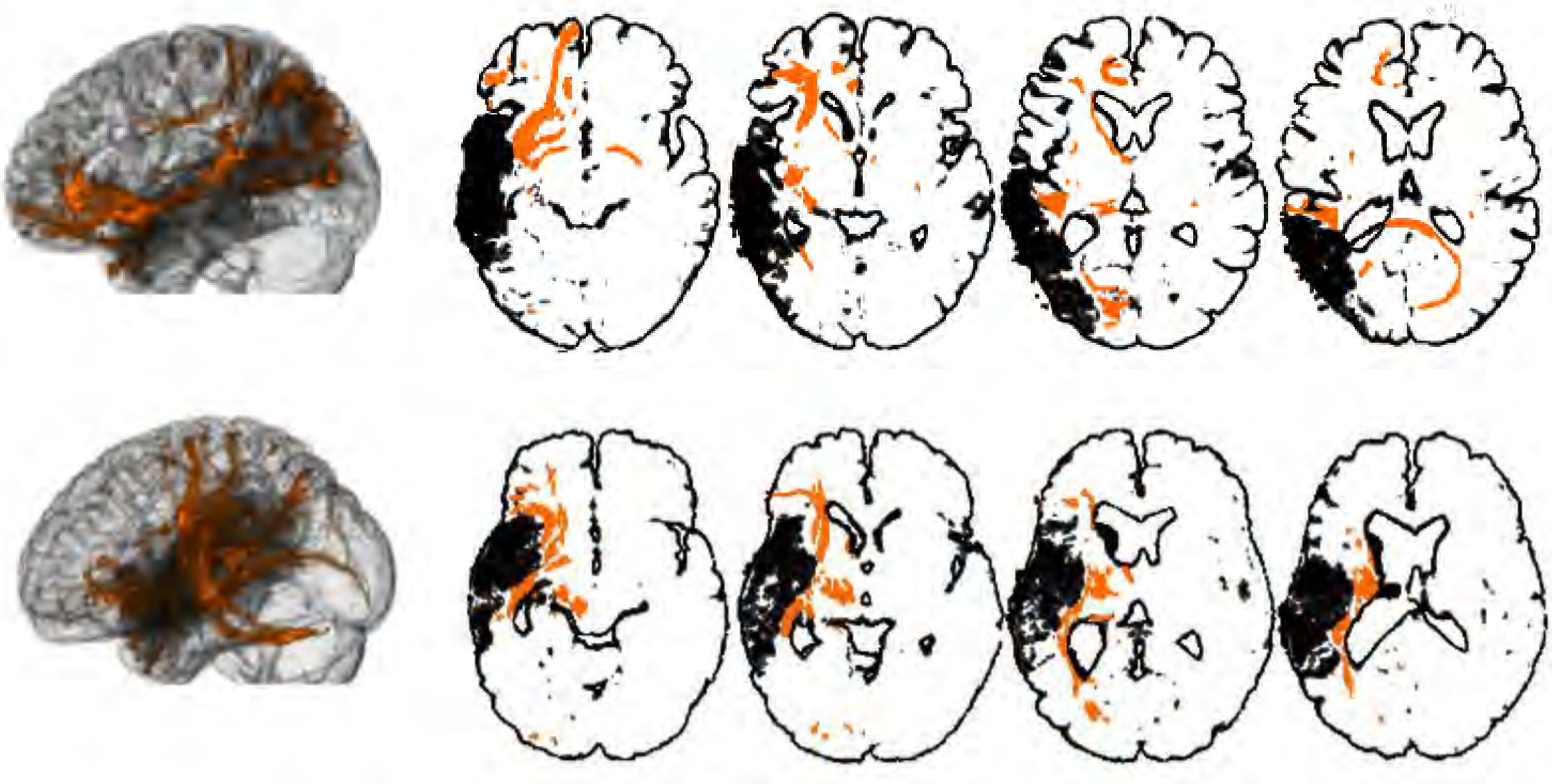
Clinical Motivation



Bonilha et al, Behav Neurology 2007

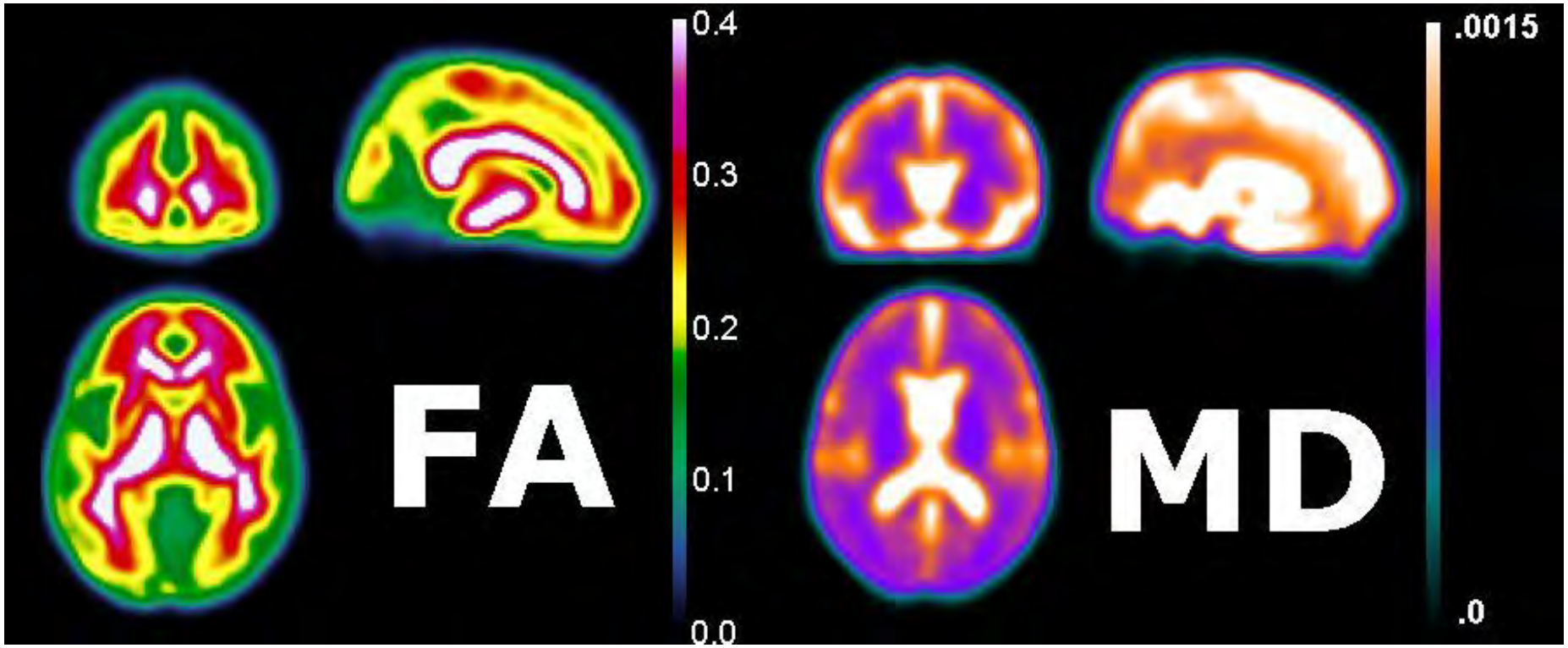


Bonilha & Fridriksson, Brain 2007



Bonilha et al, Behavioral Neurology, 2015

What is the connectome?



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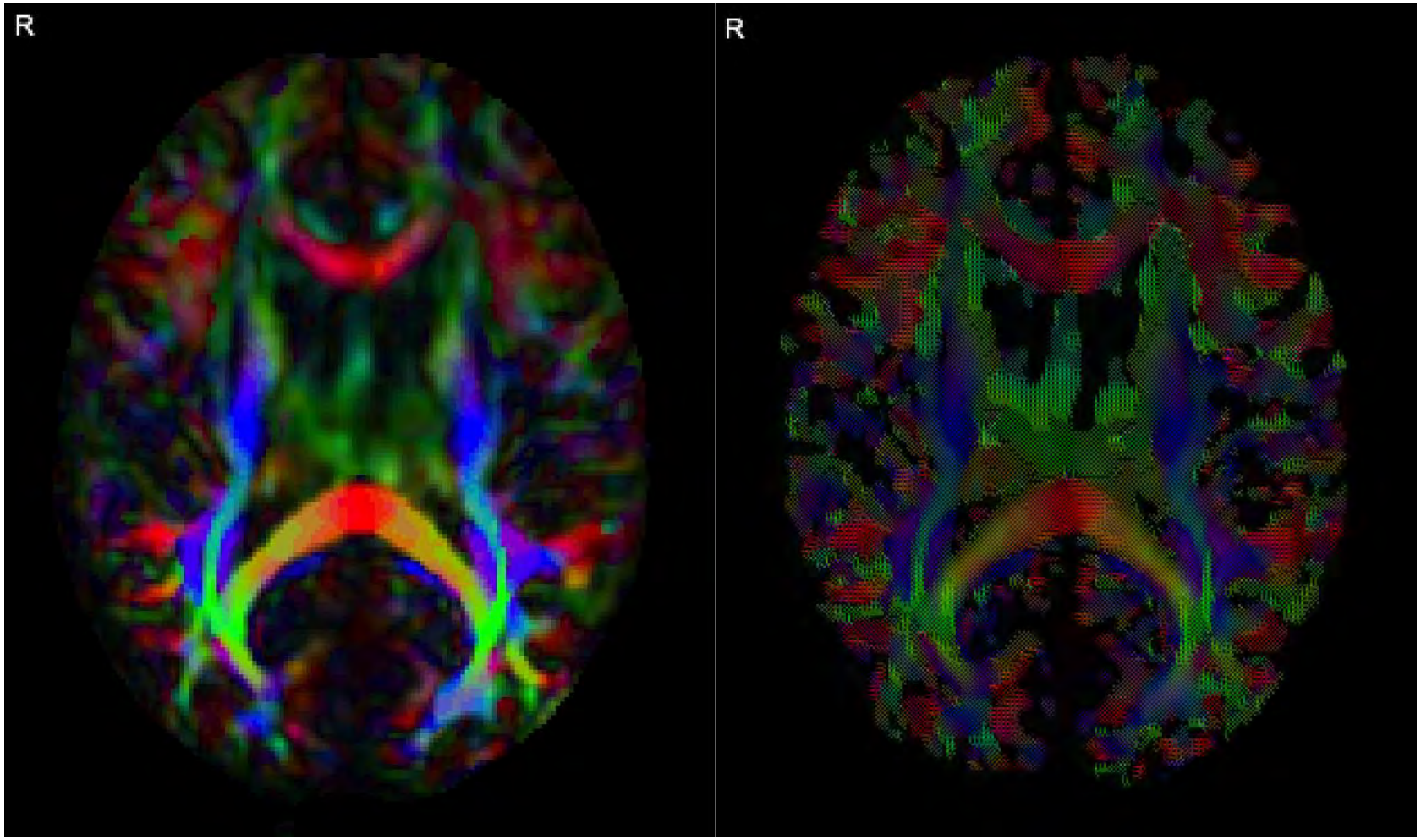
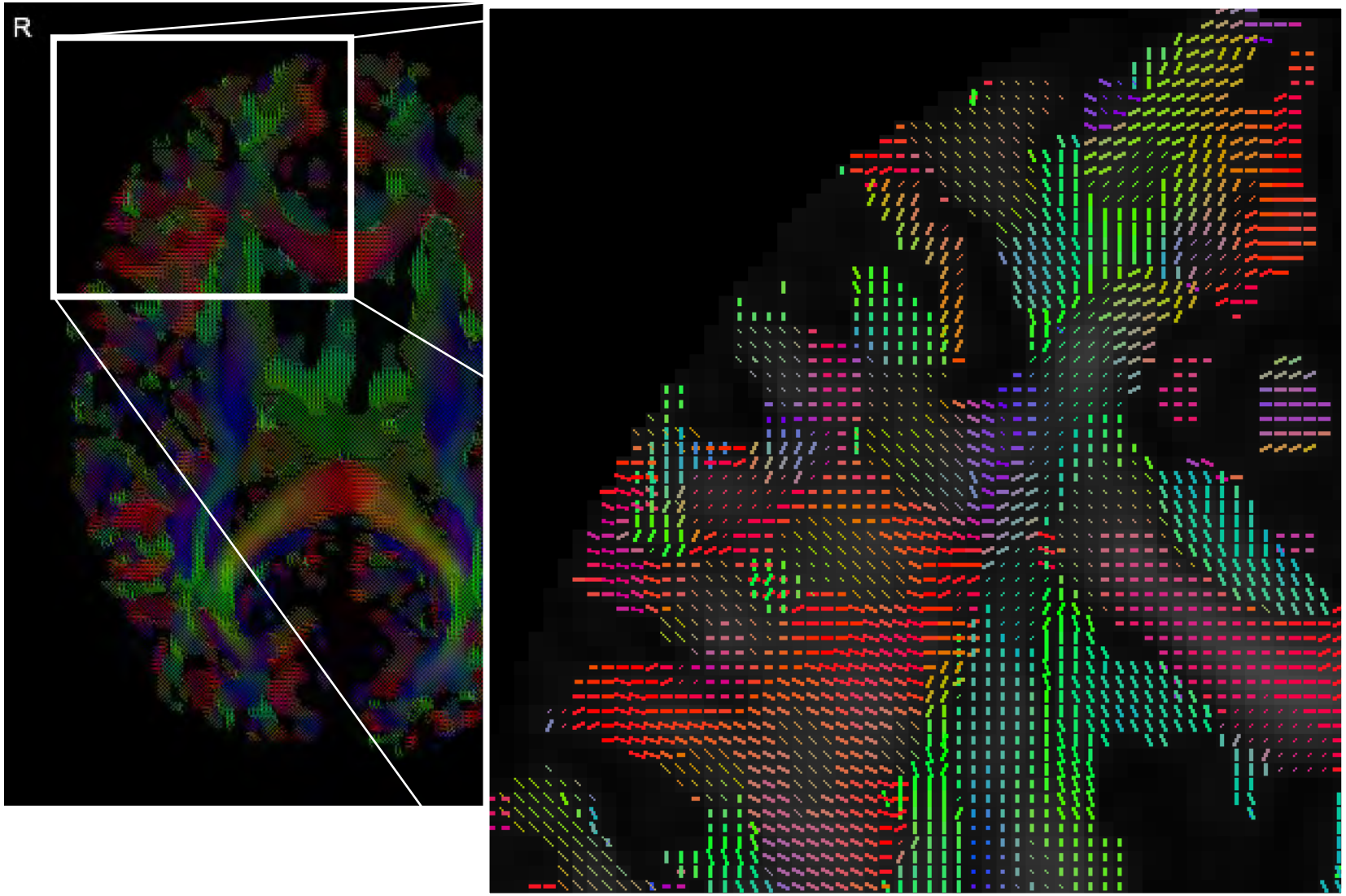
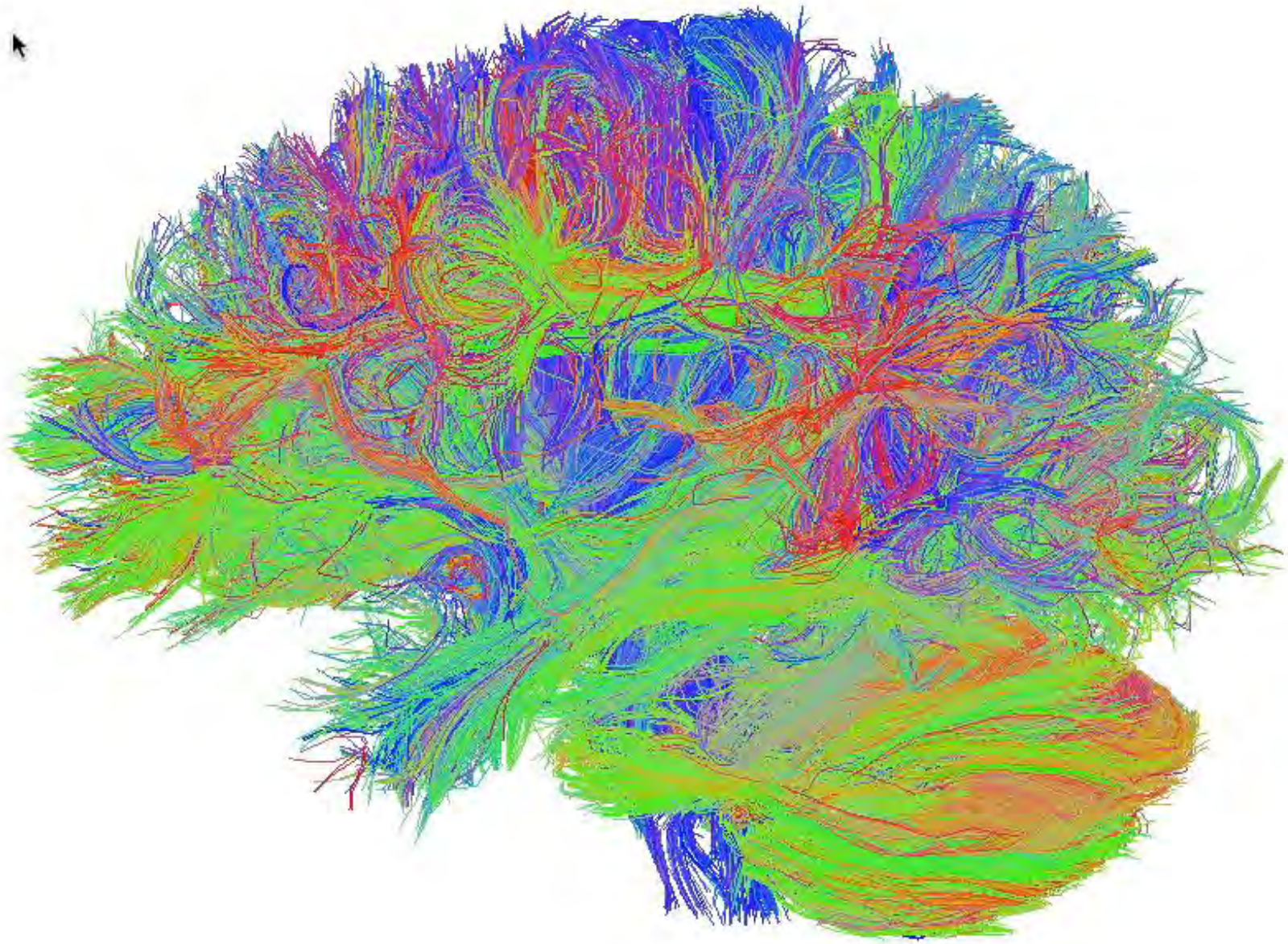
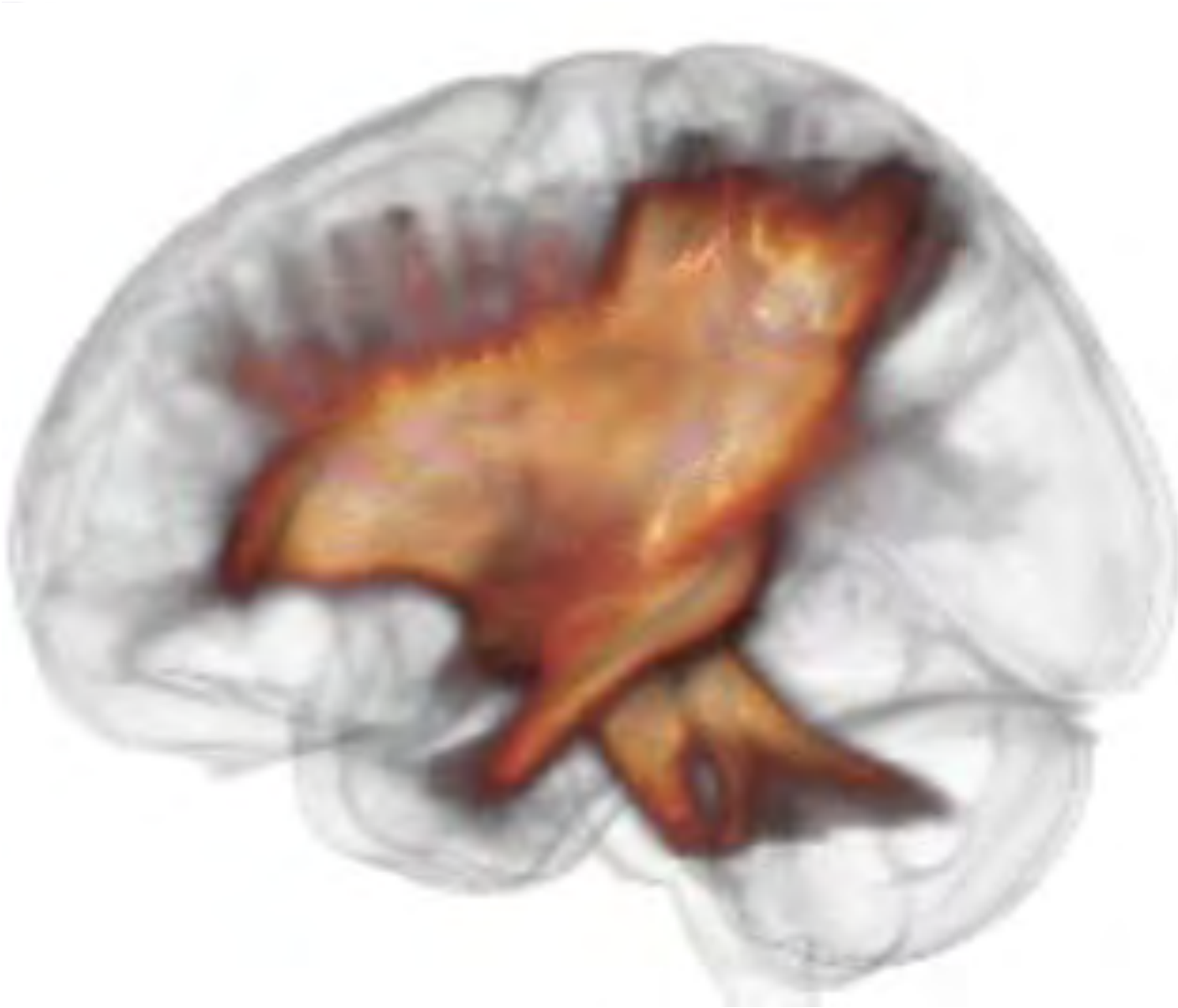


What is the connectome?







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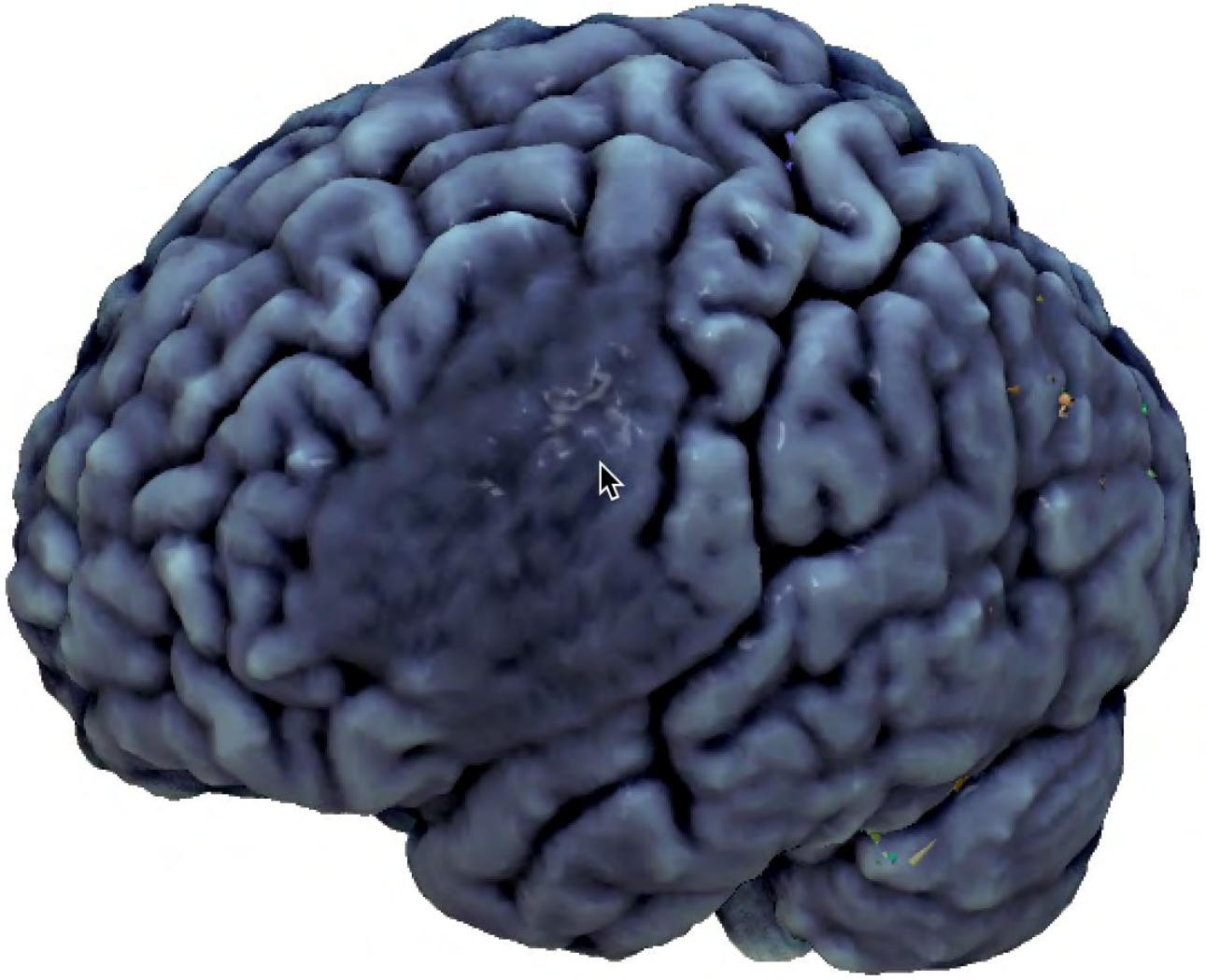

Surfice - https://github.com/neurolabusc/surf-ice


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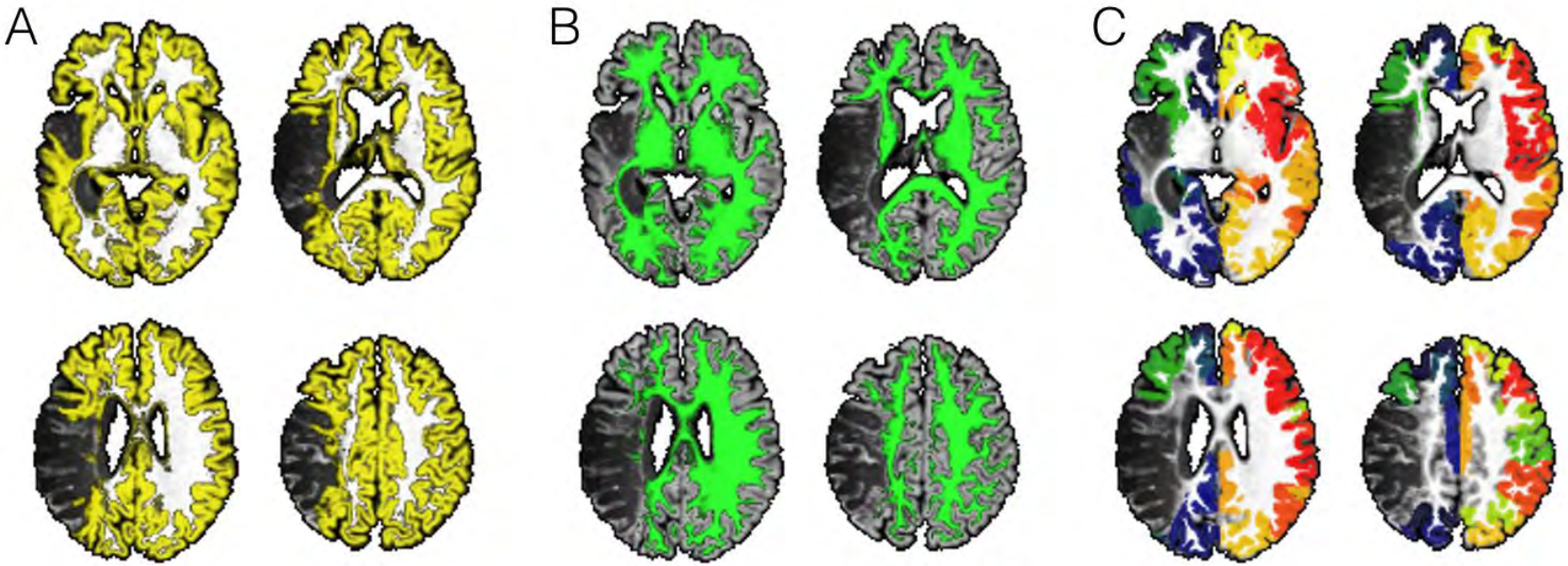
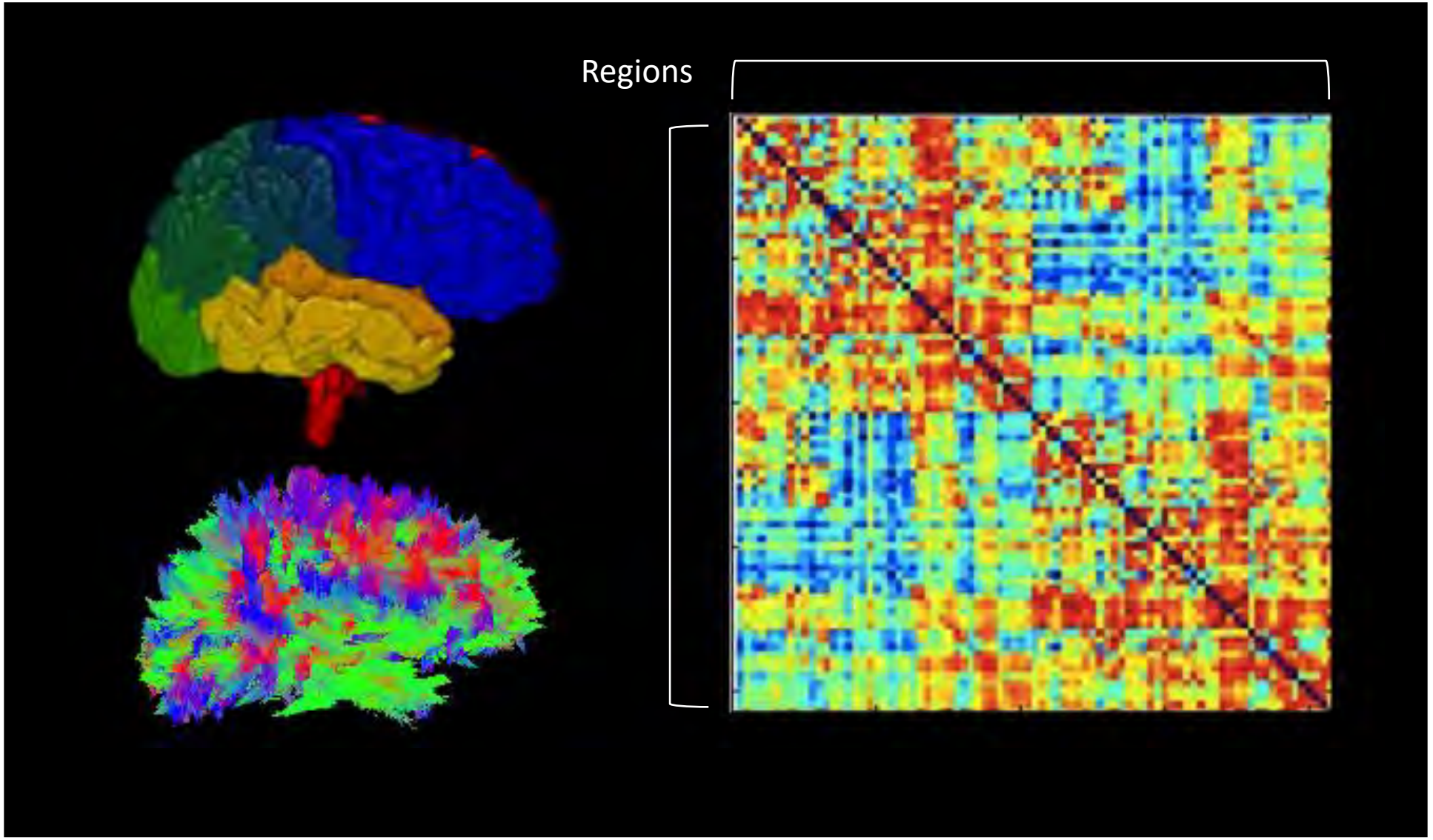
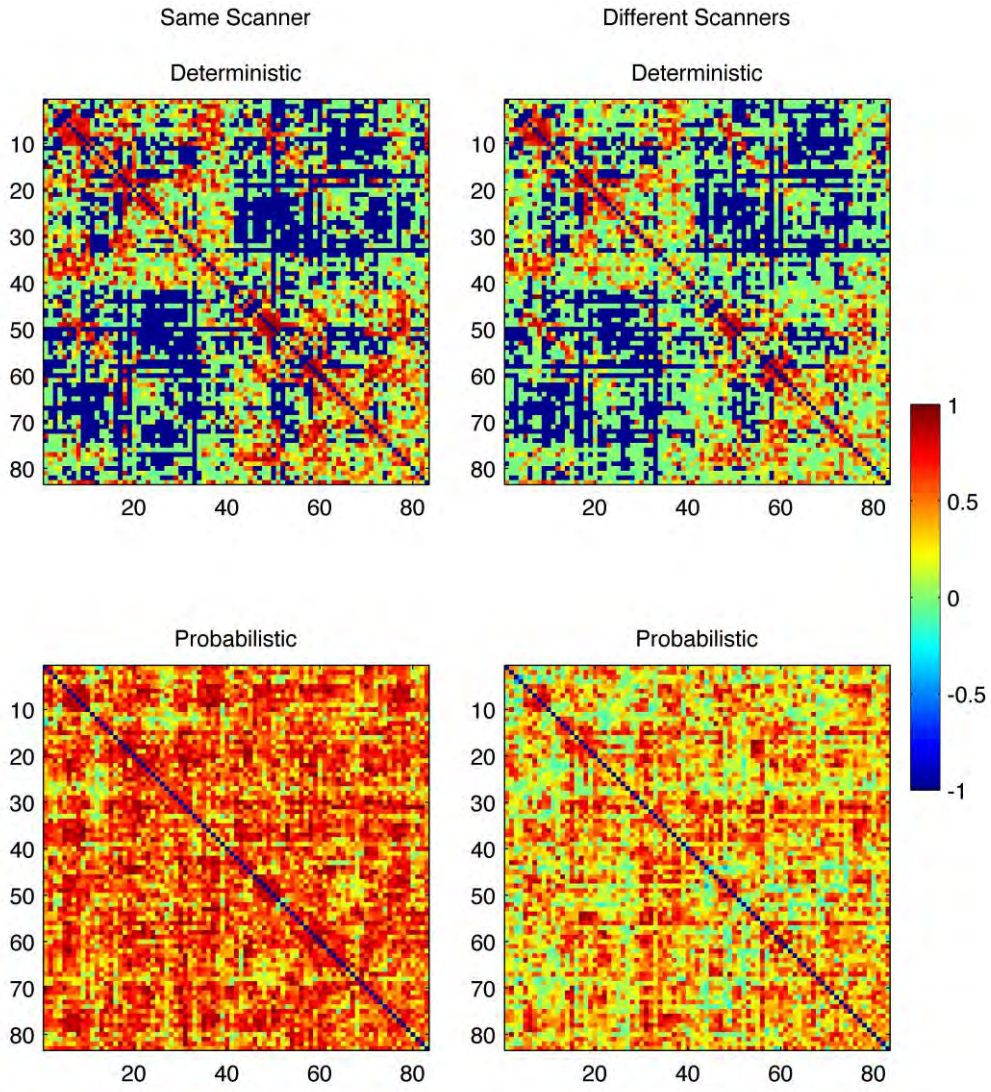
Connectome and brain lesions



SPM Clinical Toolbox - https://www.nitrc.org/projects/clinicaltbx/


Regions

Connectome reproducibility?



Bonilha et al, PLOS One, 2015

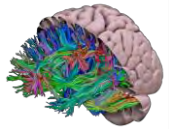
Identifying Subnetwork Fingerprints in Structural Connectomes: A Data-Driven Approach

Brent C. Munsell[1], Eric Hofesmann[1], John Delgaizo[2], Martin Styner[3], Leonardo Bonilha[2]

[1] College of Charleston, Department of Computer Science
[2] Medical University of South Carolina, Department of Neurology
[3] University of North Carolina, Department of Psychiatry

Diffusion Tensor Imaging

White matter is composed of bundles of myelinated axons that connect gray matter regions. Water movement is less constrained along these bundles, which allow us to detect white matter fiber tracts [2].

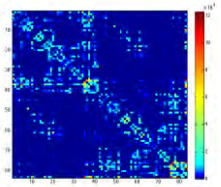


Brain Connectome

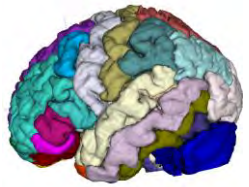
Computational analyses of neuroimaging data now permit the definition of whole brain maps of connectivity, commonly referred to as the brain connectome [2].

The brain connectome provides unprecedented information about neuronal network architecture across the entire brain with millimetric precision.

In general, the connectome is reconstructed using white matter fiber tractography from diffusion tensor imaging (DTI) based on an anatomical parcellation (atlas) of the human brain.



Example connectivity matrix based on 83 region parcellation of the human brain

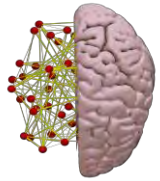


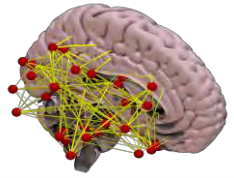
Example 83 region parcellation of the human brain that is used to create the connectome.

Network Analysis

A connectome is a weighted undirected graph, where nodes in the graph represent brain regions (defined in brain atlas), and the edge that connects two different nodes is weighted by a value that represents the fiber density [2].

To better understand how the brain network is organized, network analysis algorithms are applied to the connectome to reveal the underlying network architecture of the brain, which has typically been used to quantify network architecture differences between healthy individual [1].



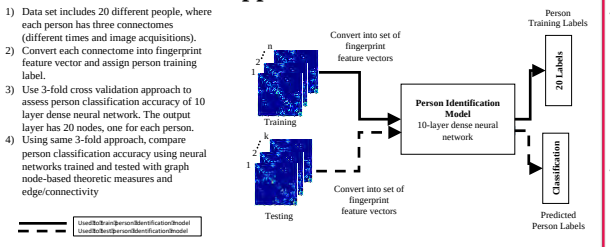


Research Topic

Identifying person identification patterns, commonly called fingerprints, in connectome data that can accurately identify one person from another is focus of our research [3-4].

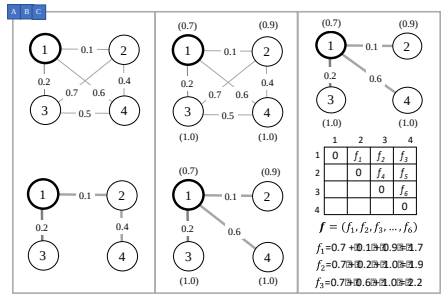
Person identification Approach

1) Data set includes 20 different people, where each person has three connectomes (different times and image acquisitions).
2) Convert each connectome into fingerprint feature vector and assign person training label.
3) Use 3-fold cross validation approach to assess person classification accuracy of 10 layer dense neural network. The output layer has 20 nodes, one for each person.
4) Using same 3-fold approach, compare person classification accuracy using neural networks trained and tested with graph node-based theoretic measures and edge/connectivity



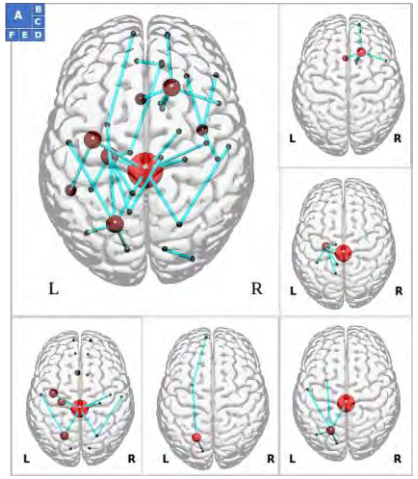
Fingerprint Feature Vector

- Instead of using region-to-region connectivity values in the connectome, a new fingerprint feature based on Dijkstra's shortest path algorithm that represents a subnetwork is used.
- Unlike a shortest path algorithm that only uses region-to-region connectivity values to compute the shortest pathway, i.e. one with the least delay between two brain regions, this shortest path algorithm is modified to include a hub-delay that is based on a graph-theoretic measure, such as Eigenvector centrality.
- Conceptually the fingerprint feature represents a pathway of communication that combines both region-to-region and hub delay information.



Examples that illustrate the difference between the (a) shortest path algorithm, and the (b) modified version of the shortest path algorithm that combines connectivity delays with hub delays. In (a) and (b) the start node is node-1, and in (b) the Eigenvector centrality hub measure is provided in the parenthesis either directly above or below the node. Lastly, (c) provides an index to subscript mapping example that is used to calculate the fingerprint features, and the example fingerprint feature values found by the modified shortest path when node-1 is the start node.

Connectome Fingerprint



(a) The connectome fingerprint defined by all 16 majority fingerprint features (b-d) local sub-networks centered at a brain region that is highly connected, (e) a sub-network that spans the entire length of the left hemisphere, and (f) individual brain regions, or brain regions that define a sub-network that are in both the left and right hemispheres.

Conclusions

- 93% classification accuracy
- Development of a new fingerprint feature
- Backpropagation technique to identify person identification fingerprint
- Computational approach can be an important step towards personalized medicine in the context of neurological diagnosis and management

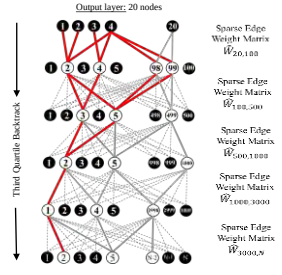
References

[1] Cormen, T., et al. (2009). Introduction to Algorithms, Third Edition, The MIT Press.
[2] Rubinov, M. and O. Sporns (2010). "Complex network measures of brain connectivity: uses and interpretations." Neuroimage 52(3): 1059-1069.
[3] Finn, E. S., et al. (2015). "Functional connectome fingerprinting: identifying individuals using patterns of brain connectivity." Nat Neurosci 18(11): 1664-1671.
[4] Yeh, F.-C., et al. (2016). "Quantifying Differences and Similarities in Whole-Brain White Matter Architecture Using Local Connectome Fingerprints." PLoS Comput Biol 12(11).

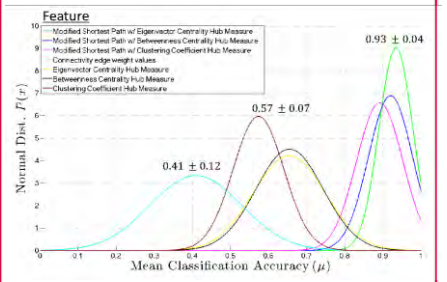
Neural Network Backpropagation

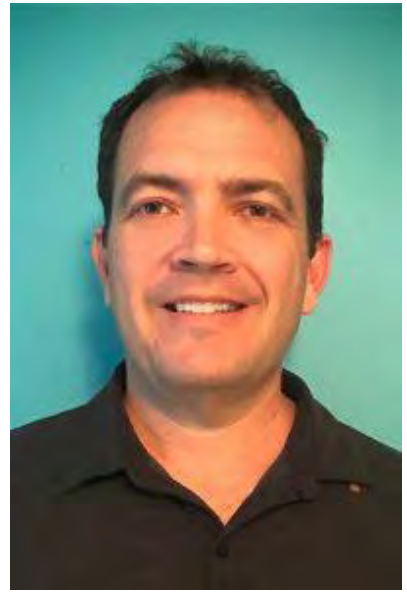
Backtracking technique that identifies a select number of fingerprint features that have the greatest contribution to classification accuracy.

Collectively, the selected fingerprint features can then be joined at intersecting brain regions that will create one or more subnetworks that form our data-driven connectome fingerprint.



Person Classification Accuracy

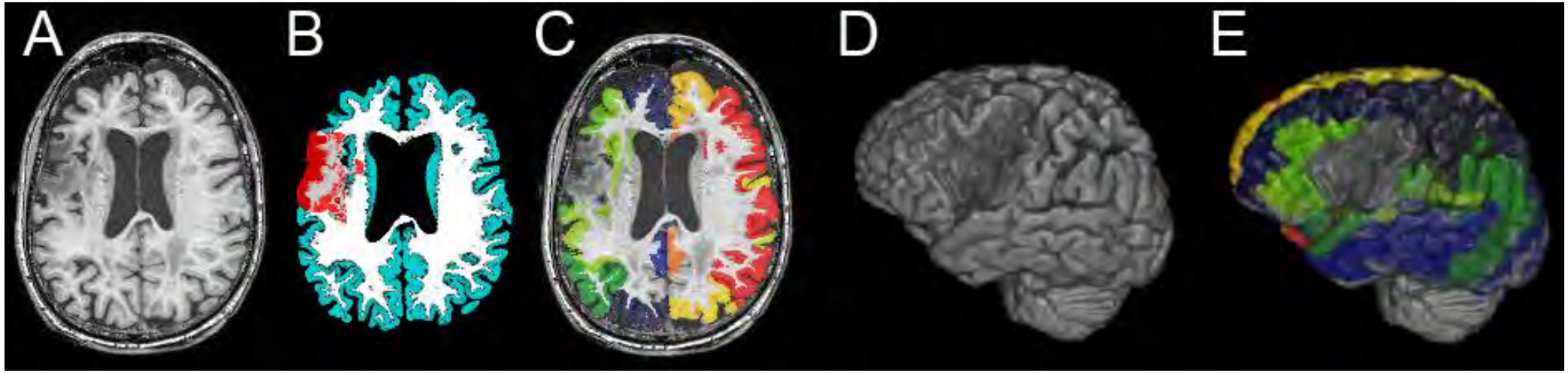


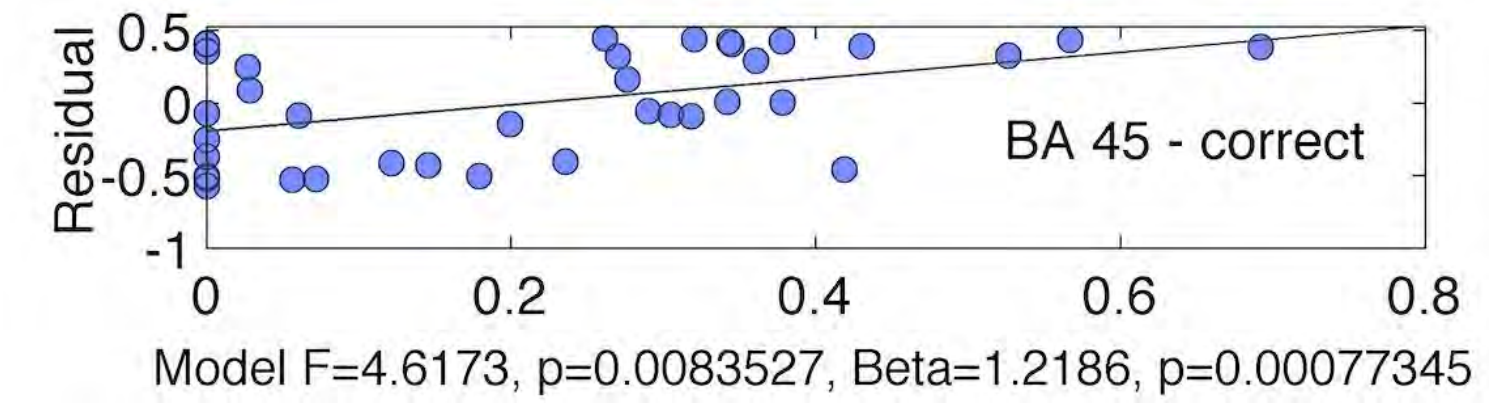


Brent Munsell

http://blogs.cofc.edu/compsci/2017/04/24/eric-hofesmann-captures-best-of-the-best-at-ssm-undergraduate-research-poster-session/

Connectome and Aphasia

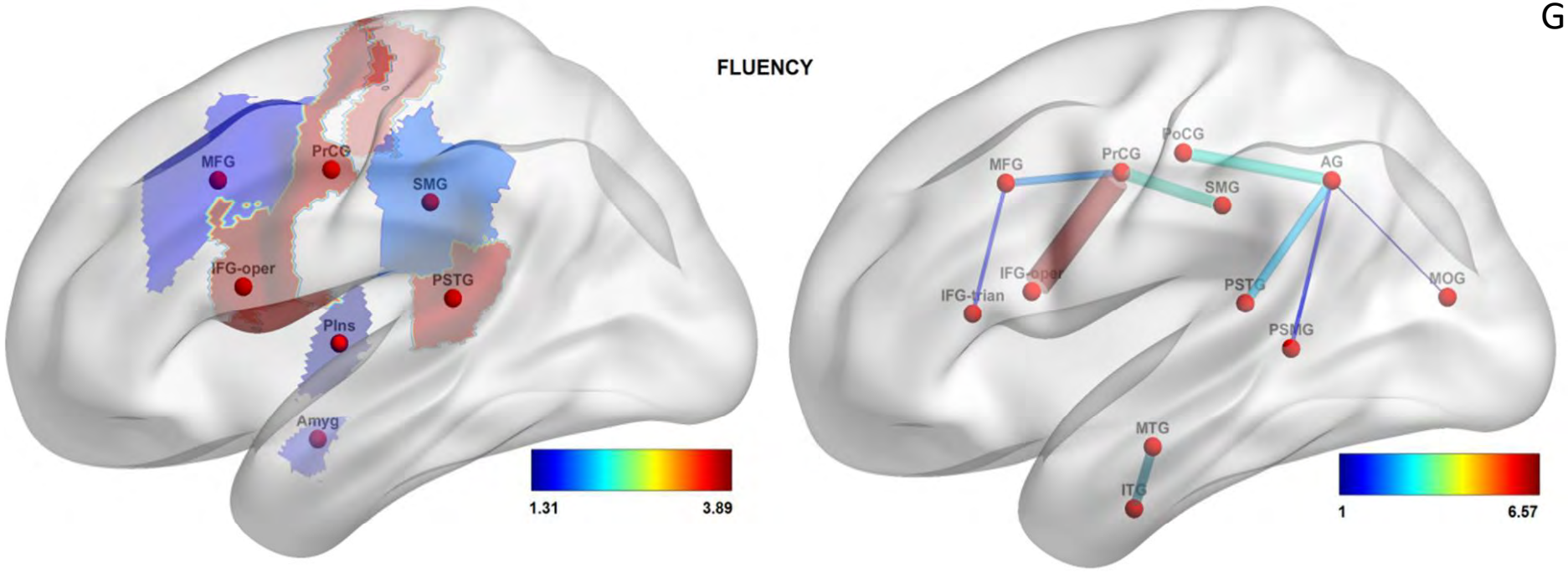




Bonilha et al, Stroke, 2014

Connectome and Aphasia

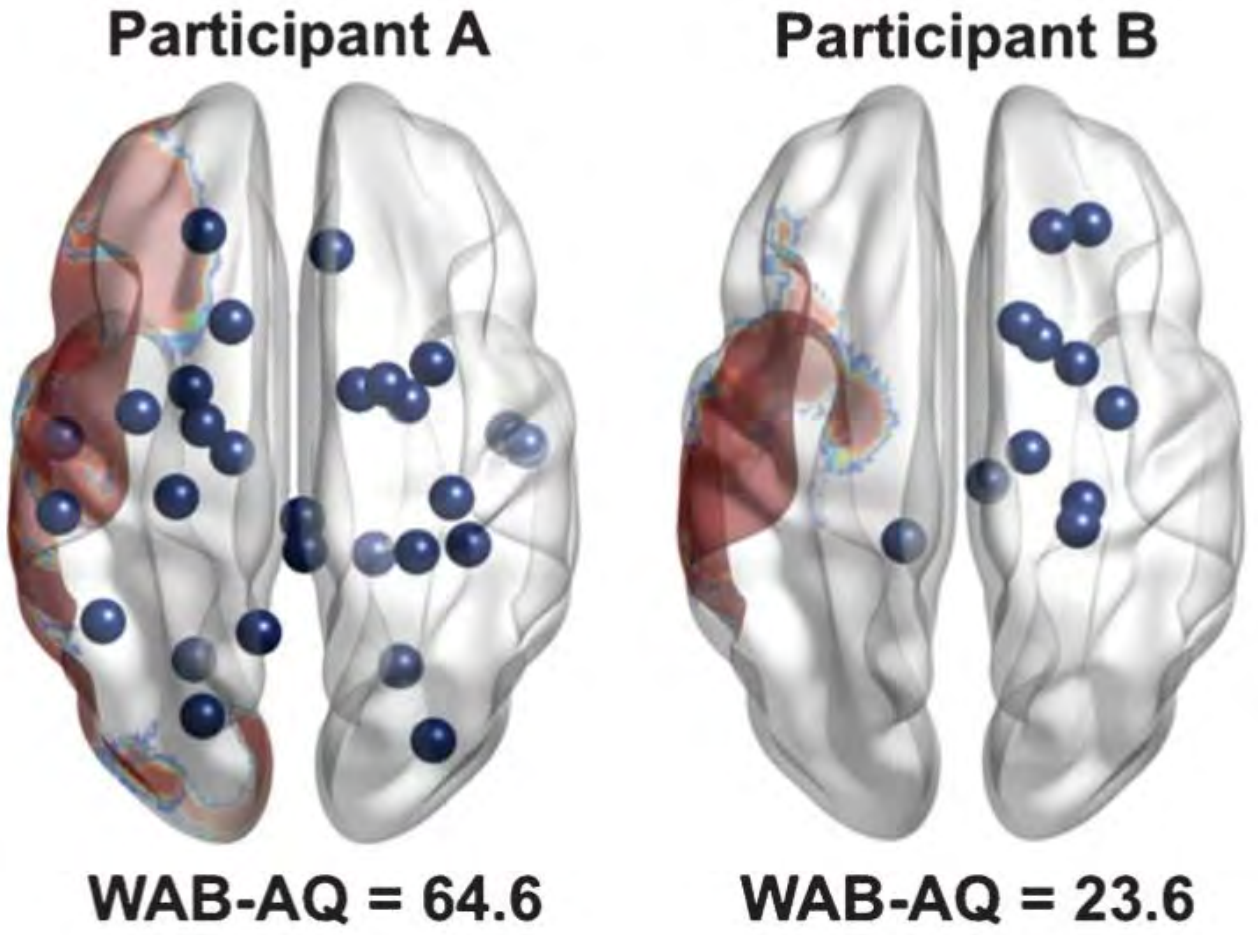
Grigori Yourganov



Yourganov et al, J Neuroscience, 2016

Connectome and Aphasia

Zeke Gleichgerrcht



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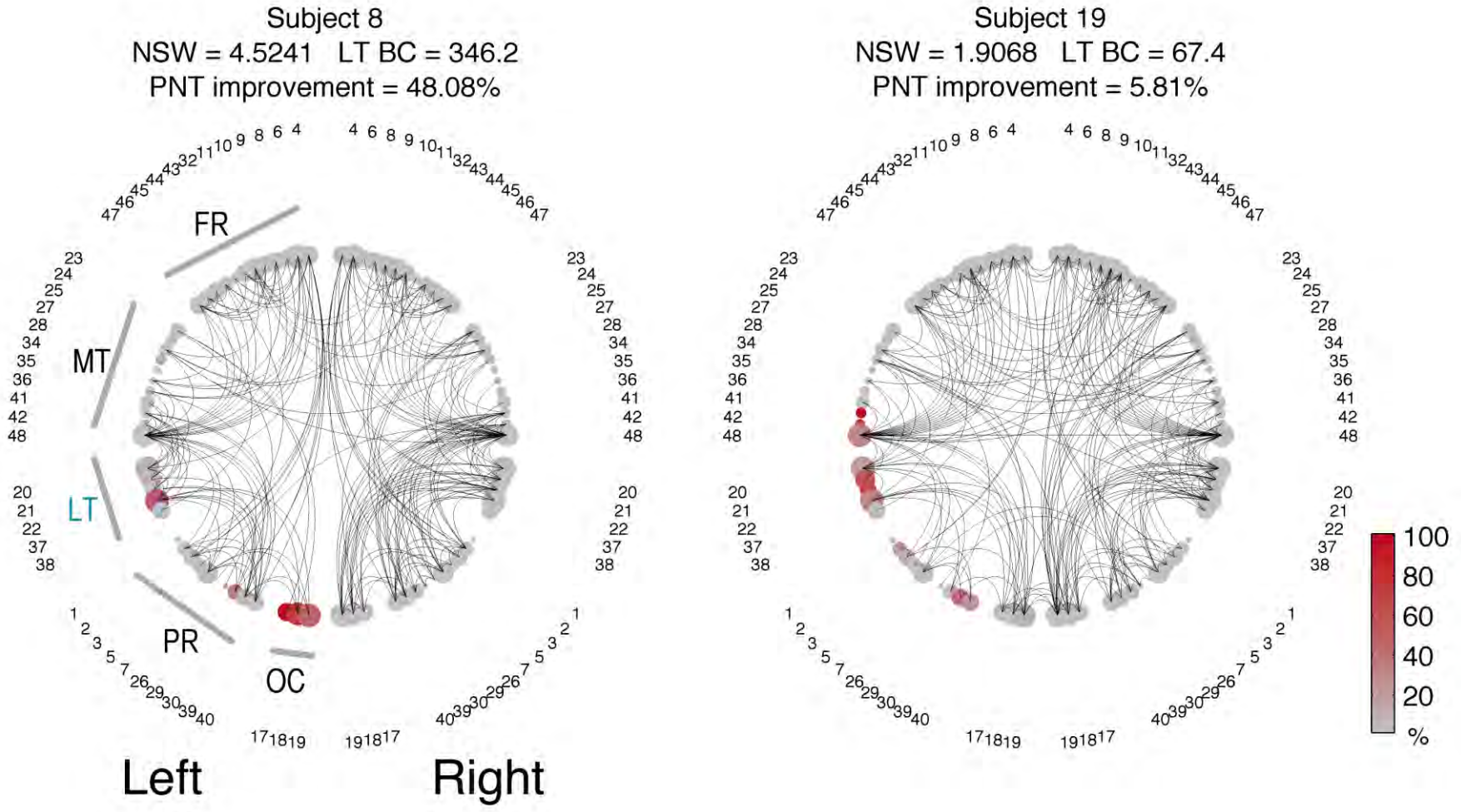
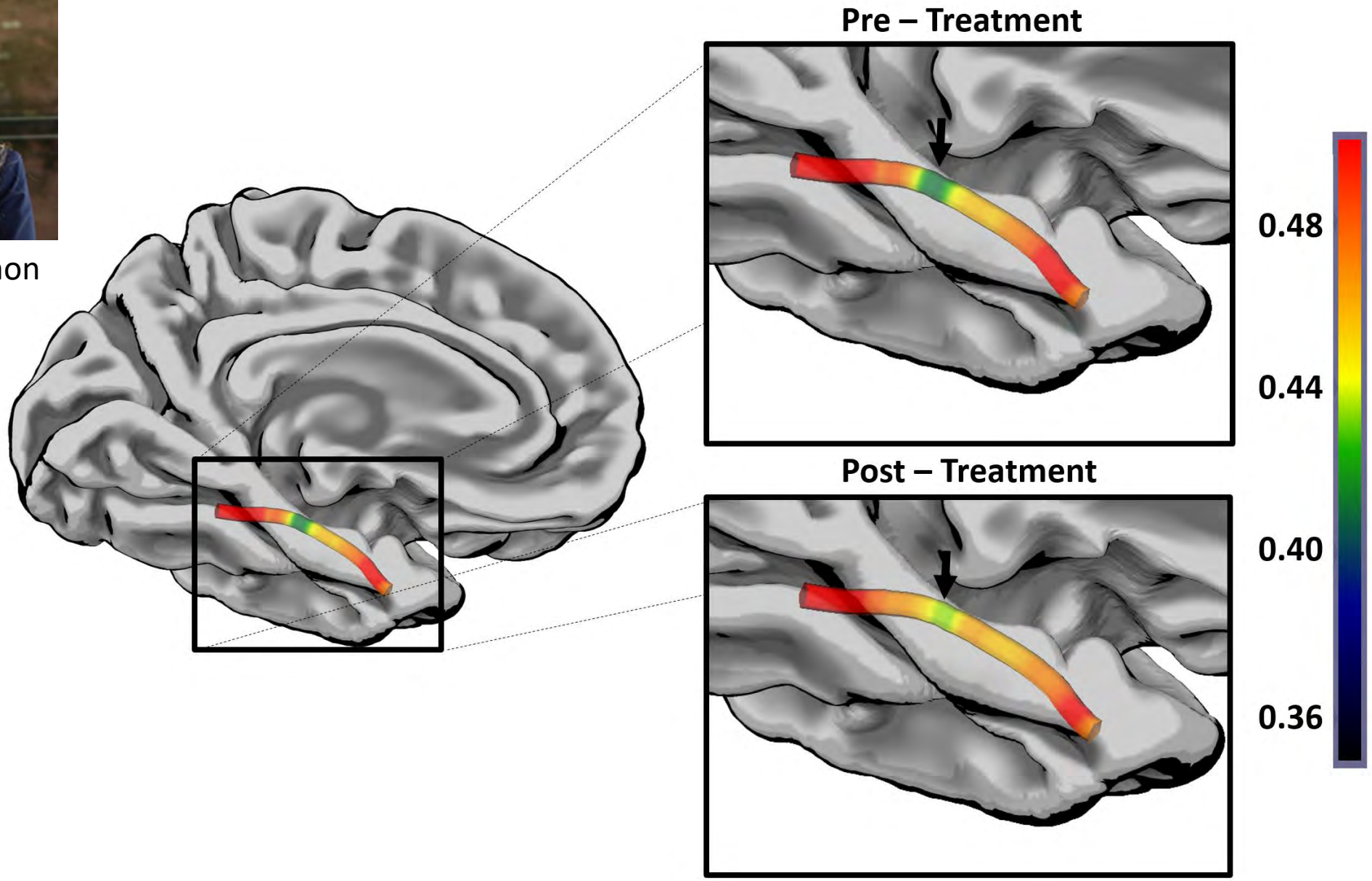
Connectome and Aphasia

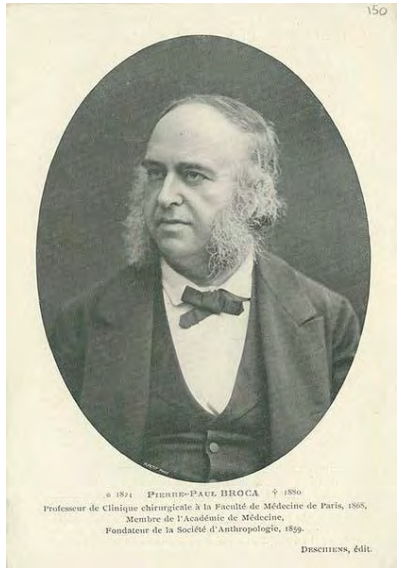


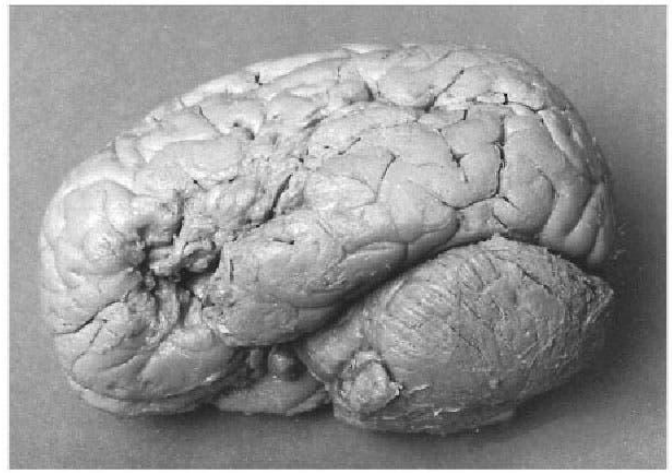
Bonilha et al, Neurorehabilitation and Neural Repair, 2015

Emilie McKinnon

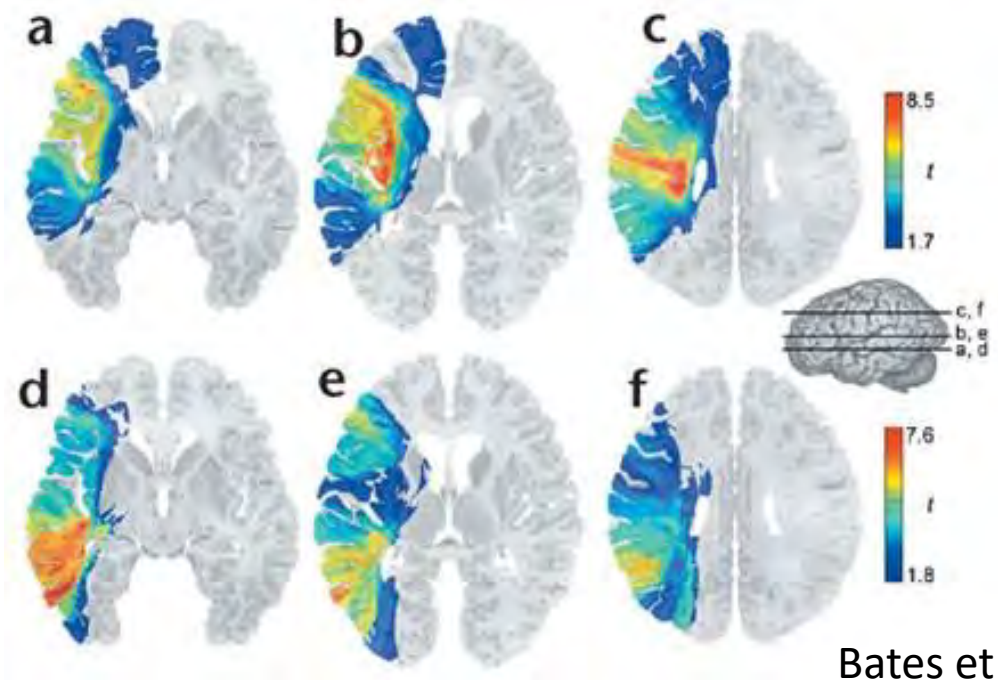


McKinnon et al. – Annals of Neurology 2017

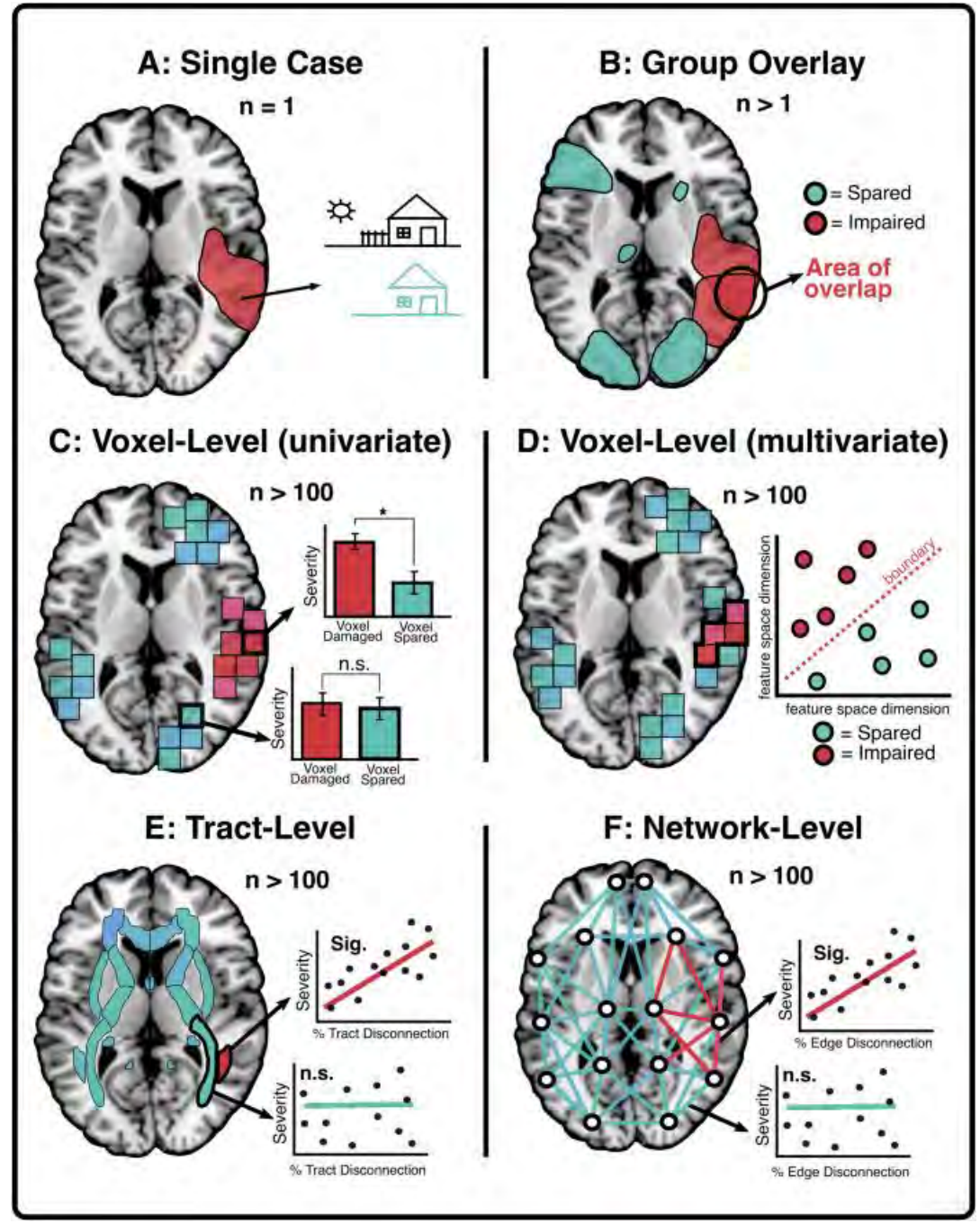




https://www.lindahall.org/about/news/scientist-of-the-day/paul-broca/



Bates et al. Nature 2003



Moore et al. Cortex 2024

Predicting Outcomes of Language Rehabilitation (POLAR) - NIDCD P50 DC014664 – Project 1

Other factors

Lisa Johnson

Available online at www.sciencedirect.com

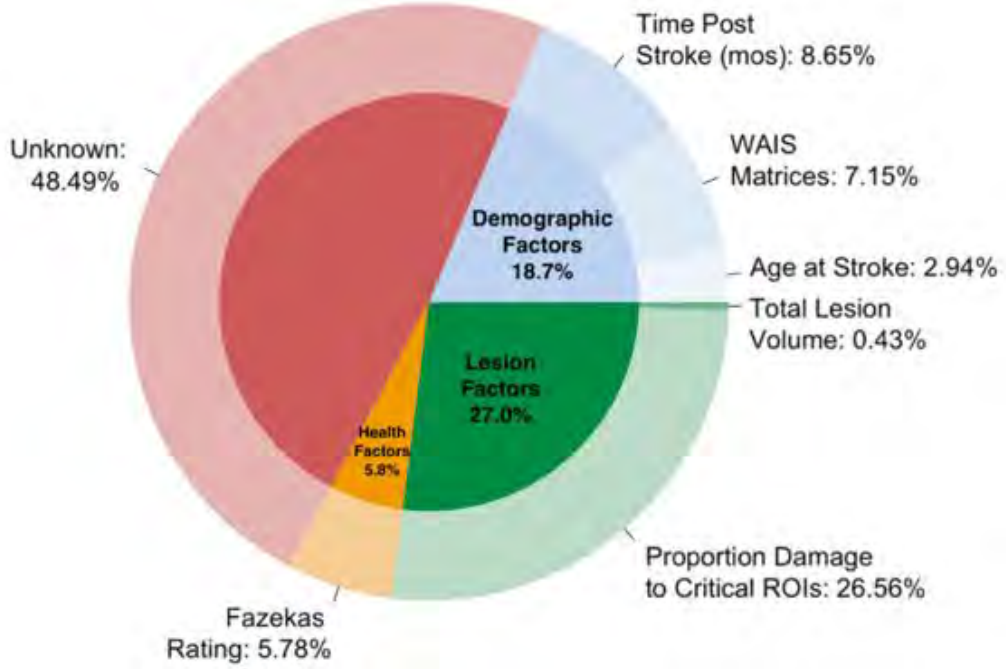
ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research Report

Predictors beyond the lesion: Health and demographic factors associated with aphasia severity

Lisa Johnson [a,*], *Samaneh Nemati* [a], *Leonardo Bonilha* [c], *Chris Rorden* [b], *Natalie Busby* [a], *Alexandra Basilakos* [a], *Roger Newman-Norlund* [b], *Argye E. Hillis* [d], *Gregory Hickok* [e] *and Julius Fridriksson* [a]



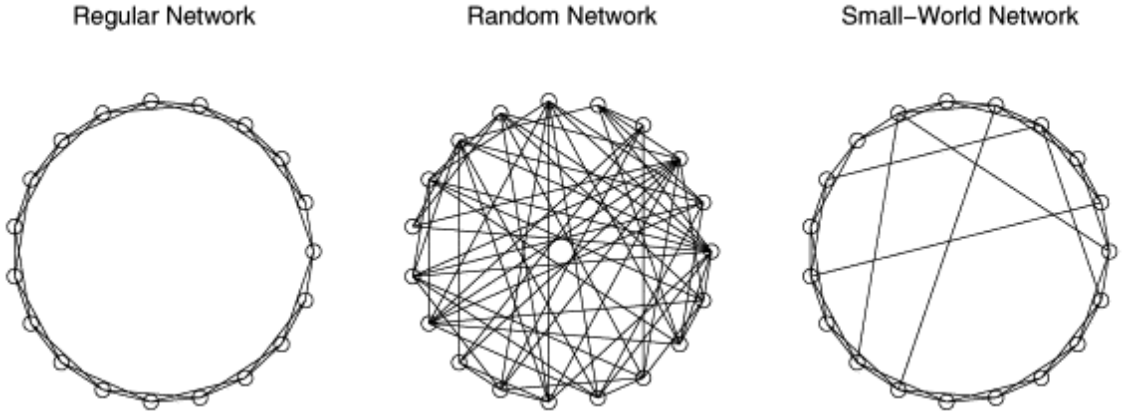
Cortex
Volume 154, September 2022, Pages 375-389

doi:10.1093/brain/awz251 BRAIN 2019: 142; 3190–3201 | 3190

BRAIN
A JOURNAL OF NEUROLOGY

Long-range fibre damage in small vessel brain disease affects aphasia severity

Janina Wilmskoetter,[1,*] Barbara Marebwa,[1,*] Alexandra Basilakos,[2] Julius Fridriksson,[2] Chris Rorden,[3] Brielle C. Stark,[4] Lisa Johnson,[2] Gregory Hickok,[5] Argye E. Hillis[6] and Leonardo Bonilha[1]



Bohland et al, Neurocomputing, 2001

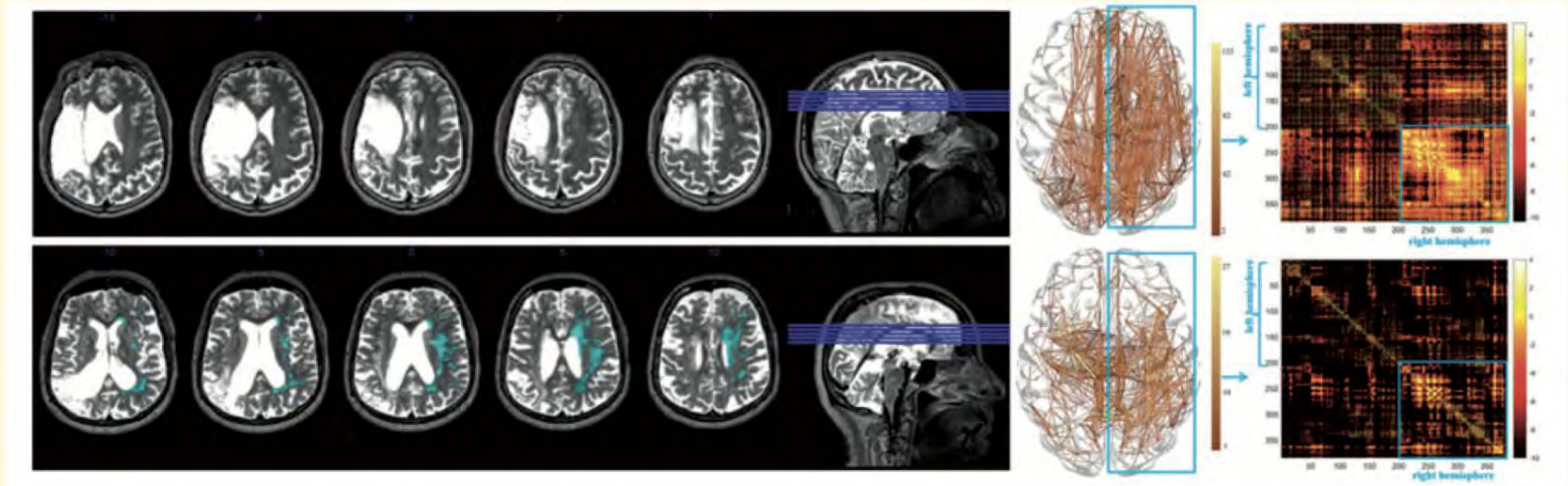


Figure 2 T_2-weighted MRI images from two patients of the study sample. Examples of PVH and deep WMH ratings (*left*: WMH are highlighted in light blue), as well as the corresponding fibre tracking and structural connectome matrix (*right*: *x*- and *y*-axes correspond to the AICHA region of interest numbers, warmer colours represent higher connectivity between regions of interest). Patient 1 (*top row*) did not present with WMH; Patient 2 (*bottom row*) presented with the most severe scores (3 for PVH and 3 for deep WMH). The connectome matrices show that the more severe WMH scores for Patient 2 coincided with fewer connections, particularly in brain areas with long range projections such as the frontal lobe, compared to Patient 1.

Janina Wilmskoetter

Archives of Rehabilitation Research and Clinical Translation (2023) 5, 100302

ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Rehabilitation Research and Clinical Translation

Archives of Rehabilitation Research and Clinical Translation 2023;5:100302

Available online at www.sciencedirect.com

OPEN ACCESS

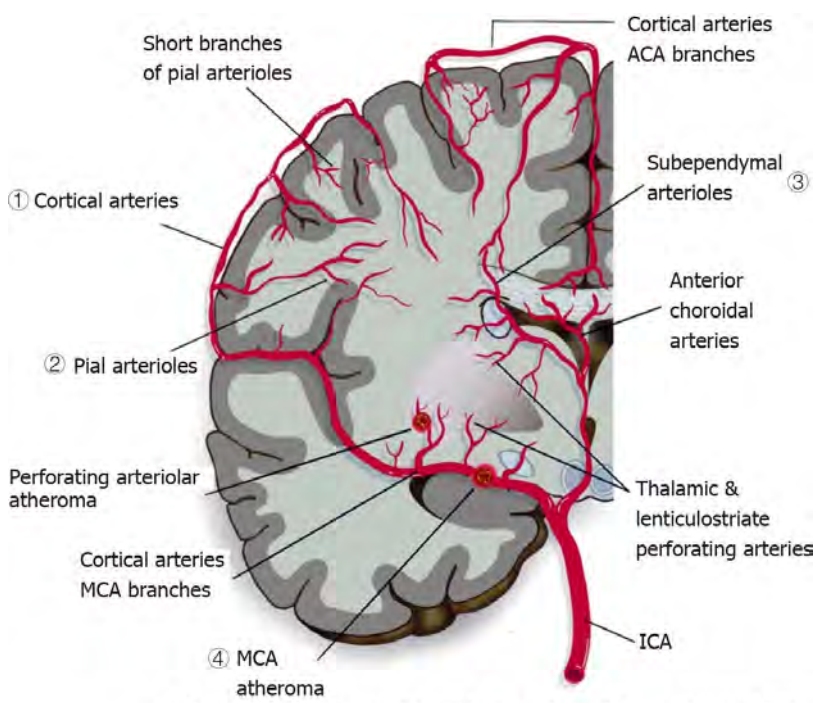
Original Research

Longitudinal Progression of White Matter Hyperintensity Severity in Chronic Stroke Aphasia

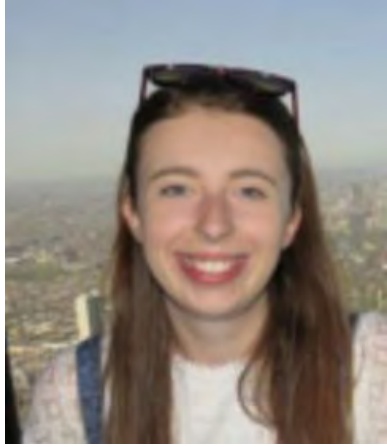
Check for updates

Natalie Busby, PhD [a], Roger Newman-Norlund, PhD [b], Janina Wilmskoetter, PhD [c], Lisa Johnson, PhD [a], Chris Rorden, PhD [b], Makayla Gibson, BS [a], Rebecca Roth, BA [d], Sarah Wilson, MA [a], Julius Fridriksson, PhD [a], Leonardo Bonilha, MD, PhD [d]

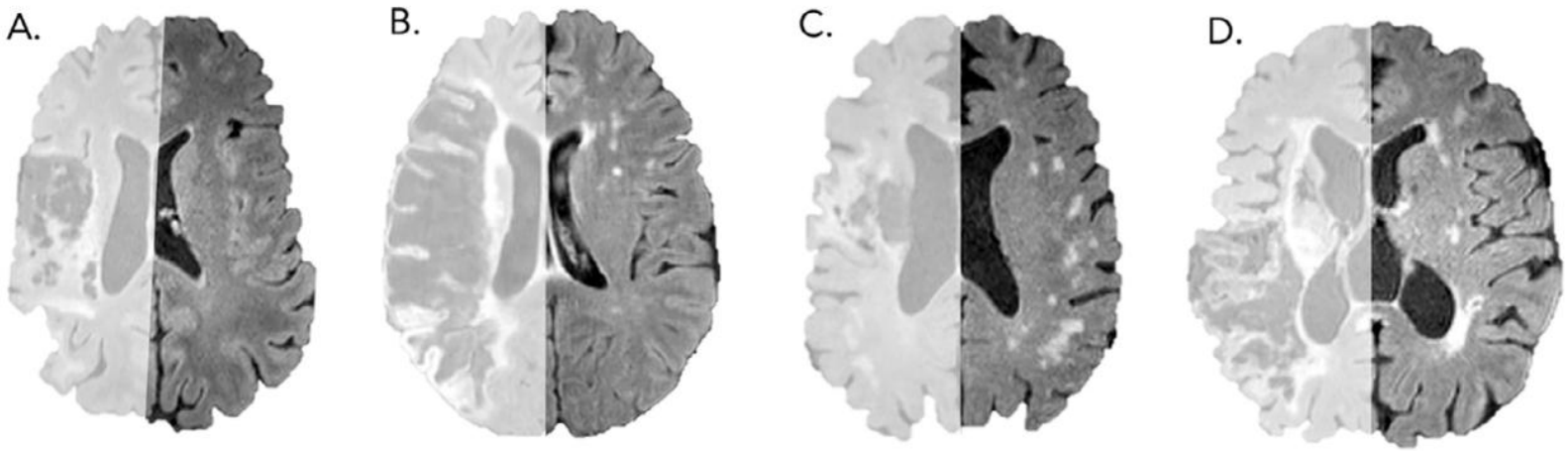
[a] *Department of Communication Sciences and Disorders, University of South Carolina, Columbia, SC*
[b] *Department of Psychology, University of South Carolina, Columbia, SC*
[c] *Department of Neurology, Medical University of South Carolina, Charleston, SC*
[d] *Department of Neurology, Emory University, Atlanta, GA*

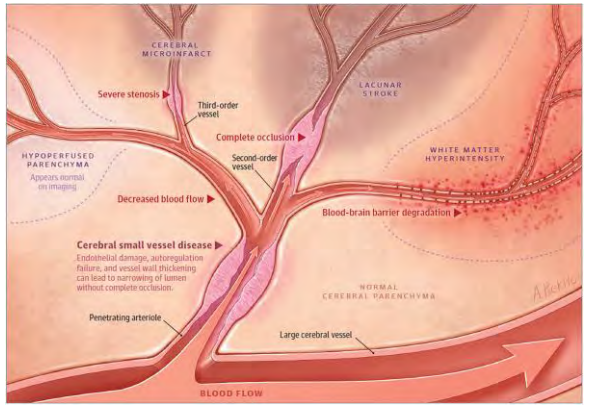


DOI: 10.12998/wjcc.v10.i24.8450 **Copyright** ©The Author(s) 2022.



Natalie Busby





Regenhardt et al, Jama Neurology, 2018

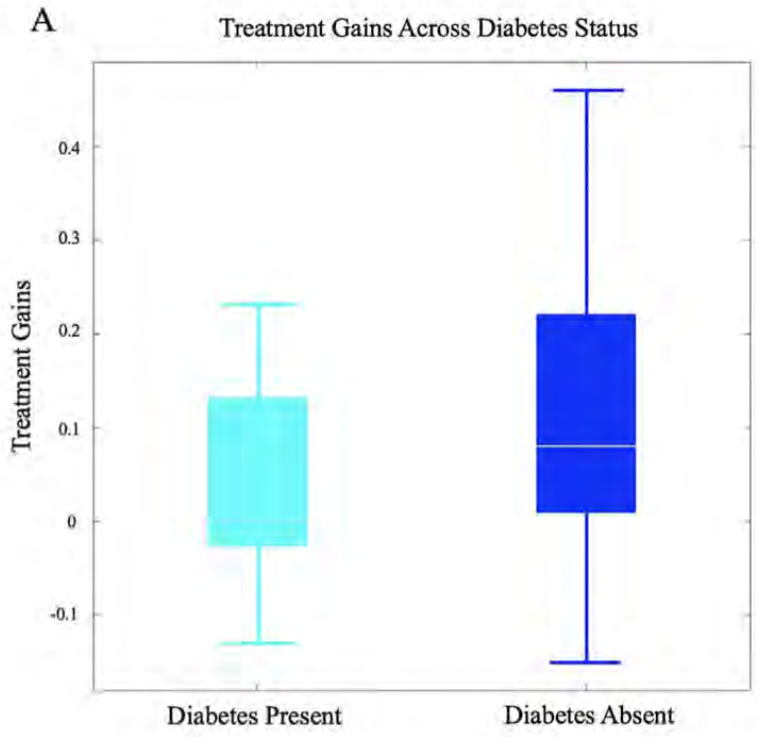
Cerebral Cortex, 2023, **33**, 8557–8564
https://doi.org/10.1093/cercor/bhad140
Advance access publication date 3 May 2023
Original Article

Rebecca Roth

Natalie Busby

Diabetes, brain health, and treatment gains in post-stroke aphasia

Rebecca Roth[1], Natalie Busby[2], Janina Wilmskoetter[3], Deena Schwen Blackett[4], Ezequiel Gleichgerrcht[4], Lisa Johnson[2], Chris Rorden[5], Roger Newman-Norlund[5], Argye E. Hillis[6], Dirk B. den Ouden[2], Julius Fridriksson[2], Leonardo Bonilha[1,*]



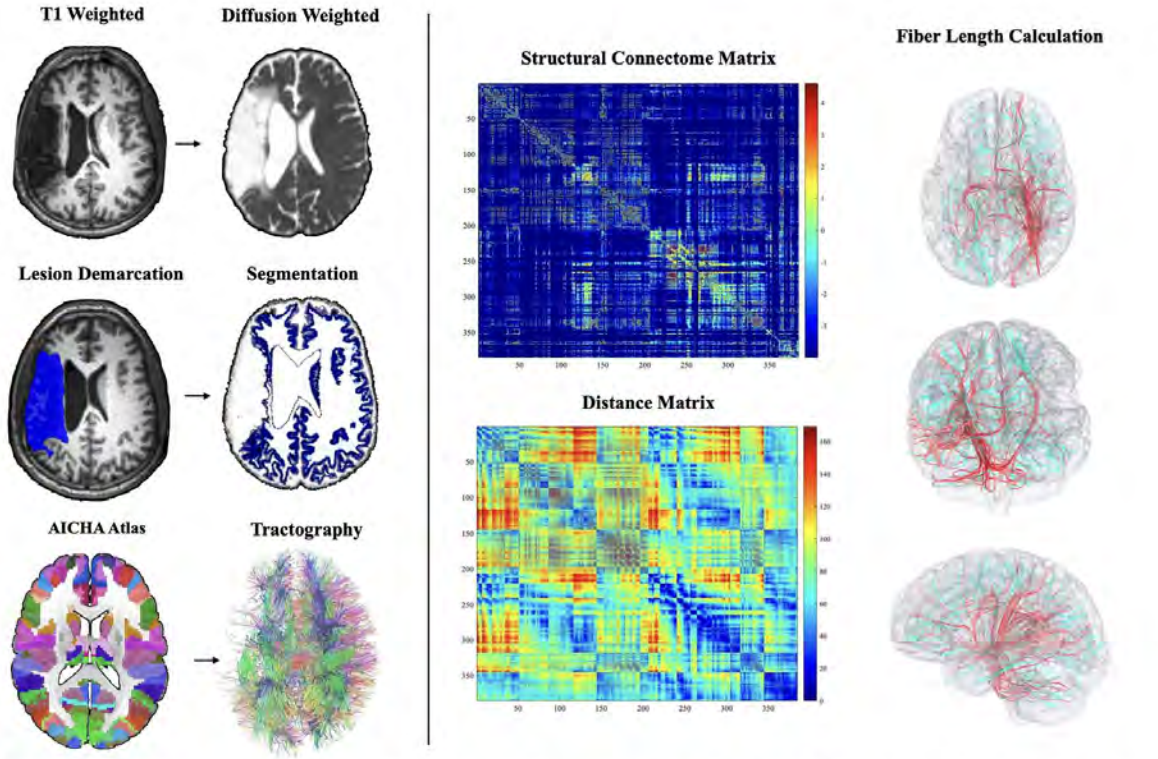
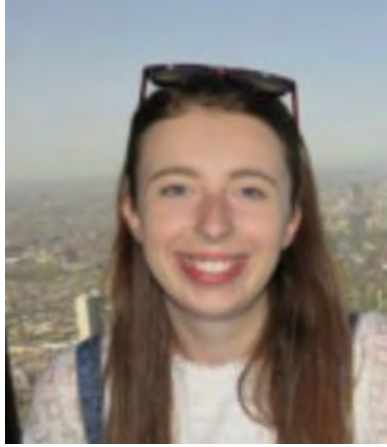


Fig. 2. Schematic of imaging methods used from using the T1 weighted, diffusion weighted, and AICHA atlas to constructing a whole brain connectome and tractography, then calculating the distance of each area, followed by categorizing fiber length.

Stroke

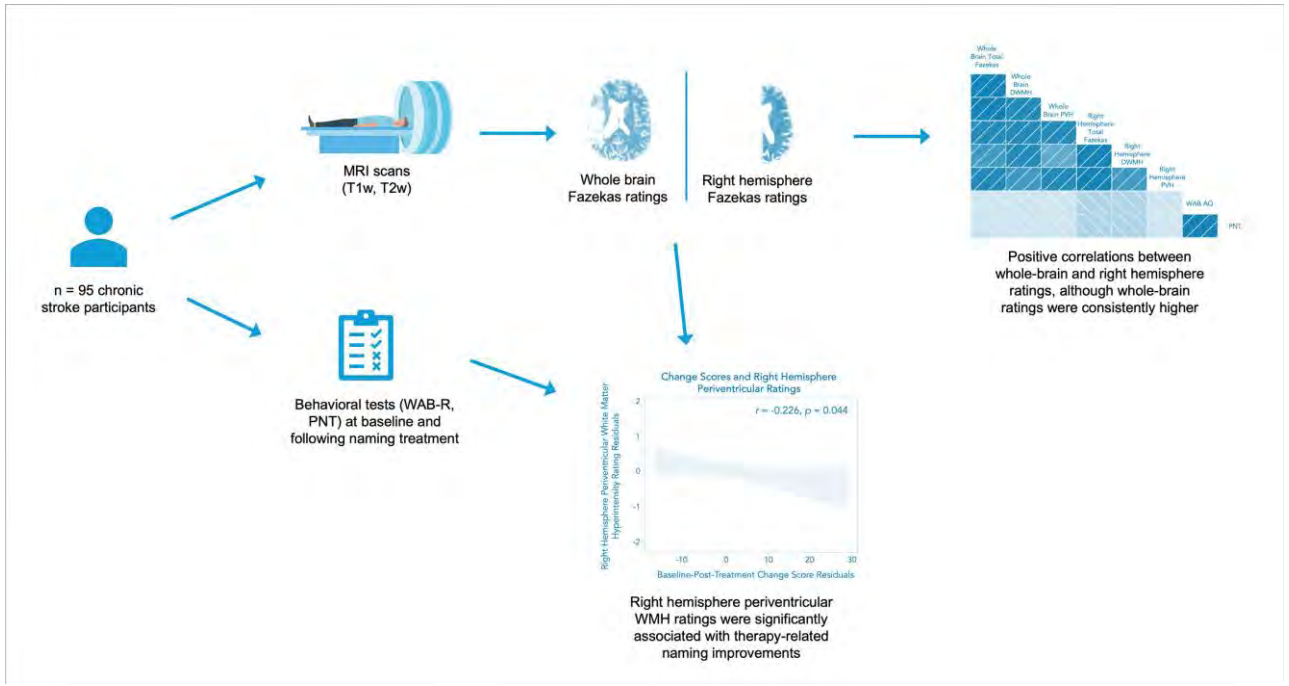


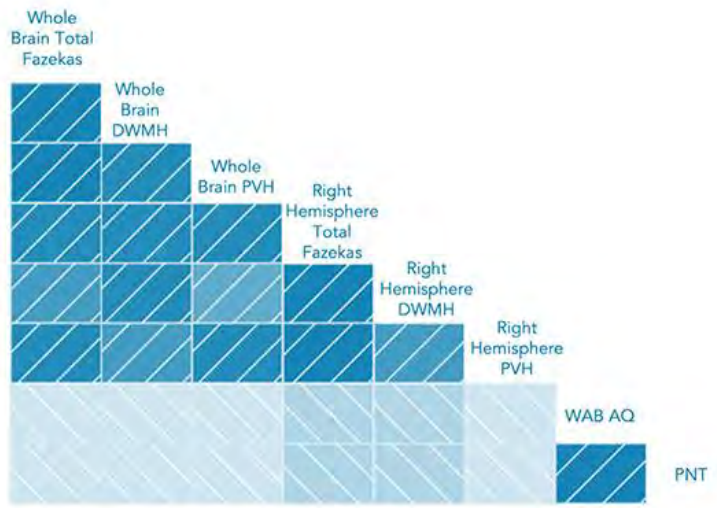
Natalie Busby

ORIGINAL CONTRIBUTION

White Matter Hyperintensity Load Independent From the Stroke Lesion Is Associated With Chronic Aphasia Severity and Treatment Outcome

Natalie Busby, PhD; Sigfus Kristinsson, PhD; Lisa Johnson, PhD; Rebecca Roth, BA; Argye E. Hillis, MD, MA; Roger Newman-Norlund, PhD; Chris Rorden, PhD; Julius Fridriksson, PhD; Leonardo Bonilha, MD, PhD

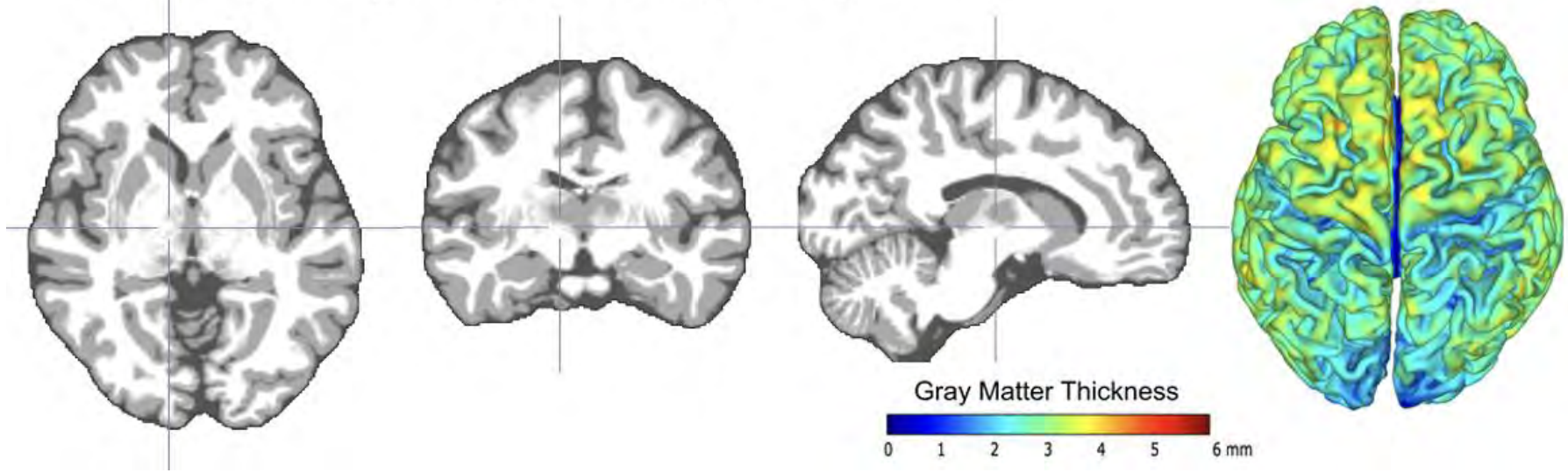




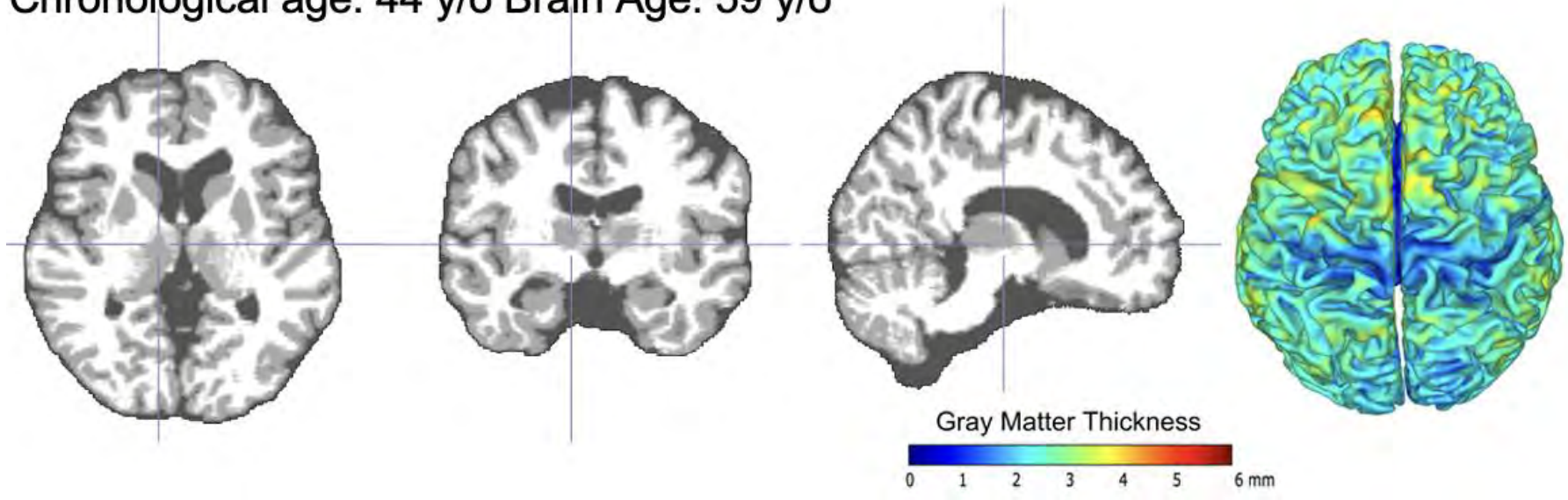
Positive correlations between whole-brain and right hemisphere ratings, although whole-brain ratings were consistently higher

Brain Health – Brain Age

Chronological age: 44 y/o Brain Age: 43 y/o

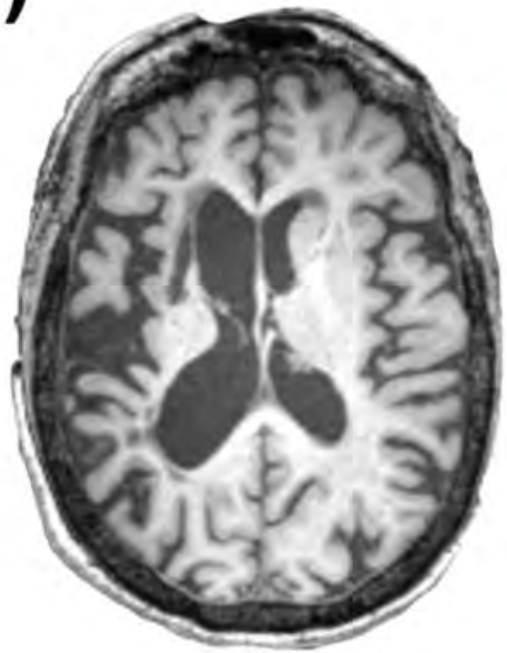


Chronological age: 44 y/o Brain Age: 59 y/o

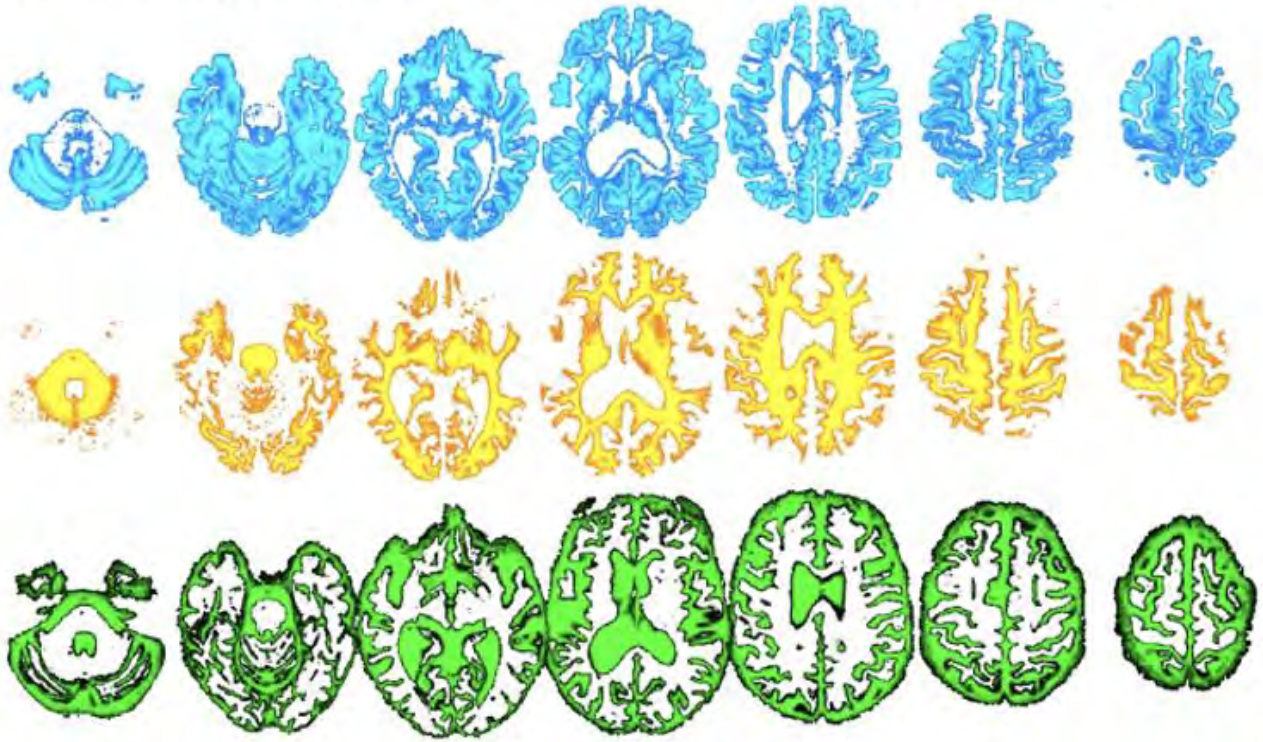


Janina Wilmskoetter

C)



Brain age (84y) > Chron. age (71y)



GM

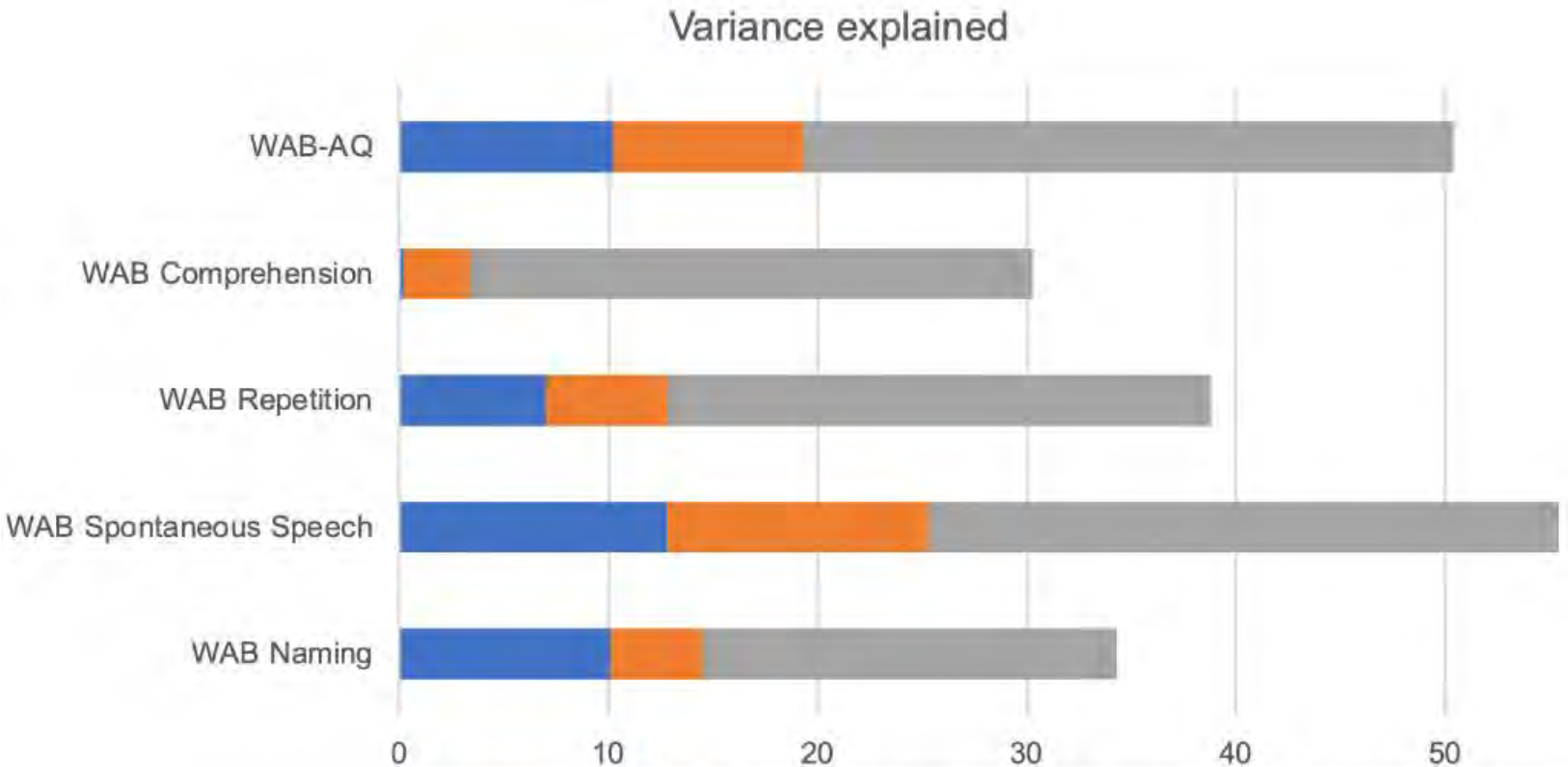
WM

CSF

Brain Age and Aphasia

Sigfus Kristinsson

Natalie Busby



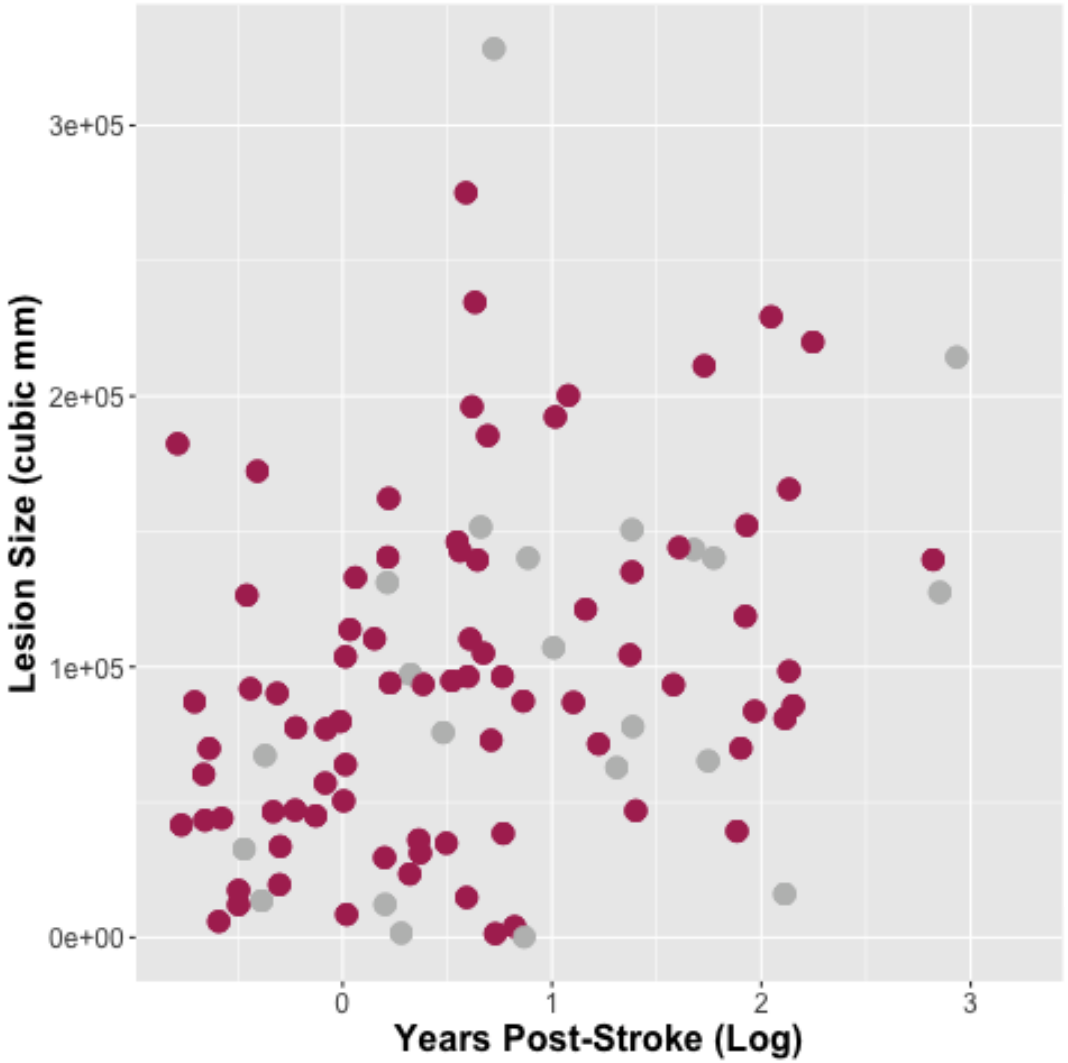
	WAB Naming	WAB Spontaneous Speech	WAB Repetition	WAB Comprehension	WAB-AQ
Age	10.1	12.8	7	0.2	10.2
PBA	4.4	12.5	5.8	3.2	9.1
Lesion Volume	19.8	30.1	26	26.9	31.1

Treatment improvements in the PNT was predicted by PBA
T = -2.3095, p = 0.0259, 11.2% of variance explained

- controlling for baseline performance, chronological age, and lesion volume.

Busby et al., Neurology. 2023 Mar 14;100(11)

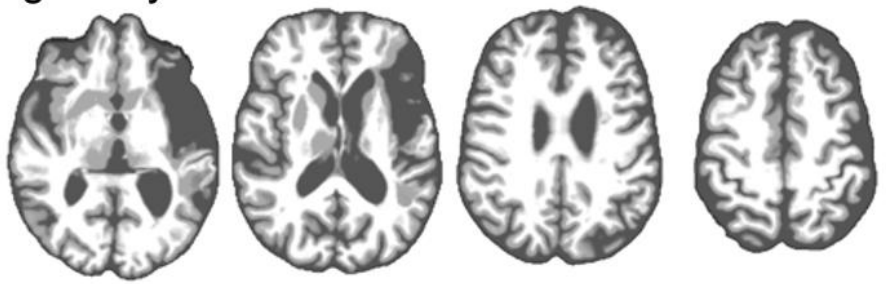
Lesion expansion



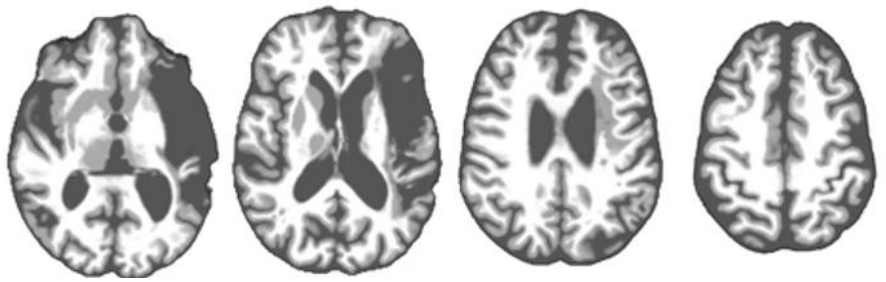
Sigfus Kristinsson

Lisa Johnson

Scan 1 - Age: 72 y/o Brain Age: 73 y/o



Scan 2 (5 years and 10 months later)- Age: 77 y/o Brain Age: 82 y/o



Johnson et al., Submitted

Lesion expansion

Sigfus Kristinsson wins national award to support stroke research

Posted on: February 24, 2025; Updated on: February 19, 2025

February 24, 2025 / *Erin Bluvas, **bluvase@sc.edu***

The **Department of Communication Sciences and Disorders**' (COMD) newest assistant professor **Sigfus Kristinsson** is the recipient of the Lawrence M. Brass, MD, Clinical Research Training Scholarship in Stroke. Funded by the American Heart Association and the American Brain Foundation in collaboration with the American Academy of Neurology, this award provides $150,000 in funding over a two-year period to support early career investigators conducting clinical studies related to stroke, vascular neurology, and neurocritical care.

Sigfus Kristinsson is an assistant professor in the Department of Communication Sciences and Disorders.

Aphasia treatment?

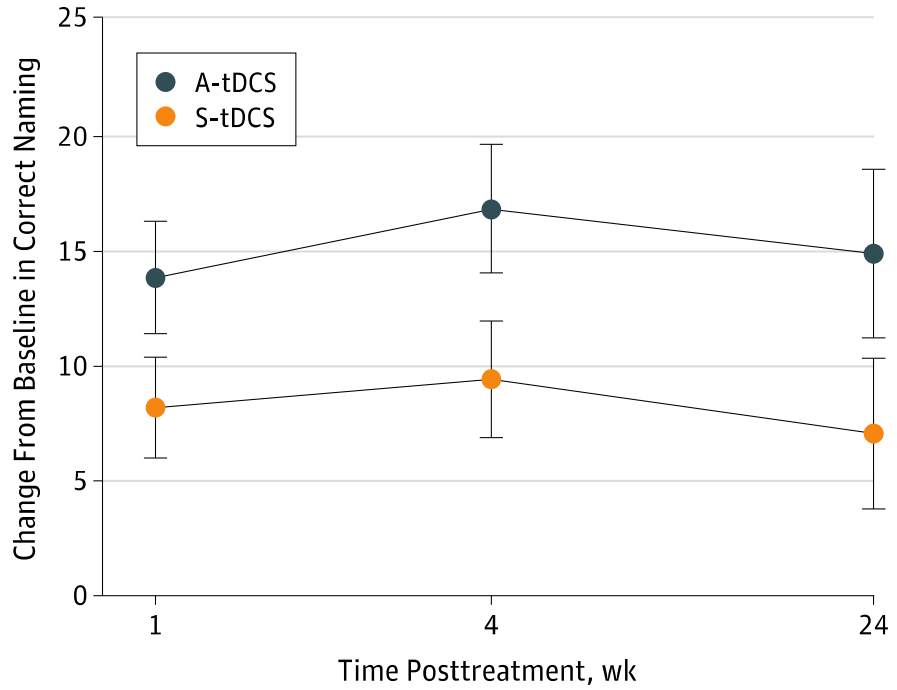
Research

JAMA Neurology | Original Investigation

Transcranial Direct Current Stimulation vs Sham Stimulation to Treat Aphasia After Stroke

A Randomized Clinical Trial

Julius Fridriksson, PhD; Chris Rorden, PhD; Jordan Elm, PhD; Souvik Sen, MD; Mark S. George, MD; Leonardo Bonilha, MD, PhD



Neurorehabilitation and Neural Repair
Volume 35, Issue 4, April 2021, Pages 346-355

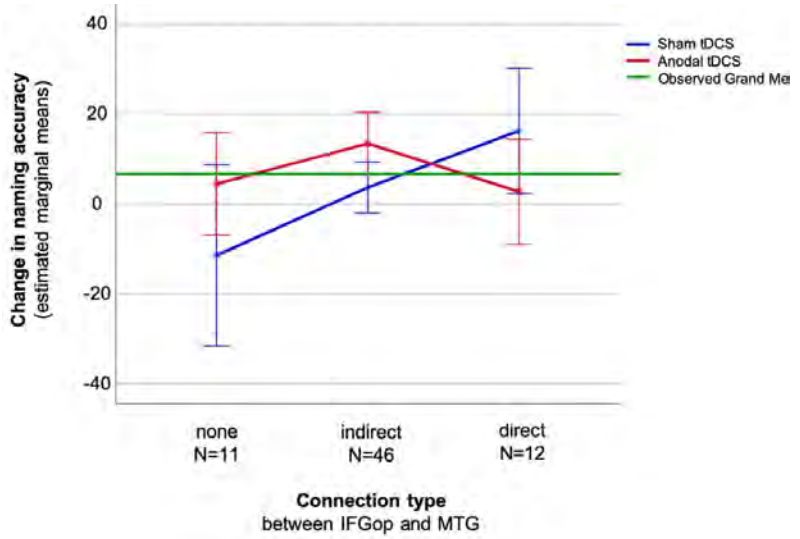
https://doi.org/10.1177/1545968321999052

SAGE journals

Original Research Article

Indirect White Matter Pathways Are Associated With Treated Naming Improvement in Aphasia

Janina Wilmskoetter, PhD [1], Julius Fridriksson, PhD [2], Alexandra Basilakos, PhD [2], Lorelei Phillip Johnson, PhD [2], Barbara Marebwa, PhD [1], Chris Rorden, PhD [2], Graham Warner, MS [1], Gregory Hickok, PhD [3], Argye E. Hillis, MD, MA [4], and Leonardo Bonilha, MD, PhD [1]



Brain health

Contents lists available at ScienceDirect

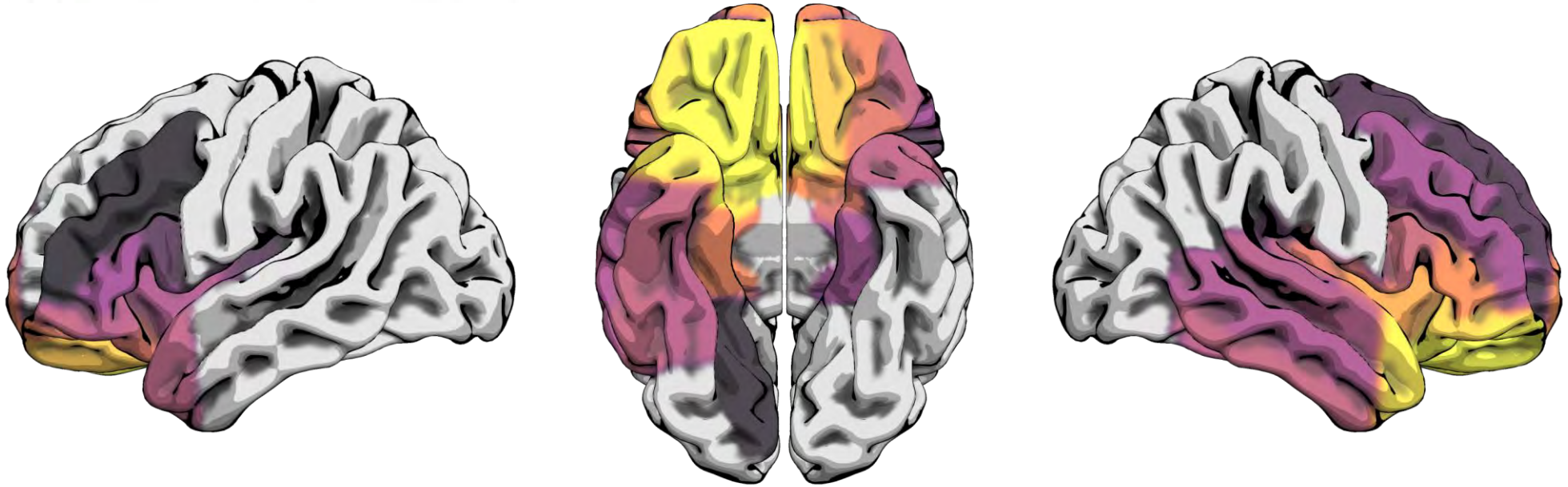
Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging.org

Epigenetic age is associated with regional brain aging along the sensorimotor-to-association axis of cortical organization

Nicholas Riccardi [a,*], Carolyn Banister [b], Natalie Busby [a], Sarah Newman-Norlund [a], Roger Newman-Norlund [c], Ida Rangus [a,d], Alex Teghipco [c], Chris Roden [c], Julius Fridriksson [a], Leonardo Bonilha [e]

Dr. Nick Riccardi



Brain health

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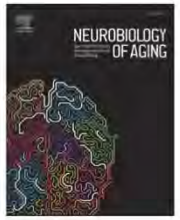
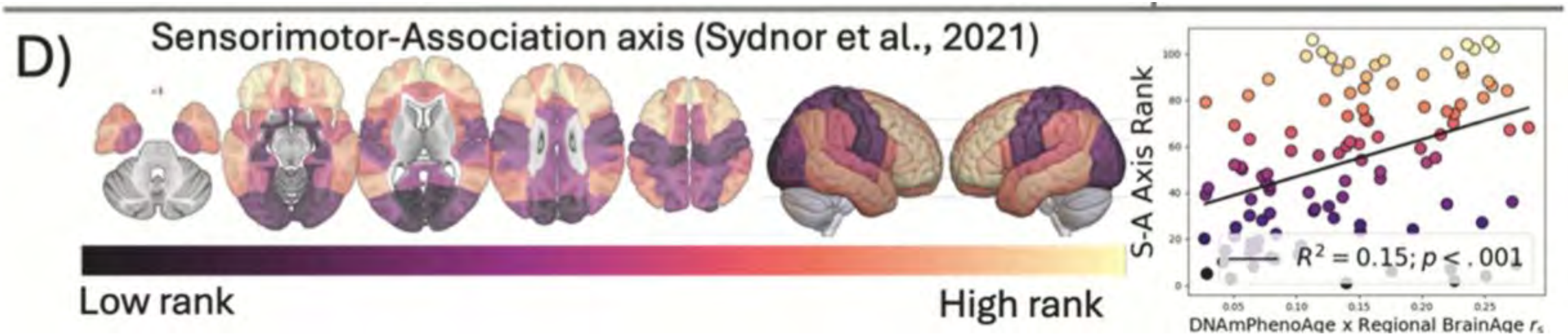


Check for updates

Epigenetic age is associated with regional brain aging along the sensorimotor-to-association axis of cortical organization

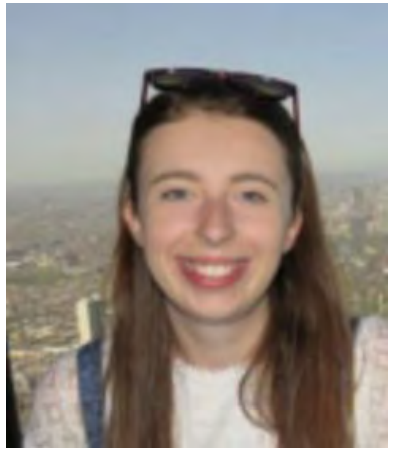
Nicholas Riccardi [a,*], Carolyn Banister [b], Natalie Busby [a], Sarah Newman-Norlund [a], Roger Newman-Norlund [c], Ida Rangus [a,d], Alex Teghipco [c], Chris Roden [c], Julius Fridriksson [a], Leonardo Bonilha [e]

Dr. Nick Riccardi



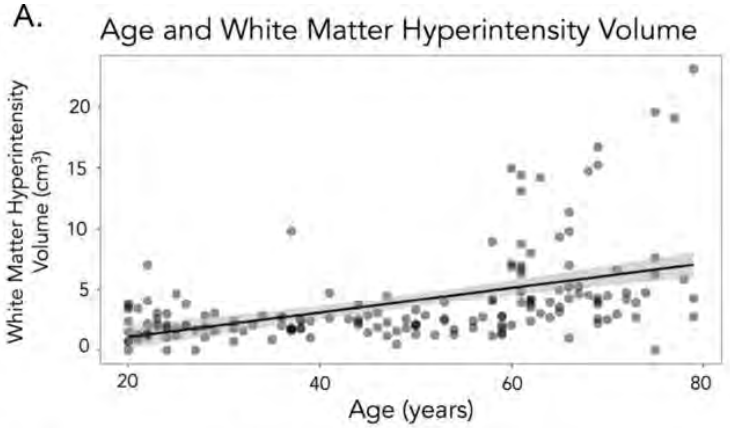
DNAmPhenoAge was related to advanced BrainAge of regions higher on the sensorimotor-to-association axis of cortical organization (F(1104) =17.5, R2 =.15, p <.001).

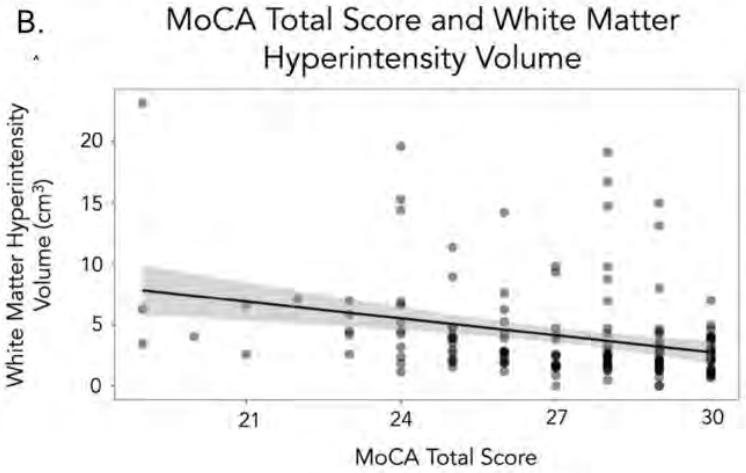
Brain health

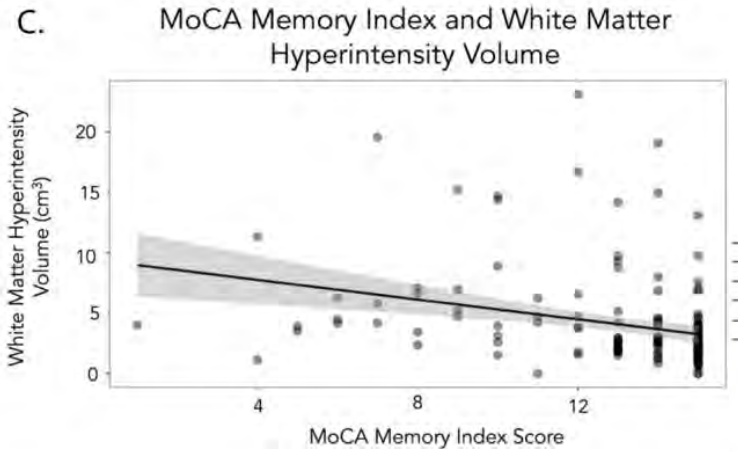


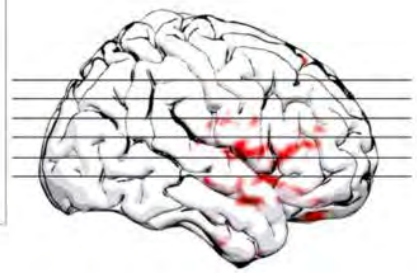
Natalie Busby

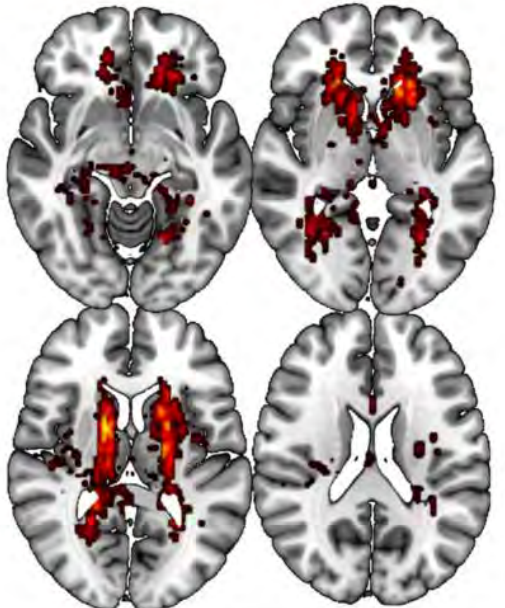
Nick Riccardi











Scientific Reports volume 15, Article number: 27736 (2025)

Brain health

communications biology

A Nature Portfolio journal

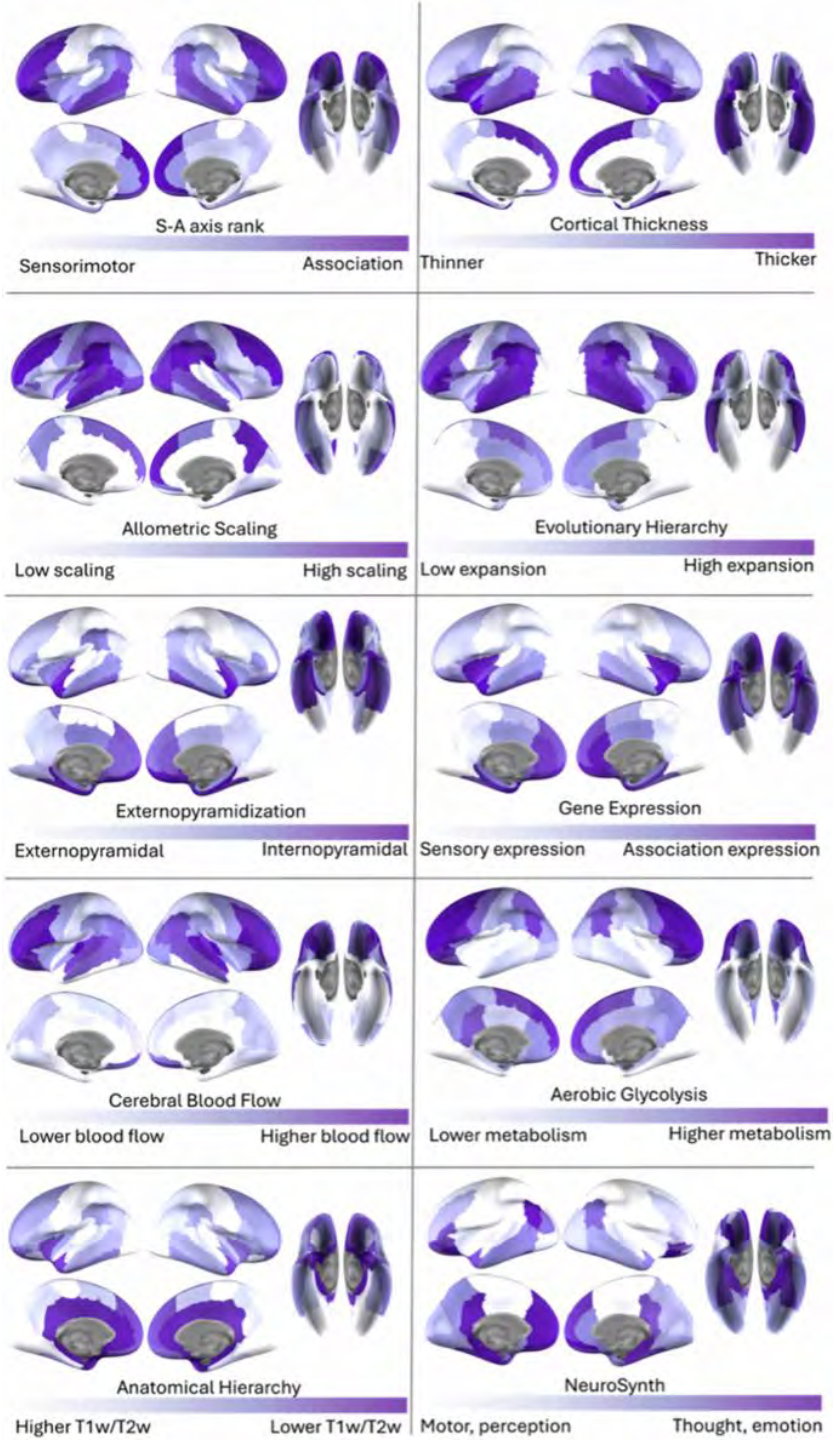
Article

https://doi.org/10.1038/s42003-025-08228-z

Distinct brain age gradients across the adult lifespan reflect diverse neurobiological hierarchies

Check for updates

Nicholas Riccardi[1], Alex Teghipco[1], Sarah Newman-Norlund[1], Roger Newman-Norlund[2], Ida Rangus[1,3], Chris Rorden[2], Julius Fridriksson[1] & Leonardo Bonilha[4]



Nick Riccardi

Brain health

communications biology

A Nature Portfolio journal

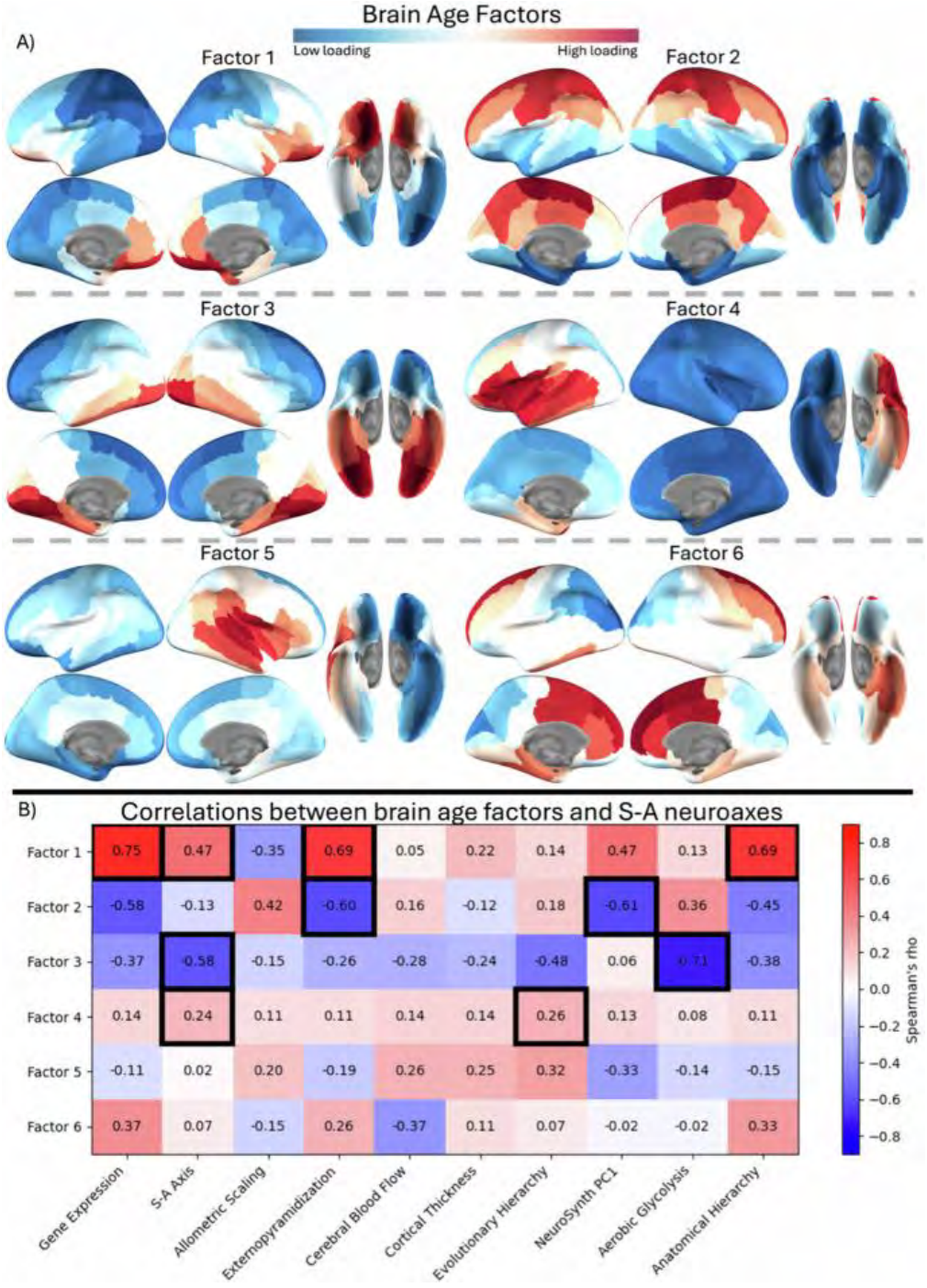
Article

https://doi.org/10.1038/s42003-025-08228-z

Distinct brain age gradients across the adult lifespan reflect diverse neurobiological hierarchies

Check for updates

Nicholas Riccardi[1], Alex Teghipco[1], Sarah Newman-Norlund[1], Roger Newman-Norlund[2], Ida Rangus[1,3], Chris Rorden[2], Julius Fridriksson[1] & Leonardo Bonilha[4]



Nick Riccardi


USC Brain Health

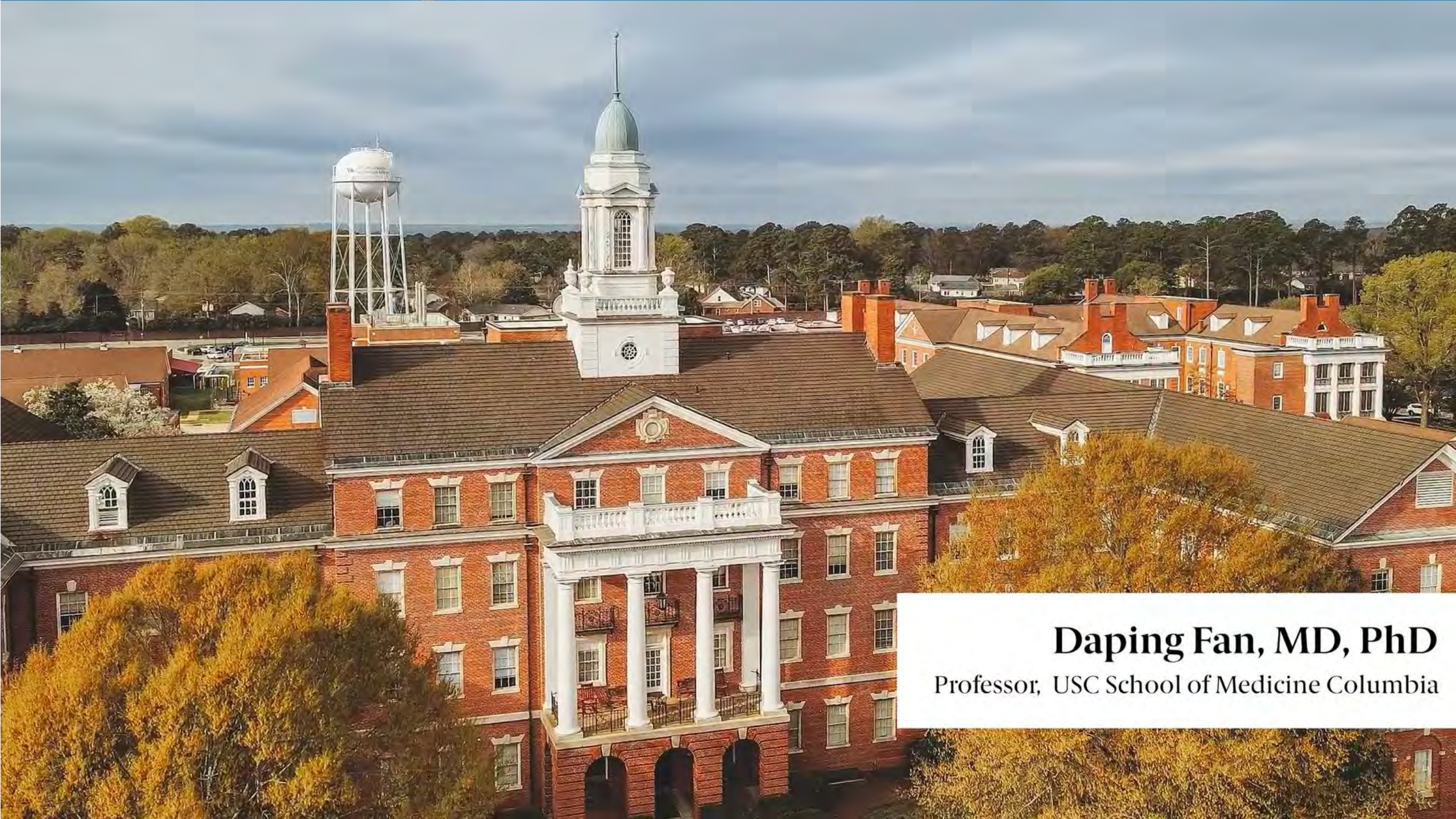
BRAIN HEALTH CENTER

Alzheimer's Disease Research Center

HELPING FAMILIES AND CAREGIVERS

Multi-disciplinary research studying and addressing the challenges experienced by those affected by Alzheimer's disease.


University of
South Carolina
College of Nursing



Daping Fan, MD, PhD

Professor, USC School of Medicine Columbia

Nicholas Riccardi, PhD

Postdoctoral Fellow
Department of Communication Sciences and Disorders,
Arnold School of Public Health

Thank you!

Questions & Discussion

USC Brain Health

PROMOTING BRAIN HEALTH: PROMOTING LIFELONG STRATEGIES TO REDUCE **ALZHEIMER'S DISEASE RISK**

Dr. Jason Yang

Dr. Jean Neils-Strunjas

Dr. James Hebert

Karilyn Tremblay

Panel Moderated by Dr. Daniela Friedman

UNIVERSITY OF South Carolina

Office for the Study of Aging
Arnold School of Public Health
UNIVERSITY OF SOUTH CAROLINA

TecHealth
Technology Center to Promote Healthy Lifestyles

Beyond the Gym: How Lifestyle Physical Activity and Sedentary Time Shape Everyday Brain Health in Older Adults

Chih-Hsiang "Jason" Yang, PhD

Department of Exercise Science

The Technology Center to Promote Healthy Lifestyles (TecHealth)

Office for the Study of Aging

Presenting at the 2025 Statewide Aging & AD Research Symposium
10/09/2025 @USC – Columbia, SC

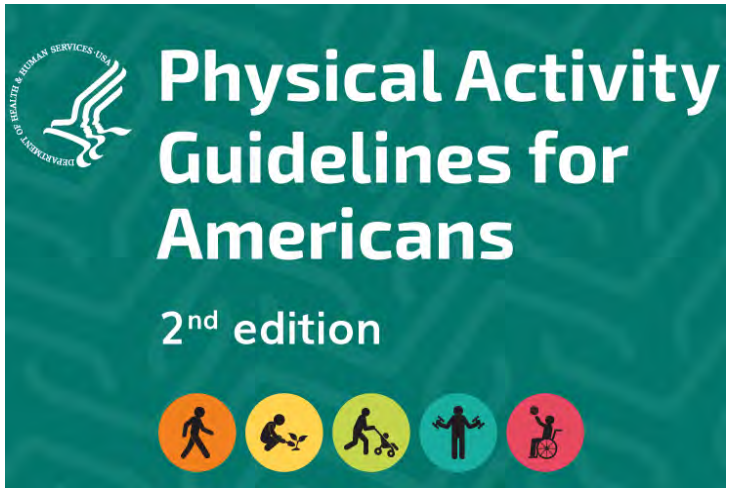
ECHO LAB

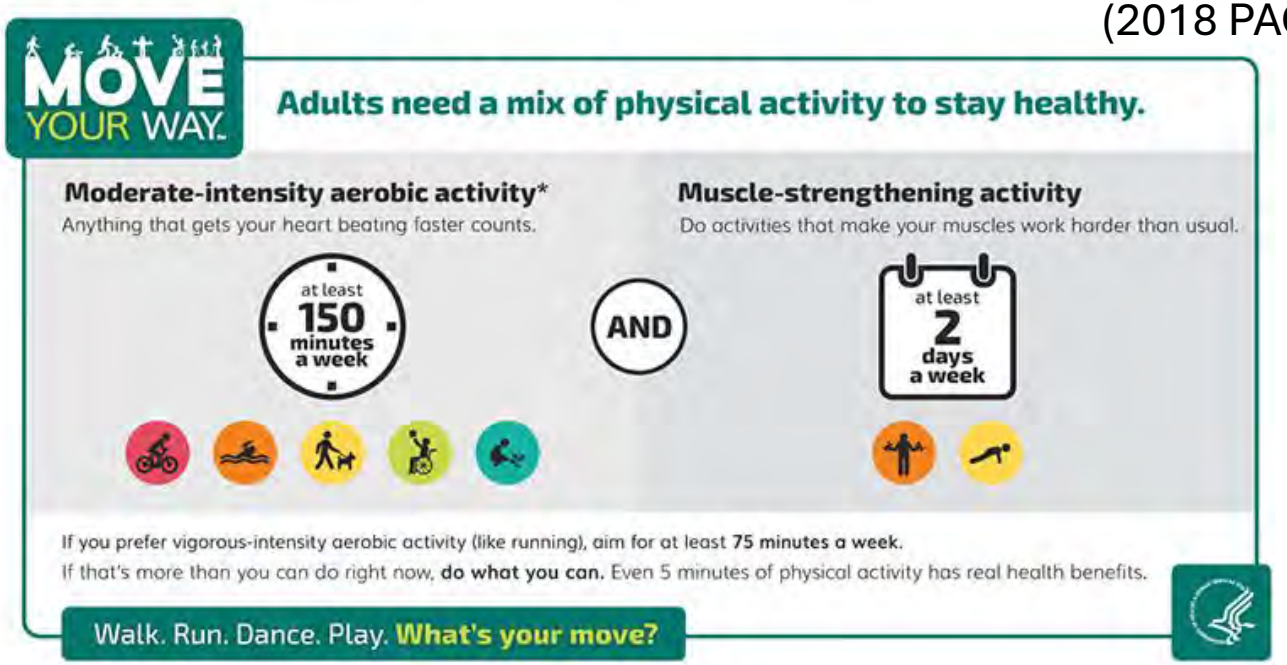
Regular physical activity engagement is beneficial for health

- Prevent Cancer
- **Enhance Brain Health** →
  - Improve cognition
  - Enhance psychological well-being and quality of life
  - Reduce the risks of dementia and Alzheimer's disease
- Enhance Cardiometabolic Health
- Prevent Weight Gain
- Reduce risks of Cardiovascular Diseases
- Reduce risks of All-cause Mortality

- Only **~20%** of adults meet current federal PA guidelines

(2018 PAGAC)





Can we target more achievable forms of lifestyle physical activities to promote brain health and active lifestyle?

Feasibility
Scalability
Motivation

Image source: https://www2.ljworld.com

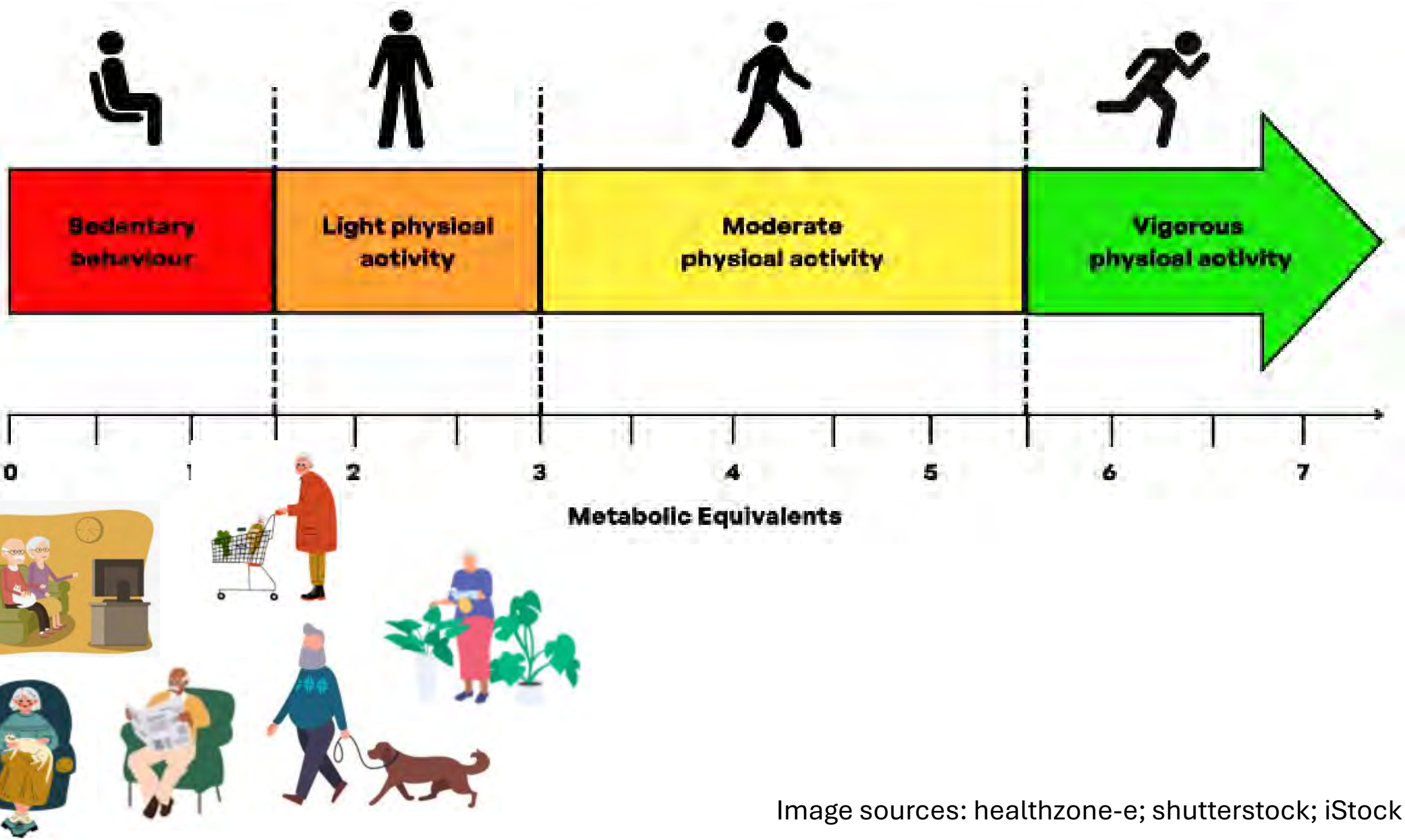


Image sources: healthzone-e; shutterstock; iStock

JAMA Network | Open™

Original Investigation | Neurology

Association of Accelerometer-Measured Light-Intensity Physical Activity With Brain Volume

The Framingham Heart Study

Nicole L. Spartano, PhD; Kendra L. Davis-Plourde, M
Charles DeCarli, MD; Joanne M. Murabito, MD, ScM

NIH National Institute on Aging

Español

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Home › News & Events › Strong association shown between being sedentary and dementia risk

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Research Highlights

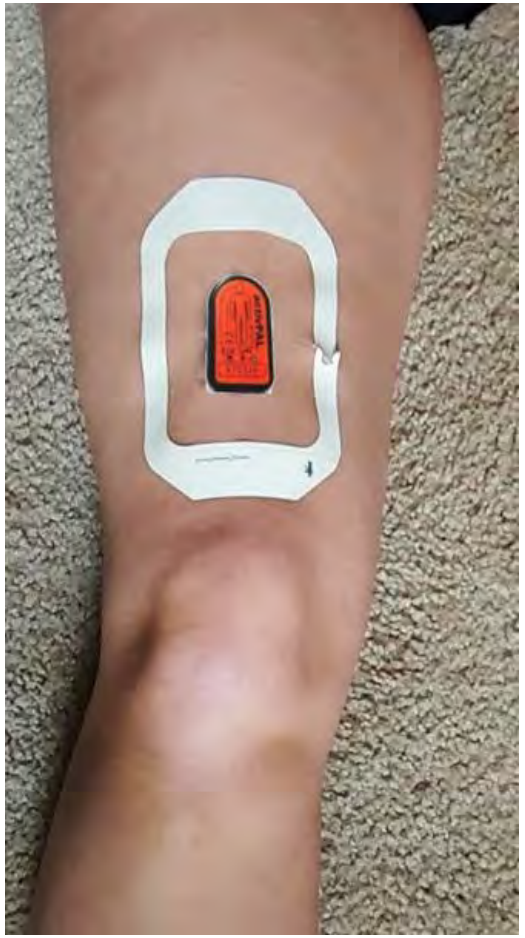
RESEARCH HIGHLIGHTS

Strong association shown between being sedentary and dementia risk

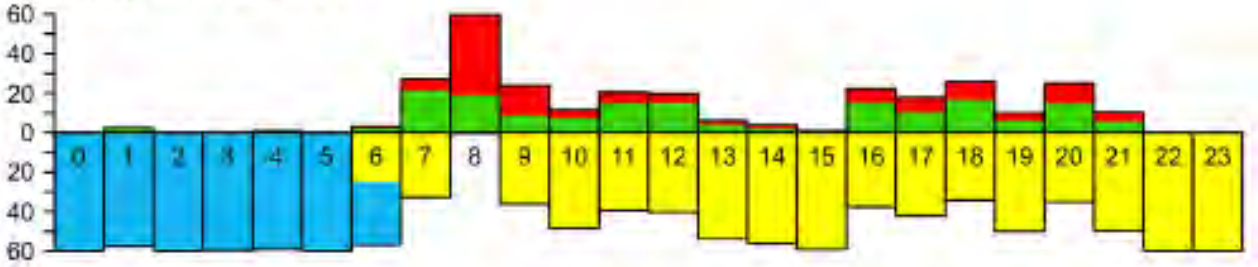
October 26, 2023

Physical Activity | Behavioral & Social Research | Dementias

Our movement activities and cognitive function fluctuate within and across days, and our daily sedentary behaviors are mostly spontaneous

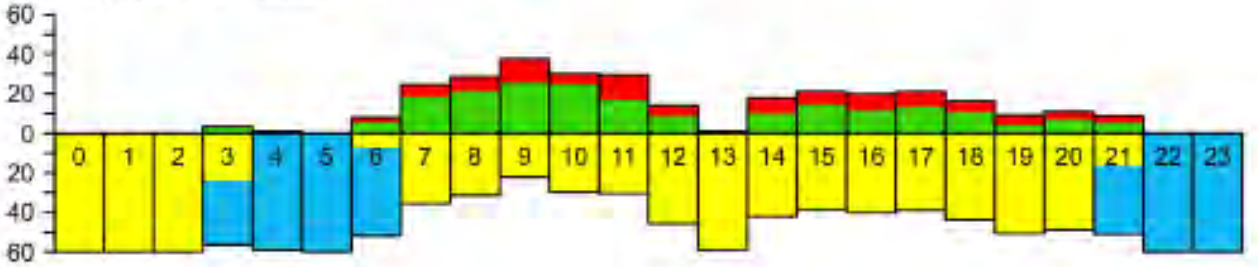


Saturday 25th Jun 2022



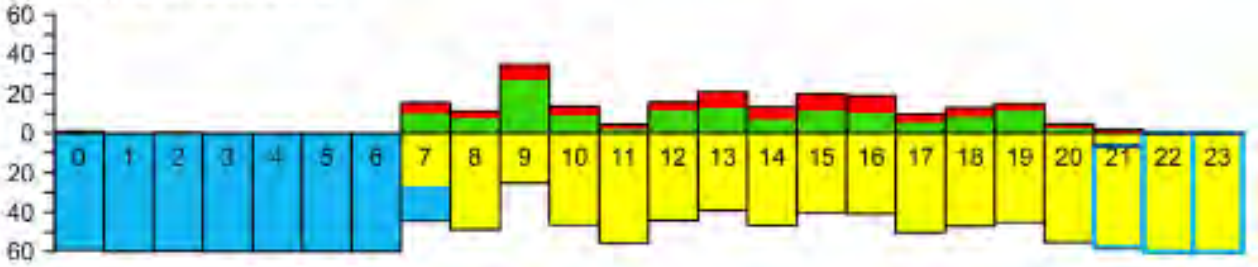
Steps
10558
Sit to Stands
77
Activity Score
34.54 MET.h

Sunday 26th Jun 2022



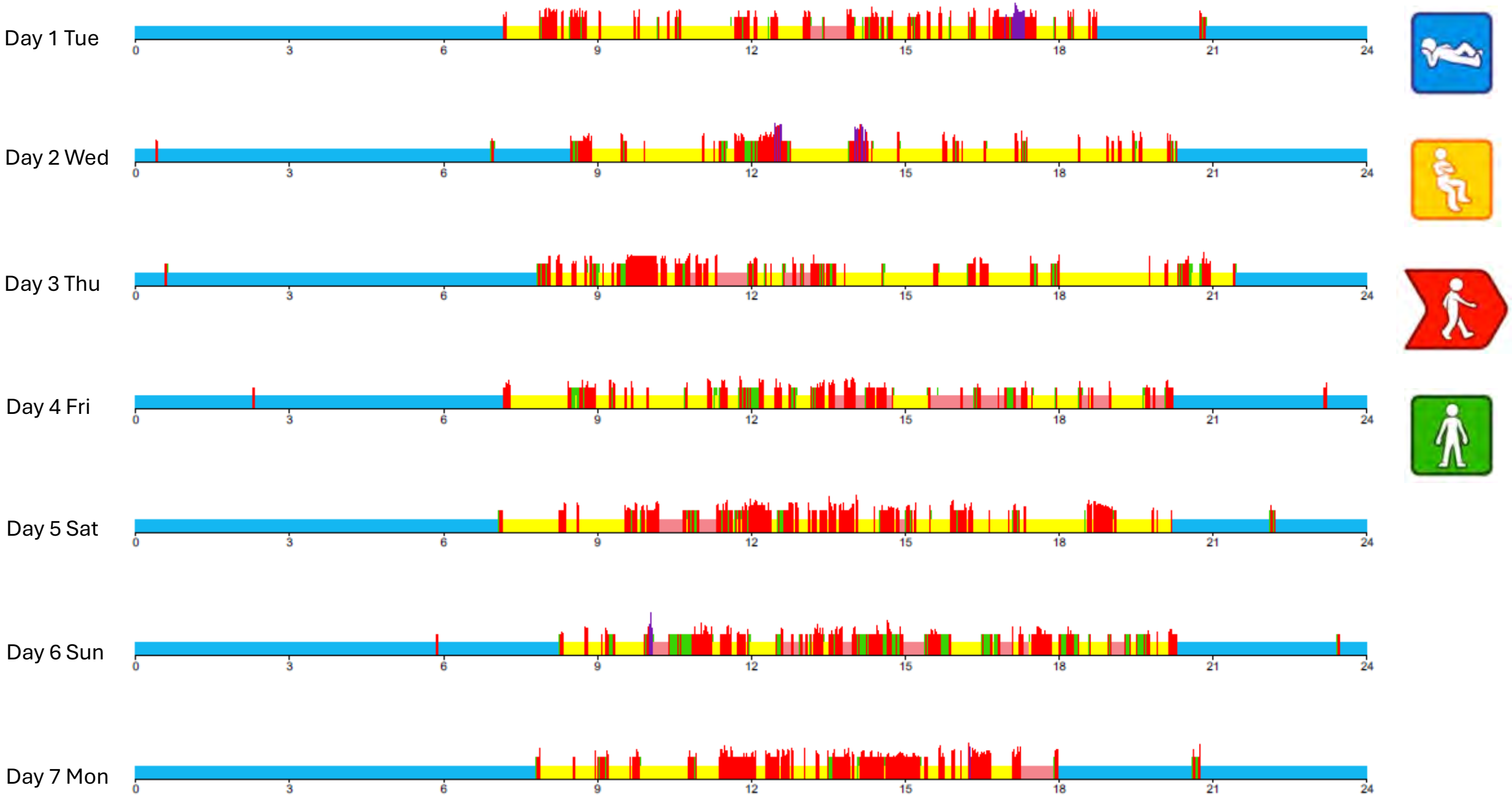
Steps
7804
Sit to Stands
84
Activity Score
33.58 MET.h

Monday 27th Jun 2022



Steps
5524
Sit to Stands
81
Activity Score
32.53 MET.h

PAL Technologies Ltd



PALtechnologies Ltd

Average time spent in each movement behavior within the 60-min time window

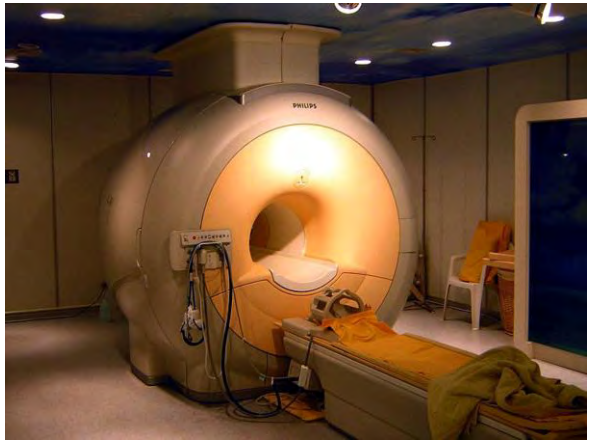
Mean=
38.6 ± 16.4
mins
(65%)

Mean =
12.9 ± 12.1
mins
(22%)

Mean =
5.52 ± 6.1
mins
(9%)

Energy Expenditure

Assessing cognitive outcome in everyday contexts



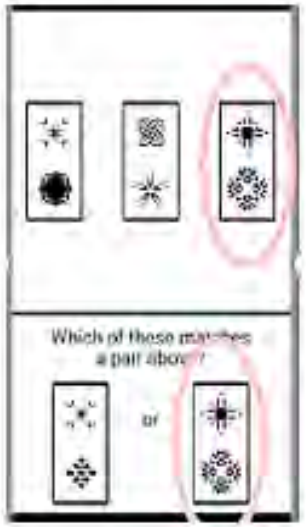
- In-lab cognitive assessments are time- and resource-consuming
- Not suitable for administrating repeatedly in naturalistic settings
- May not best represent cognition required to deal with everyday cognitively - demanding tasks (*ecological validity*)

Image credit: assistinghands.com

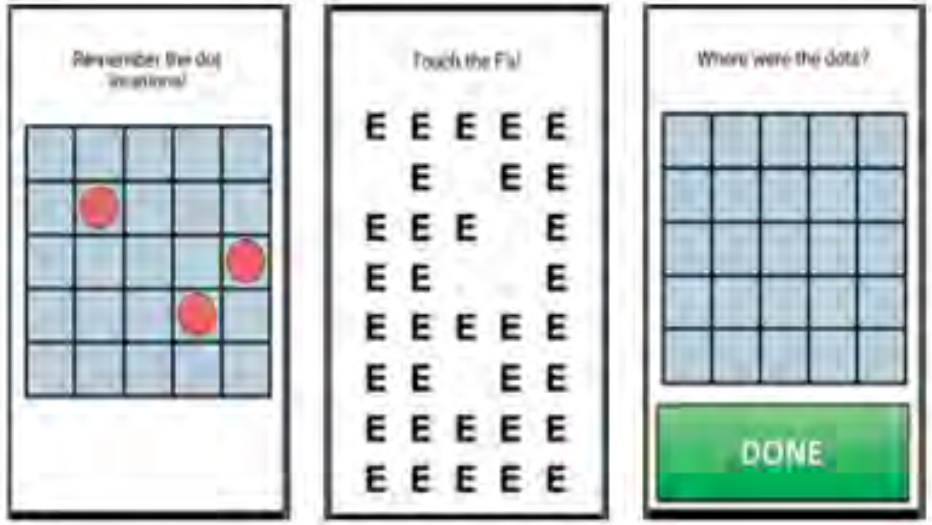
Utilize NIH-funded mobile tool to study performance-based cognition in everyday life

Ambulatory Methods for Measuring Cognitive Change (the M2C2 App)

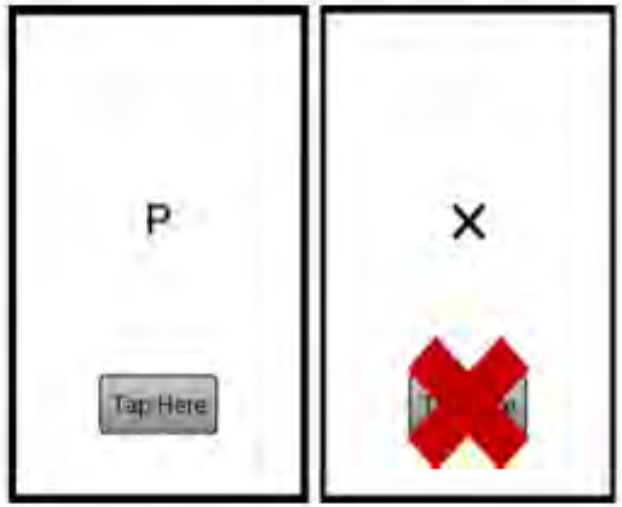
Symbol Search
(18 trials)



Grid Memory
(3 trials)



Letter Go/No-Go
(24 trials)



Subjective Cognition
(2 items)

Processing speed

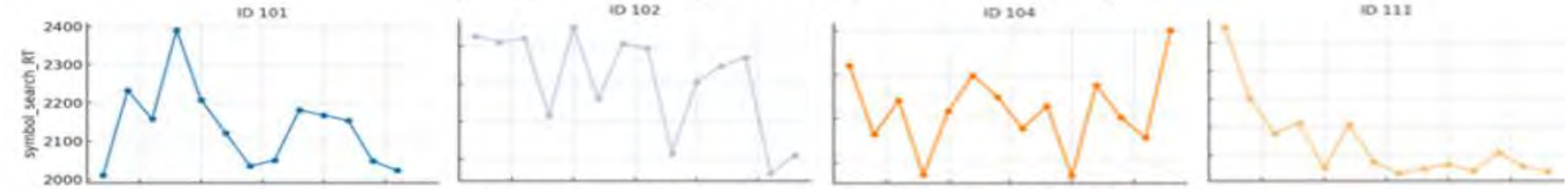
Visuospatial working memory

Inhibitory control

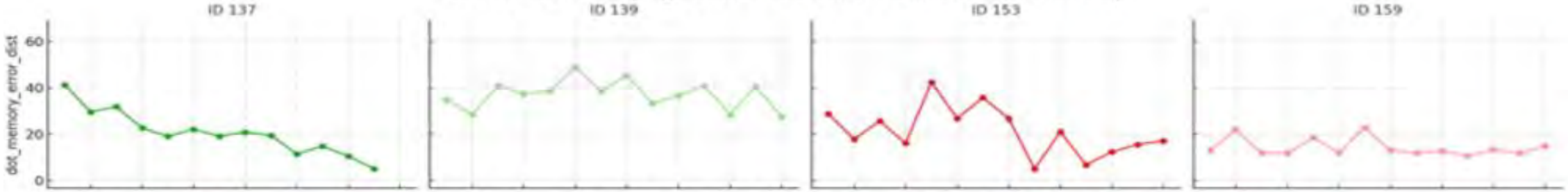
Self-report rating

(Penn State Center for Healthy Aging - U2CAG060408; PI: Sliwinski)

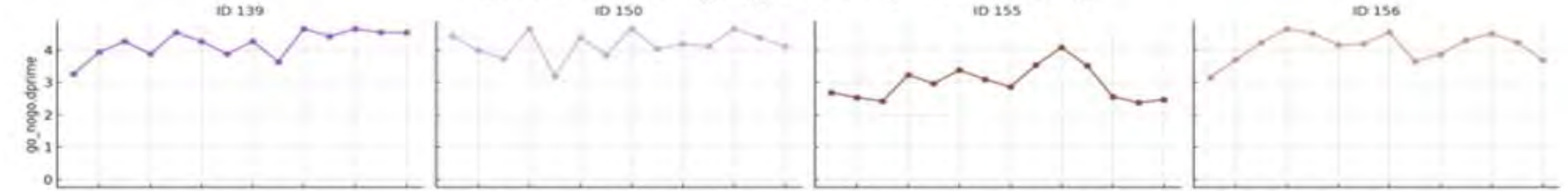
Symbol Search (y axis: response time [ms])



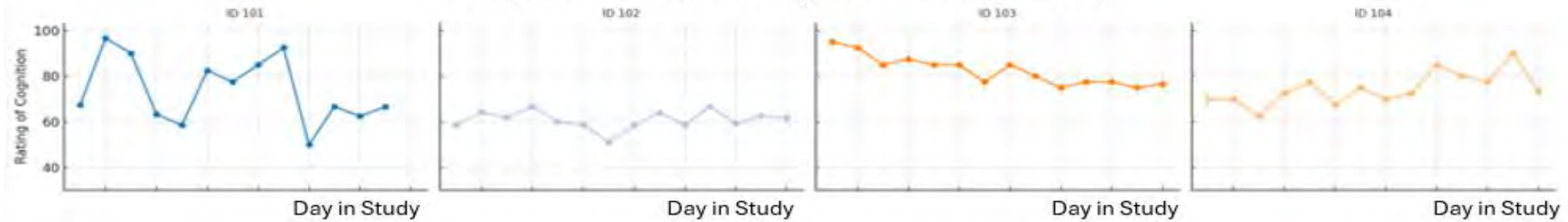
Grid Memory (y axis: sum of error distance)



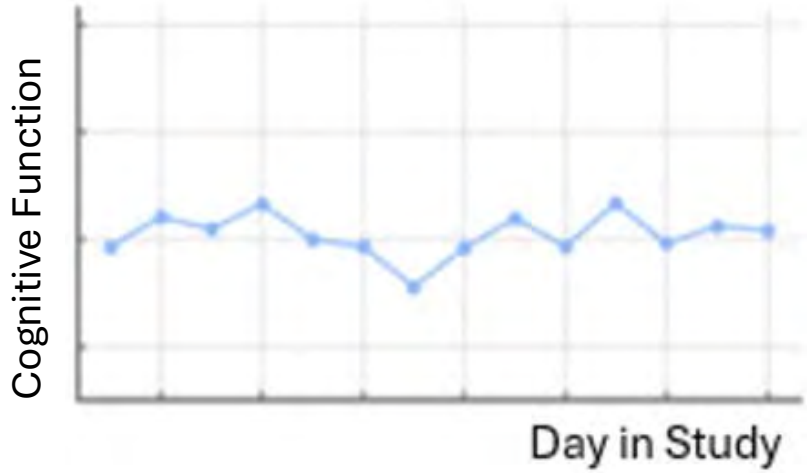
Letter Go-No-go (y axis: d prime score)

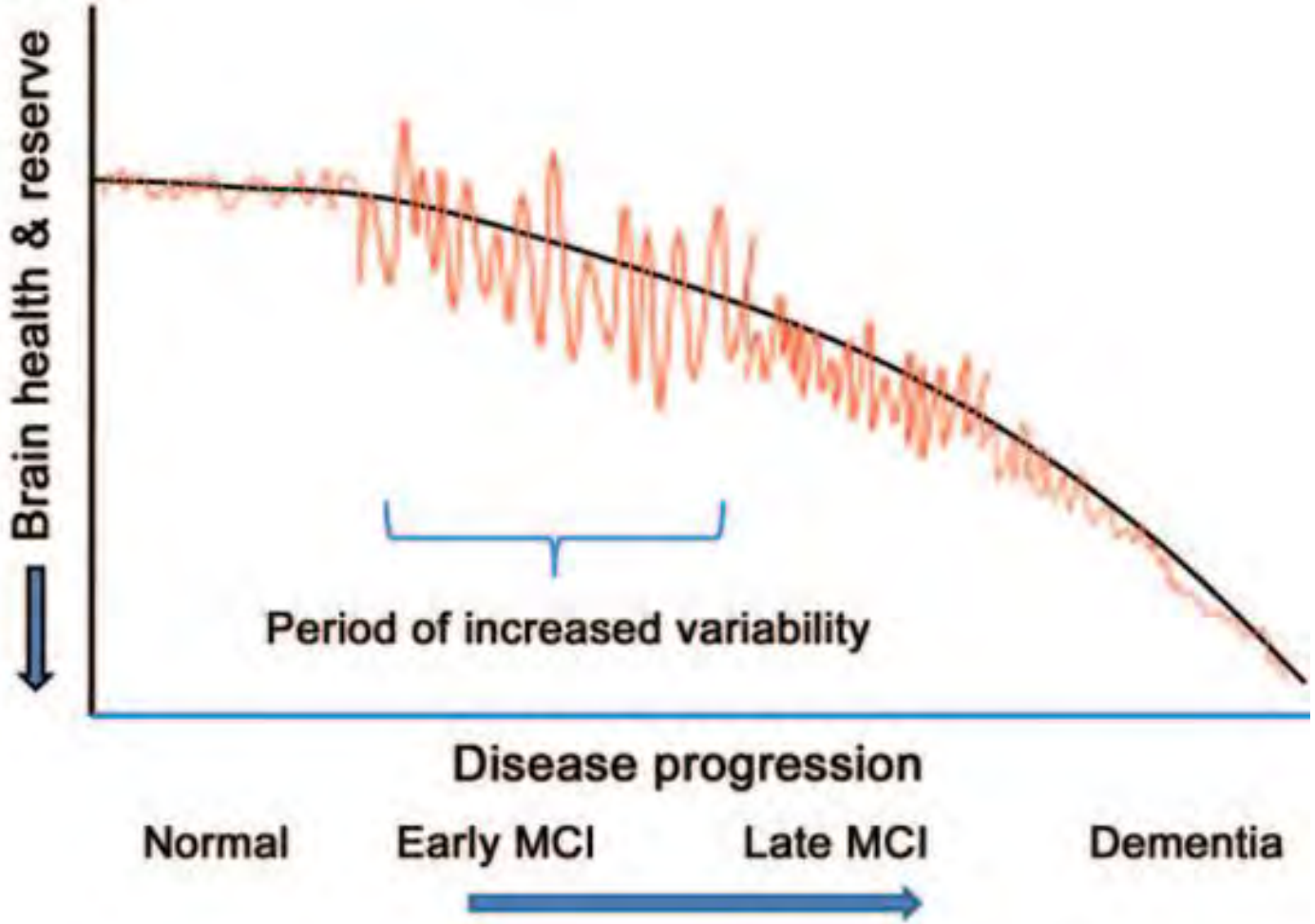


Subjective Cognition (y axis: rating score)



Beyond the mean levels, higher instability (variations) of cognitive function represents an early signal of cognitive decline.





Dodge et al. 2012

Within-Individual Variation in Cognitive Performance Is Not Noise: Why and How Cognitive Assessments Should Examine Within-Person Performance

Arabella Charlotte Vaughan and Damian Patrick Birney *

Neuropsychology
2007, Vol. 21, No. 4, 401–411

0894-4105/07/$12.00 DOI: 10.1037/0894-4105.

Implications of Within-Person Variability in Cognitive and Neuropsychological Functioning for the Interpretation of Change

Timothy A. Salthouse
University of Virginia

Neuropsychology
2010, Vol. 24, No. 6, 731–741

0894-4105/10/$12.00 DOI: 10.1037/a0019802

Both Reaction Time and Accuracy Measures of Intraindividual Variability Predict Cognitive Performance in Alzheimer's Disease

Björn U. Christ[1], Marc I. Combrinck[2] and Kevin G. F. Thomas[1]*

[1] Applied Cognitive Science and Experimental Neuropsychology Team Laboratory, Department of Psychology, University of Cape Town, Cape Town, South Africa, [2] Division of Geriatric Medicine, Groote Schuur Hospital, Department of Medicine, University of Cape Town, Cape Town, South Africa

Intraindividual Variability in Reaction Time Predicts Cognitive Outcomes 5 Years Later

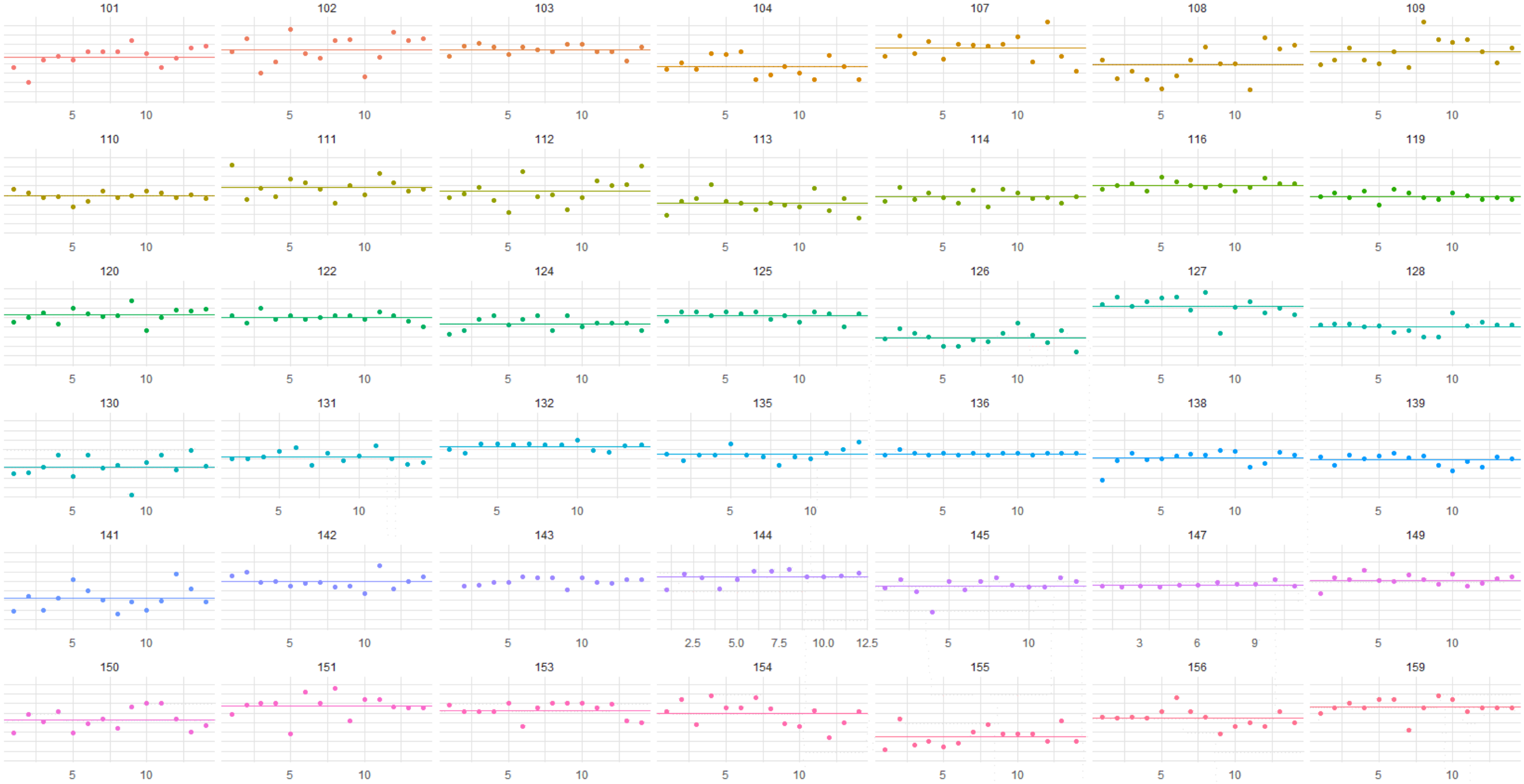
Allison A. M. Bielak
Australian National University

David F. Hultsch, Esther Strauss,
Stuart W. S. MacDonald, and Michael A. Hunter
University of Victoria

Reaction Times and Performance Variability in Normal Aging, Mild Cognitive Impairment, and Alzheimer's Disease

Ellen Gorus, MSc, PhD, Rudi De Raedt, MSc, PhD,
Margareta Lambert, MD, Jean-Claude Lemper, MD, and
Tony Mets, MD, PhD

Considering both mean levels and degree of instability of cognition



Can we observe the time sensitive associations between lifestyle physical activity, sedentary time, and cognitive outcomes in the contexts of older adults' daily lives?

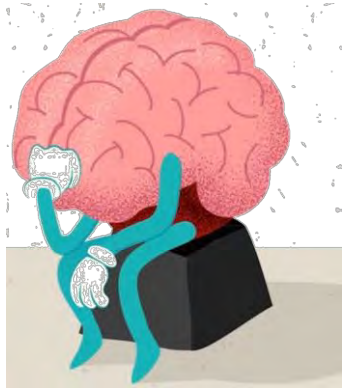
Daily lifestyle physical activity levels

Daily sedentary time

Daily Cognitive function

Mean (overall) levels

Instability (variations)



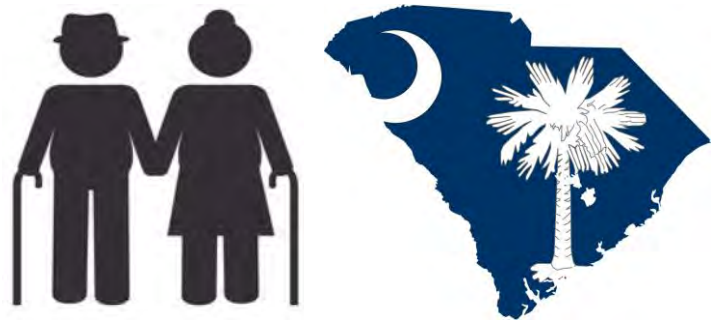
Contribute to research on this topic beyond the focus on population-level association between physical activity and brain health

- *More active older adults tend to have better mental and cognitive health in the general public*

?

Can we observe this in older adults' daily life

Participants

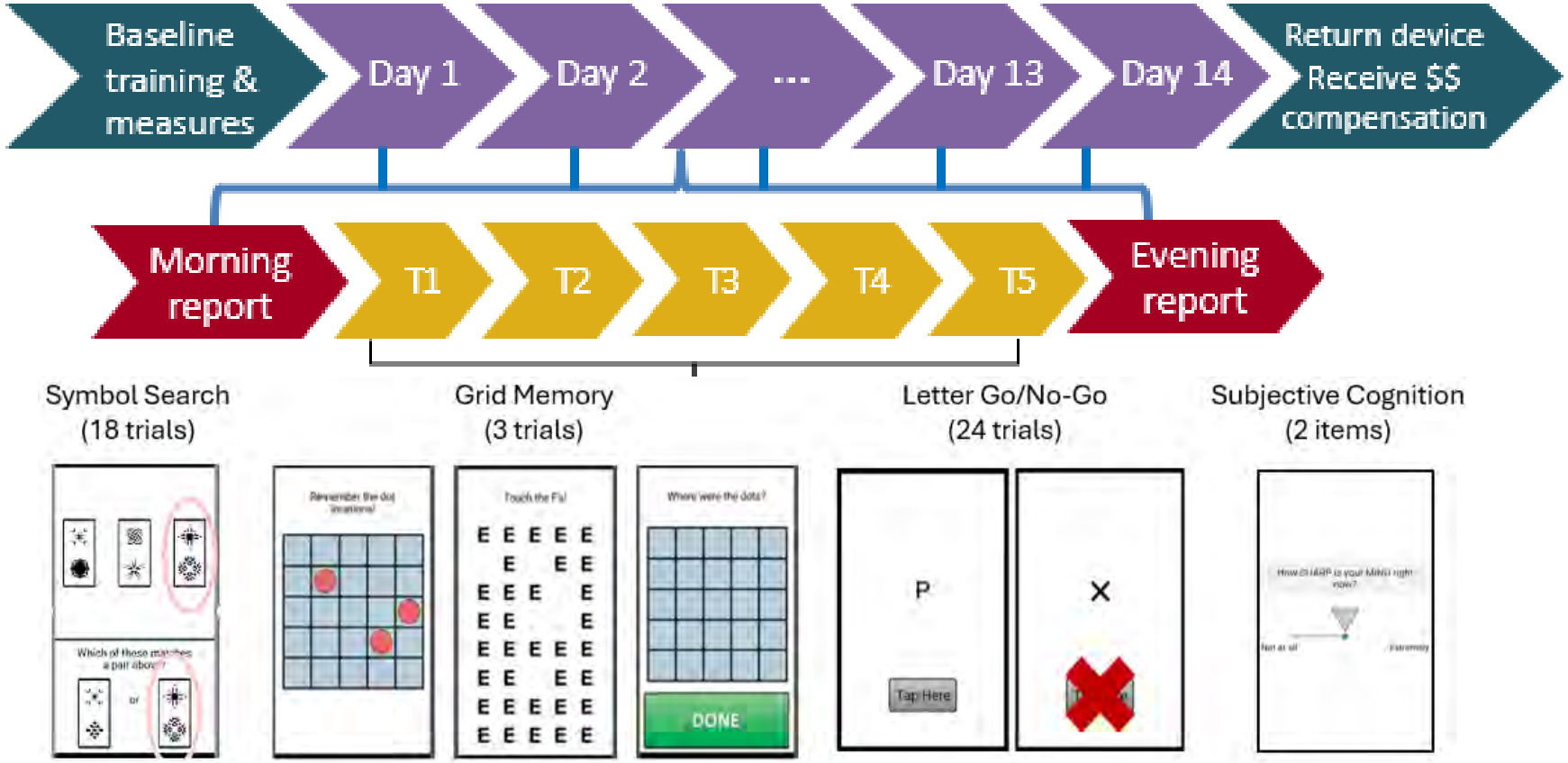


Inclusion criteria:

- Older adults with elevated risk of developing neuropsychological diseases
- Can walk independently without other person's assistance

Demographics (n=96)	Mean, SD,%
Age (Mean, SD)	68.5 ±7.04
Males (n, %)	34 (37.8%)
BMI (Mean, SD)	27.5 ± 5.50
Total observations	4,691
Mean observations/person-day	3.76 ±1.08

Day of Week	%	n of Cog. Tests
Monday	13.9%	655
Tuesday	14.6%	687
Wednesday	14.6%	688
Thursday	14.4%	675
Friday	14.3%	671
Saturday	14.0%	656
Sunday	14.1%	659



Data analysis

- **Mixed-effects location scale models** estimated whether the between-person differences and the within-person changes of daily lifestyle physical activity and sedentary time explained the mean level and the degree of variability from each cognitive outcome.
- **Covariates:** demographics, day of the week, daily accelerometer valid wear time.

Findings of **between-person differences**

(*i.e., overall lifestyle physical activity/sedentary levels*)

and **mean** cognitive function

Between-person differences in lifestyle physical activity (LPA) and **mean-level** cognition

Overall daily LPA minutes

N.S.

N.S.

N.S.

b= 1.77*

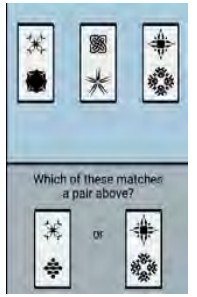
Response time (ms)

Mean error distance

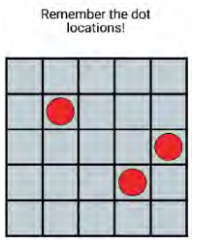
Number of accurate trials

Self-reported cognition

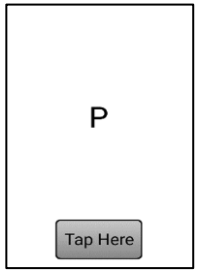
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

*p<.05

Between-person differences in daily steps and mean-level cognition

Overall daily step counts

b= -0.05**

b= -1.07*

N.S.

N.S.

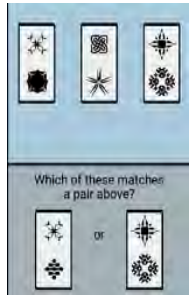
Response time (ms)

Mean error distance

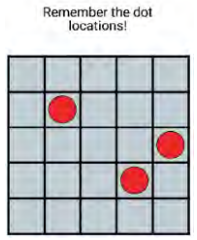
Number of accurate trials

Self-reported cognition

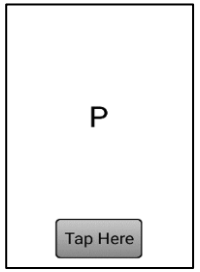
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

*p<.05, **p<.01

Between-person differences in daily sedentary time and mean-level cognition

Daily Sedentary time

N.S.

N.S.

N.S.

N.S.

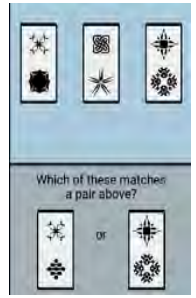
Response time (ms)

Mean error distance

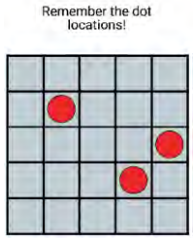
Number of accurate trials

Self-reported cognition

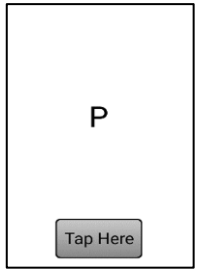
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for demographics and time trend.

Findings of **within-person changes**

(*i.e., being more or less active/sedentary on a given day*)

and **mean** cognitive function

Within-person changes of light physical activity (LPA) and mean-level cognition

Relatively more daily LPA time on a given day

N.S.

N.S.

N.S.

b= 0.39**

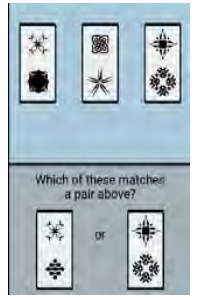
Response time (ms)

Mean error distance

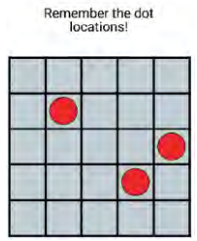
Number of accurate trials

Self-reported cognition

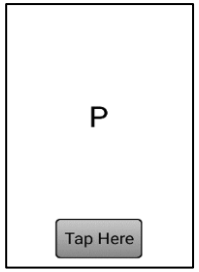
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

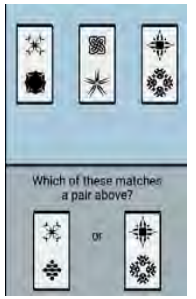
Model controlled for age, sex, day of week, and valid wear time

**p<.01

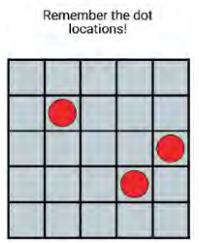
Within-person changes of daily steps and mean-level cognition

Relatively more steps on a given day

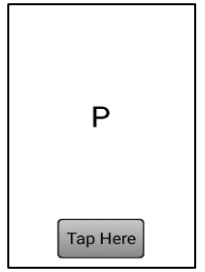
N.S. → Response time (ms) → Symbol Search Test



N.S. → Mean error distance → Dot Memory Test



N.S. → Number of accurate trials → Go-NoGo Test



b= 0.19* → Self-reported cognition → Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

*p<.05

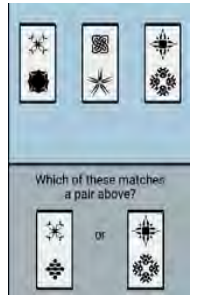
Within-person changes of daily sedentary time and mean-level cognition

Relatively more sedentary time on a given day

N.S.

Response time (ms)

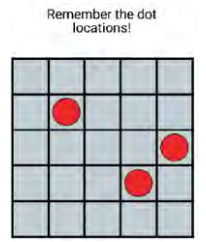
Symbol Search Test



N.S.

Mean error distance

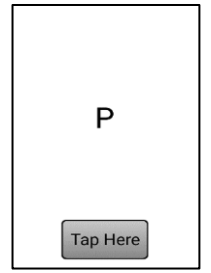
Dot Memory Test



N.S.

Number of accurate trials

Go-NoGo Test



t= -0.39**

Self-reported cognition

Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

**p<.01

Findings of **between-person differences**

(*i.e., overall lifestyle physical activity/sedentary levels*)

and **instability** of cognitive function

Between-person differences in daily light physical activity (LPA) and instability of cognition

Overall daily LPA minutes

b= -0.11**

b= -0.07*

N.S.

N.S.

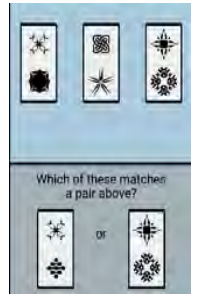
Response time (ms)

Mean error distance

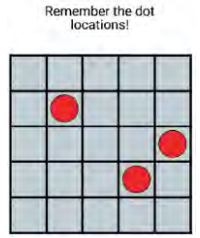
Number of accurate trials

Self-reported cognition

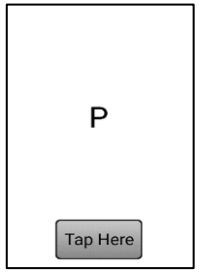
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

*p<.05, **p<.001

Between-person differences in daily steps and instability of cognition

Overall daily step counts

b= -0.08***

b= -0.04**

N.S.

b= -0.03*

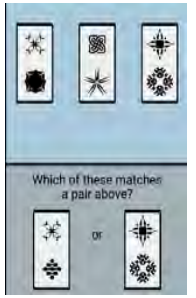
Response time (ms)

Mean error distance

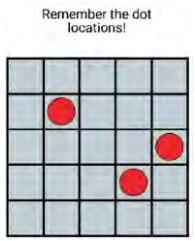
Number of accurate trials

Self-reported cognition

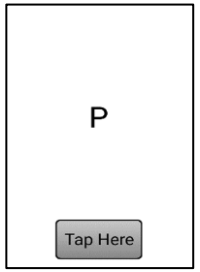
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

*p<.05, **p<.01, ***p<.001

Between-person differences in daily sedentary time and instability of cognition

Overall daily Sedentary time

N.S.

N.S.

b= 0.04*

N.S.

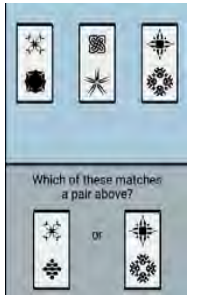
Response time (ms)

Mean error distance

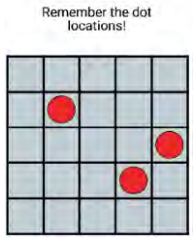
Number of accurate trials

Self-reported cognition

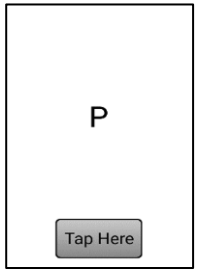
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for demographics and time trend.
*p<.05

Findings of within-person changes

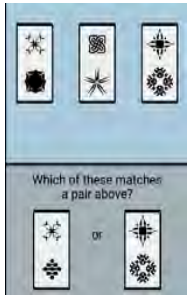
(*i.e., being more or less active/sedentary on a given day*)

and **instability** of cognitive function

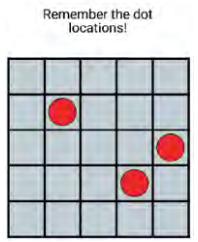
Within-person changes of light physical activity (LPA) and instability of cognition

Relatively more daily LPA on a given day

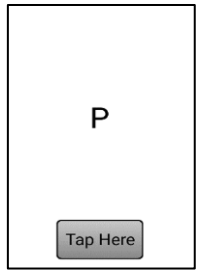
N.S. → Response time (ms) — Symbol Search Test



N.S. → Mean error distance — Dot Memory Test



N.S. → Number of accurate trials — Go-NoGo Test



b= -0.06* → Self-reported cognition — Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

*p<.05

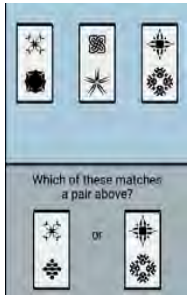
Within-person changes of daily steps and instability of cognition

Relatively more daily steps on a given day

N.S.

Response time (ms)

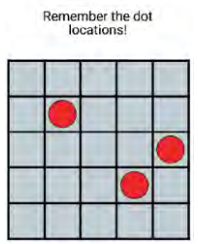
Symbol Search Test



N.S.

Mean error distance

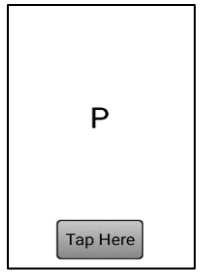
Dot Memory Test



N.S.

Number of accurate trials

Go-NoGo Test



N.S.

Self-reported cognition

Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

Within-person changes of daily sedentary time and instability of cognition

Relatively more sedentary time on a given day

b= 0.11***

b= 0.07***

b= 0.09***

b= 0.07***

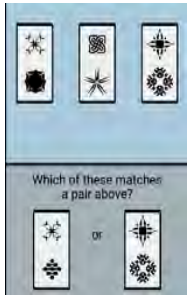
Response time (ms)

Mean error distance

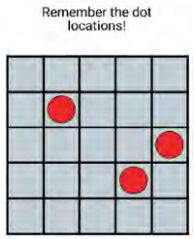
Number of accurate trials

Self-reported cognition

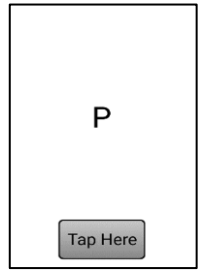
Symbol Search Test



Dot Memory Test



Go-NoGo Test



Subjective Rating

Model controlled for age, sex, day of week, and valid wear time

***p<.001

Summary

- Lifestyle physical activity (including steps) and sedentary time are linked to cognitive function both at the mean and variability levels in older adults.
- **For LPA and Steps:** more evidence on the between-person associations compared to the within-person changes
  - *sustained and regular engagement in daily activity matters more for cognitive health than short-term increases*
- **For Sedentary Time:** older adults exhibited more variability of cognitive function on days when they spent more sedentary time

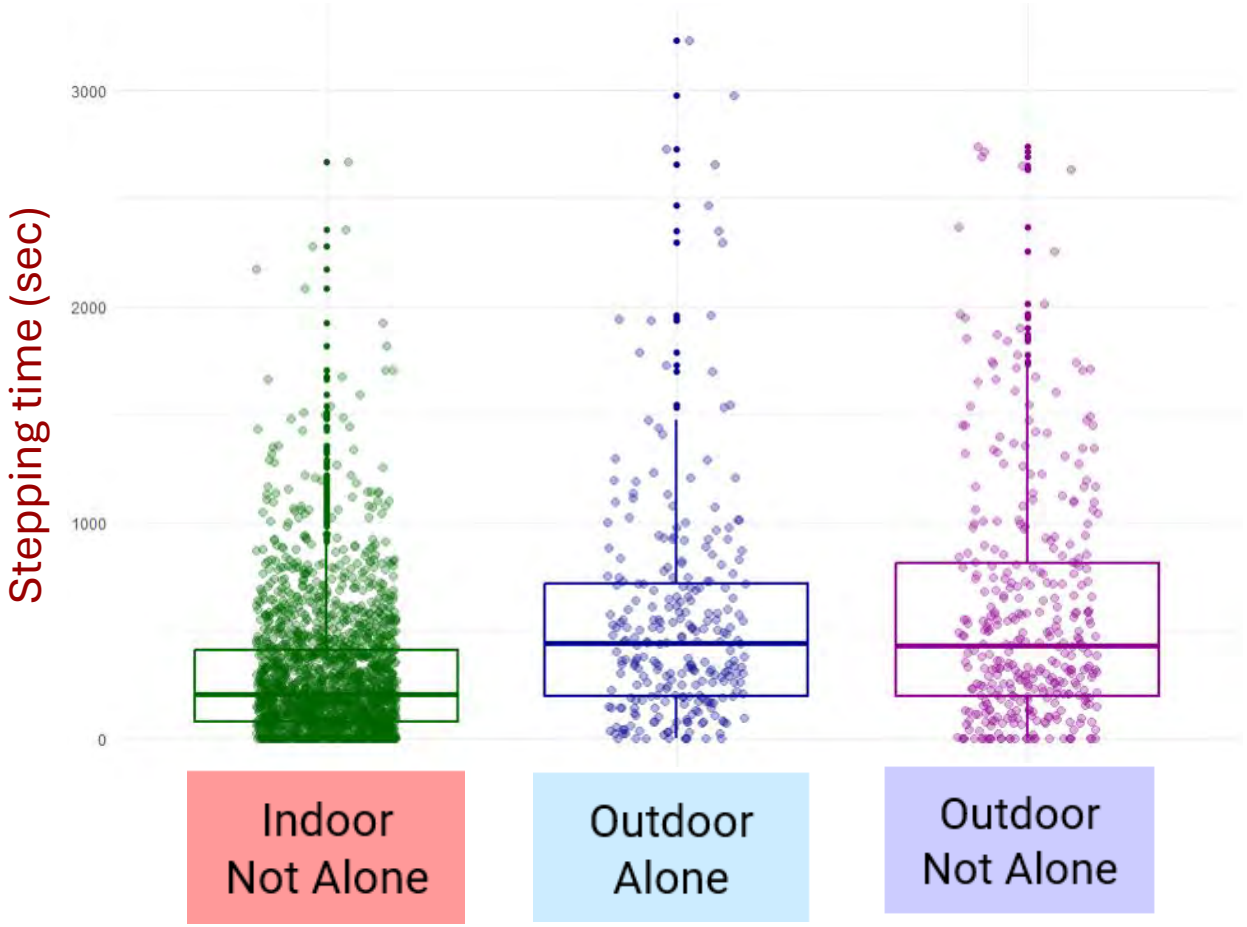
  → observed across four cognitive tests.

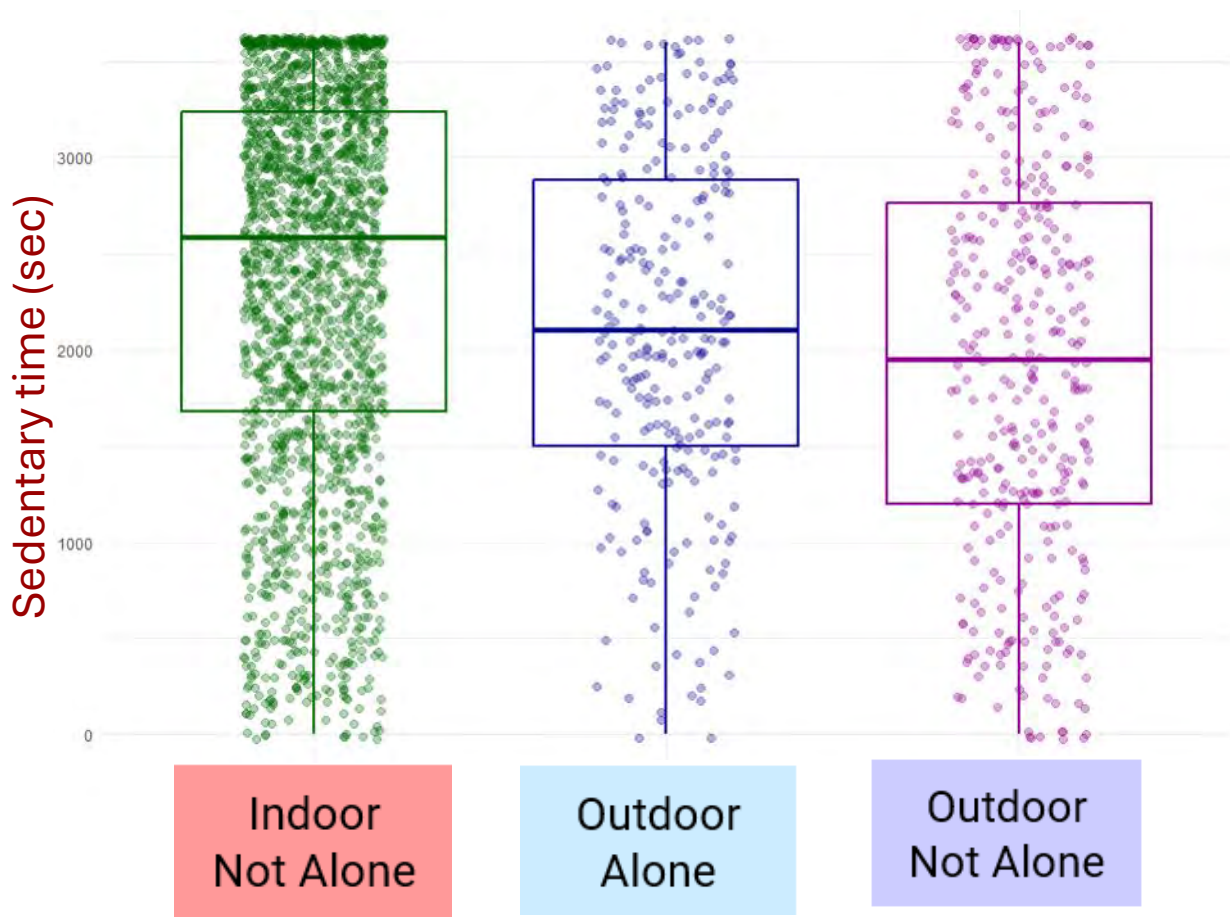
Future directions

- Include more representative older adults.
- Access lifestyle activity and cognition for a longer study period.
- Apply other direct measures of cognitive assessments.
- Making the most of real-time data capturing techniques to understand lifestyle movement behaviors in various contexts of daily life.

Context Matters!

In what context were the steps and sitting time accumulated?





Future directions

- Include more representative older adults.
- Access lifestyle activity and cognition for a longer study period.
- Apply other direct measures of cognitive assessments.
- Making the most of real-time data capturing techniques to understand lifestyle movement behaviors in various contexts of daily life.

Conclusion

- Mobile technology helps uncover the temporal and dynamic processes underlying daily cognitive function

  → More studies in this area can inform scalable behavioral preventive strategies to sustain healthy brain aging in older adults' everyday life.

Funding:

- USC Office for the Study of Aging Pilot Fund
- USC ASPIRE-I Seed Grant

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- Jonathan Hakun, PhD
- Rahul Ghosal, PhD

Participants!

ECHO LAB

Please also check out the posters from our lab!

For more information: cy11@mailbox.sc.edu

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Advance access publication: 27 June 2025
Original Research Article

Daily Movement Activities Are Associated With Within-Person Instability of Cognitive Function in Older Adults: Evidence From an Ambulatory Assessment Study

Chih-Hsiang Yang, PhD,[1,*] Donald Hedeker, PhD,[2] Jongwon Lee, MPH,[1] Halle Prine, MS,[1] Donna Coffman, PhD,[3] Jingkai Wei, PhD, MSPH,[4] and Jonathan George Hakun, PhD[5,6,]

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[2]Department of Public Health Sciences, Biological Sciences Division, The University of Chicago, Chicago, Illinois, USA.
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[4]Department of Family and Community Medicine, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, Texas, USA.
[5]Department of Neurology, College of Medicine, The Pennsylvania State University, Hershey, Pennsylvania, USA.
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Decision Editor: Michelle Putnam, PhD, MGS, FGSA

Original Paper

Ultra-brief Assessment of Working Memory Capacity: Ambulatory Assessment Study Using Smartphones

Jonathan G Hakun[1,2,3,4], PhD; Nelson A Roque[3,5], PhD; Courtney R Gerver[2], PhD; Eric S Cerino[3,6], PhD

Assessment. 2018 January ; 25(1): 14–30. doi:10.1177/1073191116643164.

Mobile Monitoring of Cognitive Change (M2C2): High-Frequency Assessments and Protocol Reporting Guidelines

Jonathan G. Hakun[a,b,c,d], Daniel B. Elbich[a], Nelson A. Roque[d,e], Scott T. Yabiku[f,g], & Martin J. Sliwinski[d,e]

Reliability and Validity of Ambulatory Cognitive Assessments

Martin J. Sliwinski[1], **Jacqueline A. Mogle**[2], **Jinshil Hyun**[1], **Elizabeth Munoz**[1], **Joshua M. Smyth**[3], and **Richard B. Lipton**[4]

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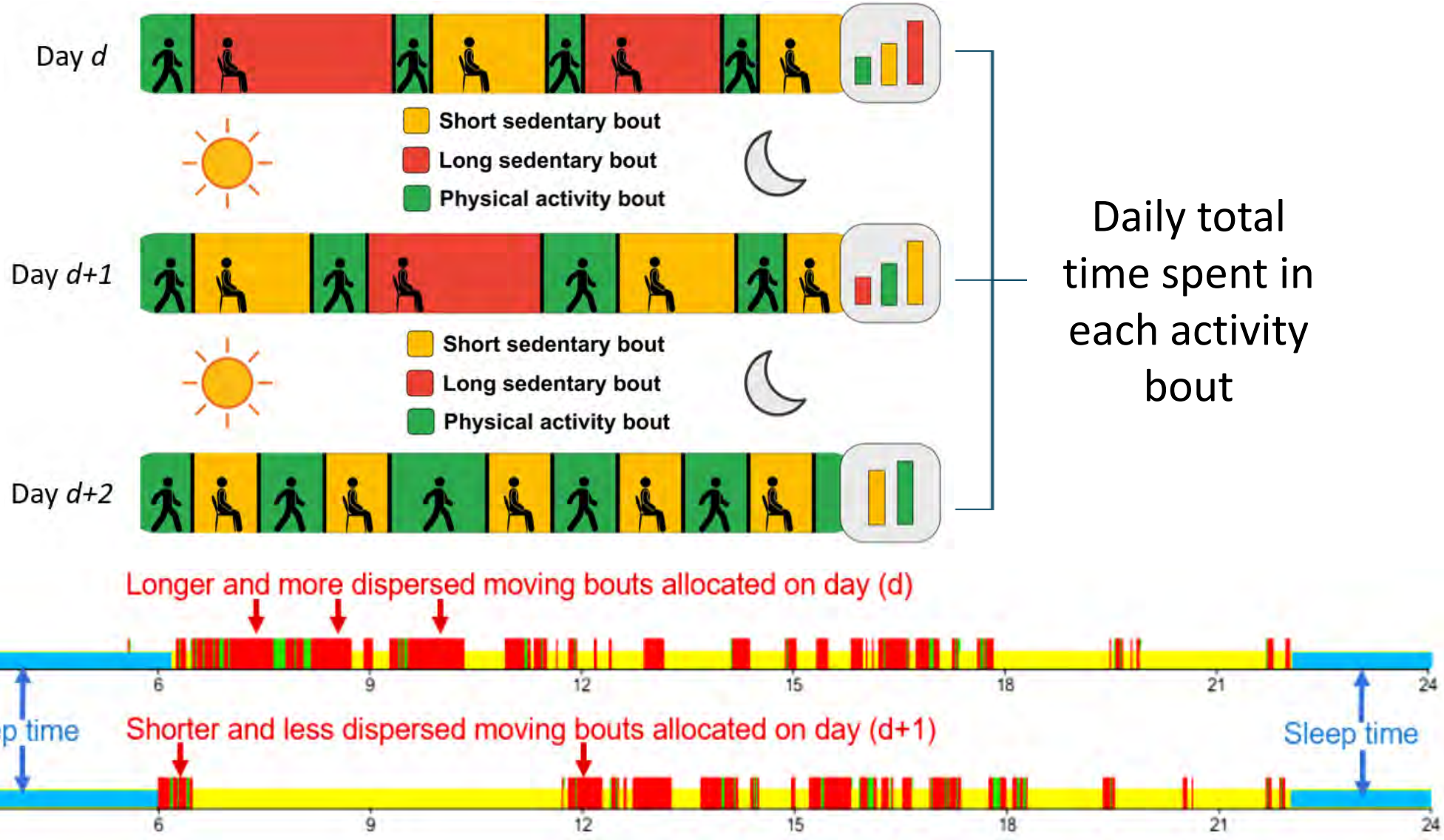
[2]College of Nursing and Center for Healthy Aging, Pennsylvania State University

[3]Department of Biobehavioral Health, Pennsylvania State University

[4]Department of Neurology, Department of Psychiatry and Behavioral Sciences, Department of Epidemiology and Population Health, Albert Einstein College of Medicine

(Penn State Center for Healthy Aging - U2CAG060408; PI: Sliwinski)

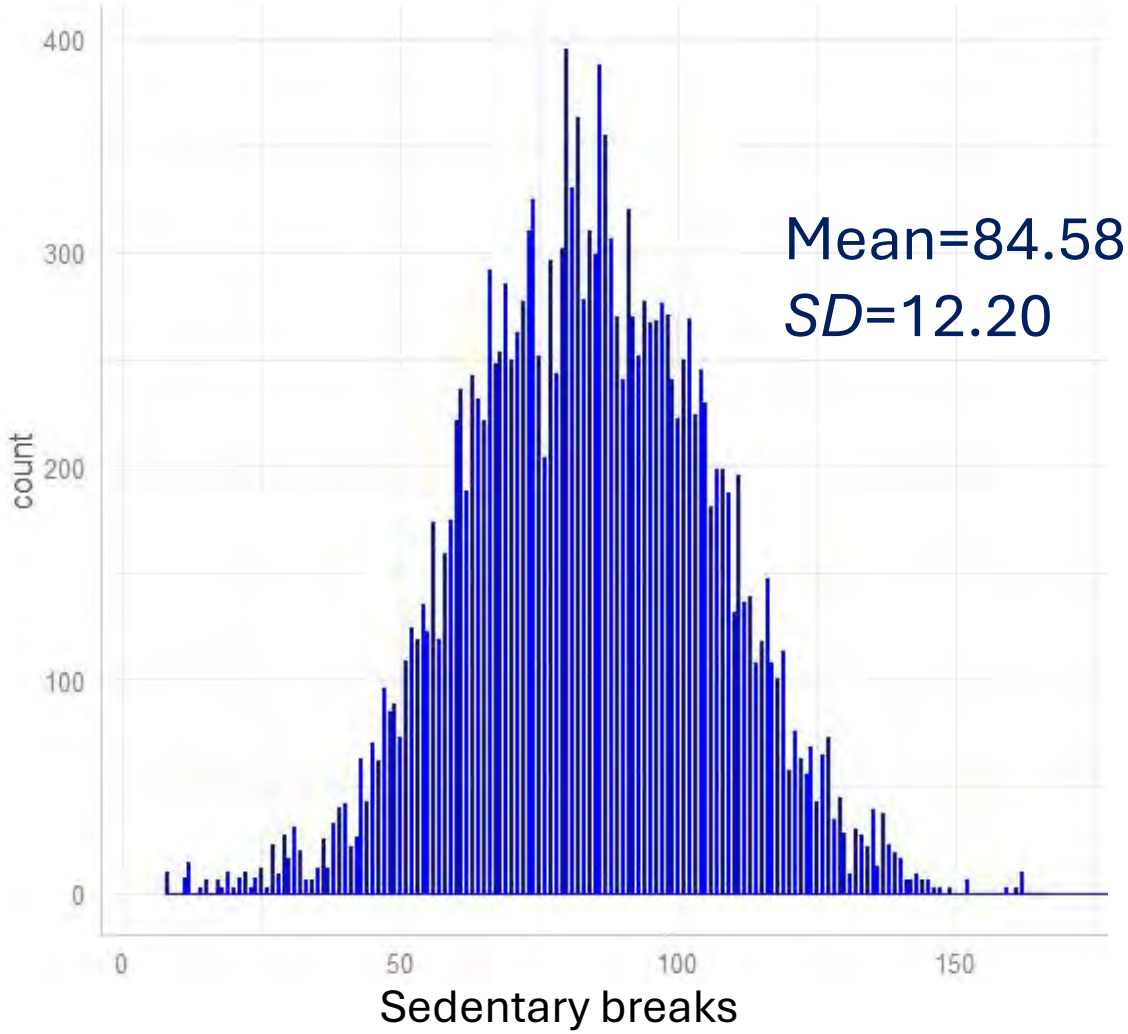
Next step – Pattern Matters



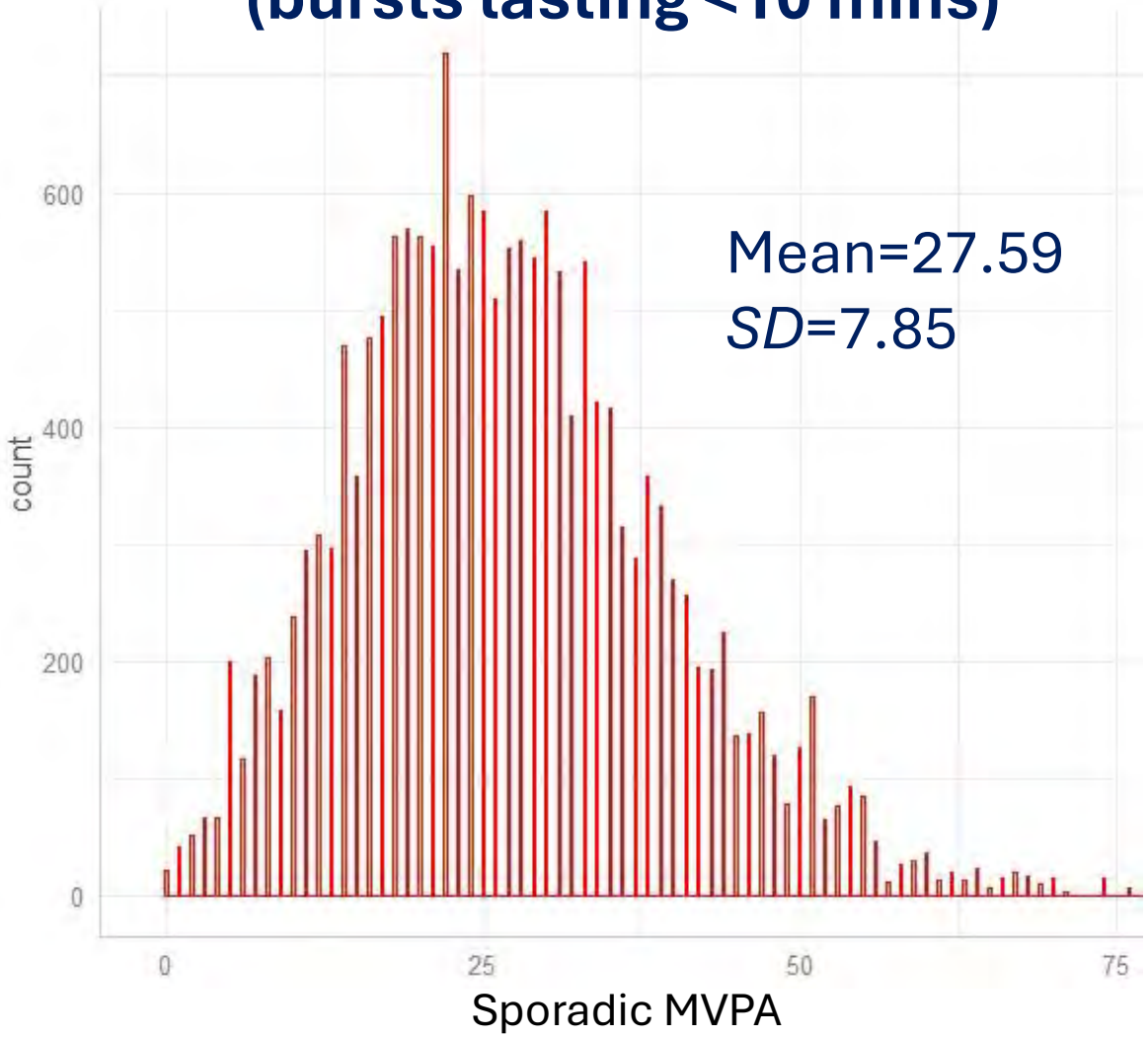
(R03AG087445; PI: Yang)

Two accelerometry-based activity outcomes

Daily sedentary breaks



Daily sporadic MVPA events (bursts lasting <10 mins)



THE COGNITIVE AND SOCIAL BENEFIT OF BOOK CLUBS

Jean Neils-Strunjas, PhD, CCC-SLP, Professor and Chair

Department of Communication Sciences and Disorders

UNIVERSITY OF South Carolina

Arnold School of Public Health

CAN MILD COGNITIVE IMPAIRMENT BE PREVENTED, REVERSED OR STABILIZED?

Yu et al. (2025) found that 74% older adults retained normal cognition and 79% with mild cognitive impairment were stable or reversed to normal cognition after 2 years.

Koepsell & Monsell (2012) found that 64% with mild cognitive impairment were stable and 16% reversed to normal cognition after 1 year.

Yu, et al. (2025); Koepsell, T. D., & Monsell, S. E. (2012)

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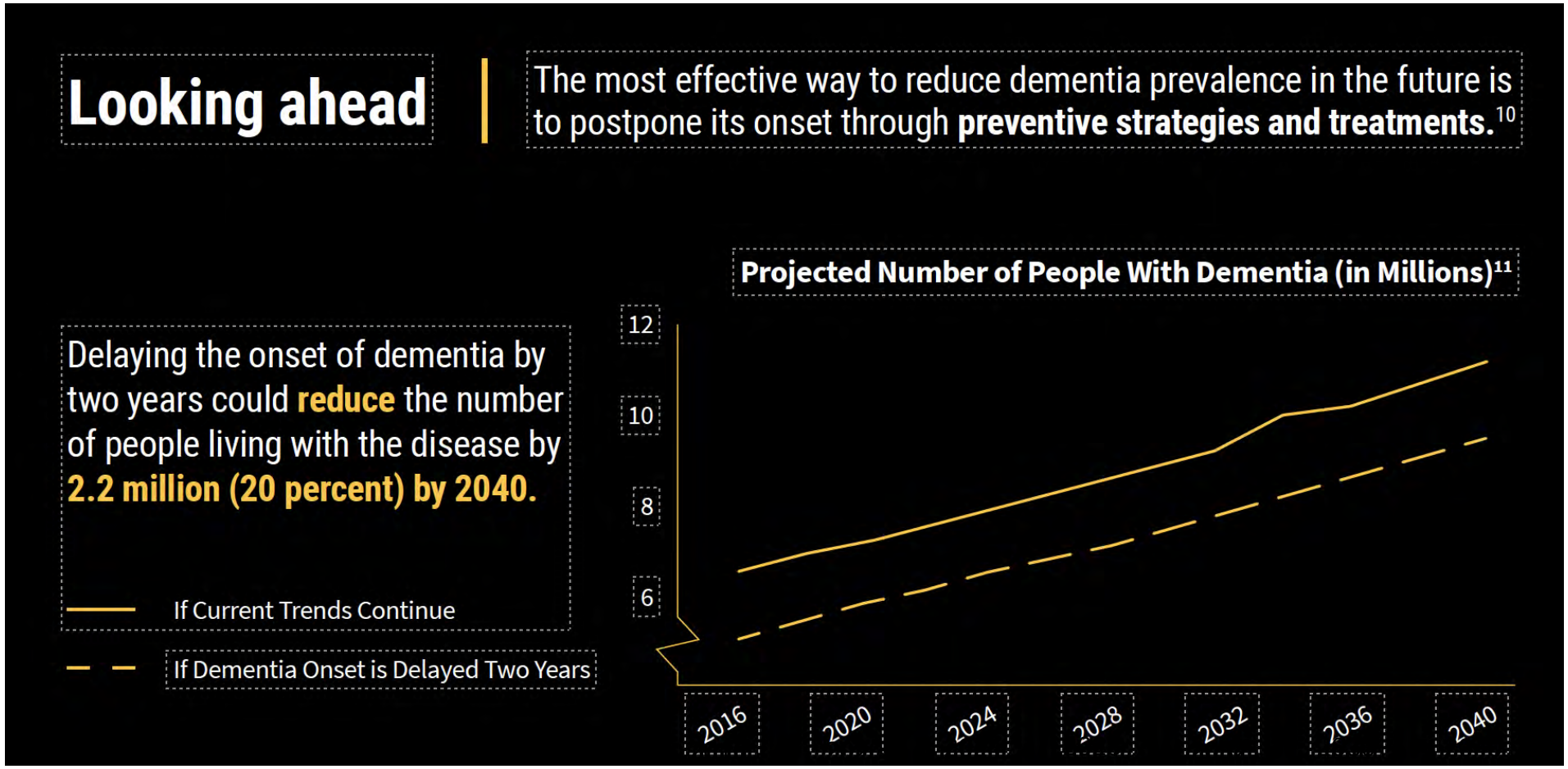
MODIFIABLE RISK FACTORS

Why they matter

UNIVERSITY OF
South Carolina

Arnold School of Public Health



HEALTH PROFESSIONALS CAN PROVIDE PREVENTATIVE STRATEGIES AND TREATMENT TO PEOPLE WITH MILD COGNITIVE IMPAIRMENT TO DECREASE RISK AND SLOW OR STOP PROGRESSION.

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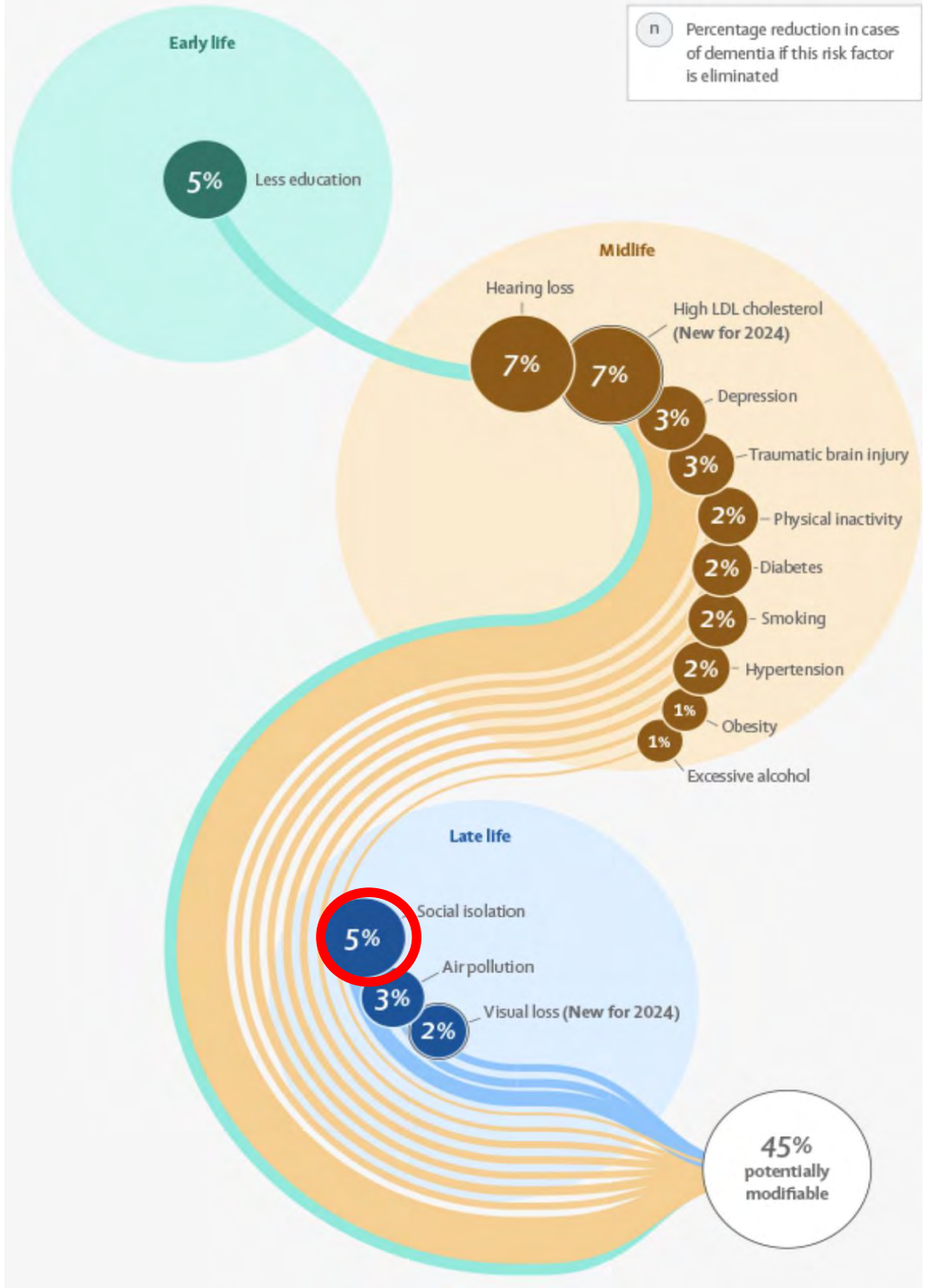
UNIVERSITY OF SOUTH CAROLINA

Everly, J., Plummer, J., Lohman, M., & Neils-Strunjas, J. (2023)

Reduce Risk Factors for Dementia



Life Stages Defined

Early life: ≤**18**

Midlife: **18-65**

Late life: **>65**

Livingston et al., 2024

UNIVERSITY OF South Carolina

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UNIVERSITY OF SOUTH CAROLINA

PROBLEM OF SOCIAL ISOLATION

- Older adults are at higher risk for social isolation because of widowhood, loss of friends, retirement, physical limitations, geographic relocation, and caregiving demands.

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Everly, J., Plummer, J., Lohman, M., & Neils-Strunjas, J. (2023)

THE ROLE OF SOCIAL ENGAGEMENT AND BOOK CLUBS

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BOOK CLUBS ARE POPULAR IN CONTEMPORARY AMERICAN SOCIETY

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Education is set earlier in life. However, lifelong learning is possible.

Older adults who engage in stimulating activities (e.g. discussion) were reported to experience better cognitive outcomes.

One study found that reading and writing were most impactful because they are novel and require active participation.

Chang, et al., 2021; Devanand et al., 2022; Karsazi, et al. 2024

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SOCIAL BOOK CLUBS MAY INCREASE COGNITIVE RESERVE

Individuals who are cognitively, socially, and intellectually active have shown to have higher levels of cognitive reserve, thus decreasing their risk of cognitive decline and dementia (Stern, 2012).

BOOK CLUBS STIMULATE:

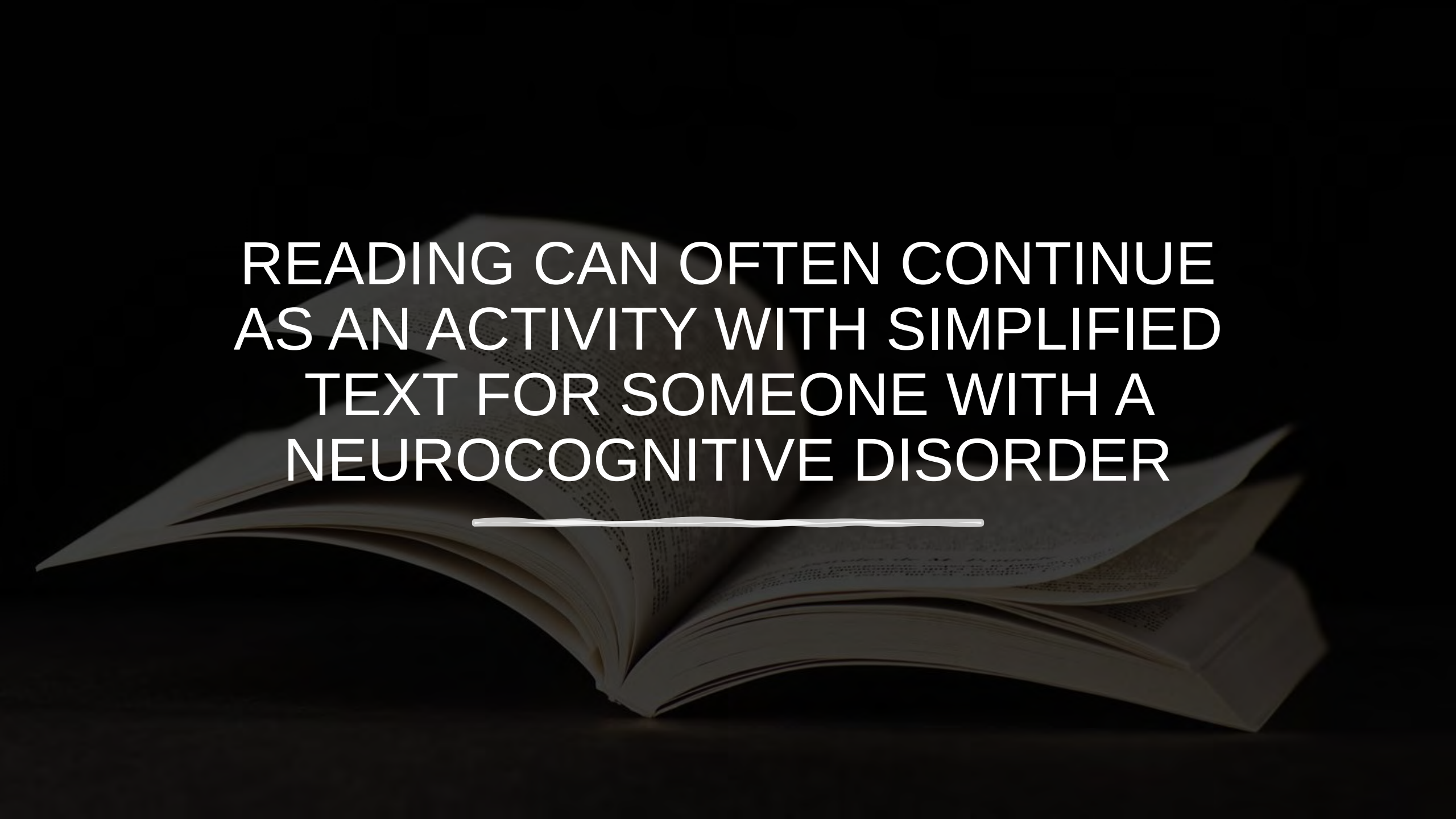
-SEMANTIC MEMORY

-EPISODIC MEMORY

-LANGUAGE COMPREHENSION

-VERBAL LANGUAGE

-CONVERSATION



READING CAN OFTEN CONTINUE AS AN ACTIVITY WITH SIMPLIFIED TEXT FOR SOMEONE WITH A NEUROCOGNITIVE DISORDER

One author wrote,

travel throws us into
a state of delight,
uncertainty and
self-discovery.

We travel to become
young fools again
and to get taken in.

These next few travel posters
may remind you of places
you have been

or they may start you dreaming
of faraway destinations.

Is there a place that you have
always dreamed of visiting?

Travel

AGING GRACEFULLY BOOK CLUBS

PURPOSE OF THE STUDY

The purpose of our pilot studies was to examine how weekly meetings in an intergenerational book club could affect older adults' subjective well-being and cognition.

We predicted that well-being and cognition would improve following participation in the book club.

OUR BOOK CLUBS INCLUDED INTERGENERATIONAL ENGAGEMENT

- community participation developed to provide resources and infrastructures that engage older adults and younger generations in innovative ways.

- research shows intergenerational programs are associated with a positive impact on social, mental, and physical health outcomes

(Krzeczkowska et al., 2021).

RESEARCH QUESTIONS

- Do senior book club members show change in cognition, wellbeing, and quality of life?
- Do book club participants experience positive emotions following their engagement?
- Can an intergenerational book club alter perceptions and attitudes between older adults and college students?
- What range of topics, particularly those related to social justice, emerge in intergenerational book club discussions?

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INTERGENERATIONAL PROGRAM DETAILS

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RECRUITMENT

- Older adult participants who responded positively to flyers describing the research and through word of mouth were included in the study if they met the age requirement of age 60 and older, reported having a COVID-19 vaccine, and had transportation to one of the book club locations.
- College and graduate students were also recruited.
- Book clubs were held in two mid-sized cities.

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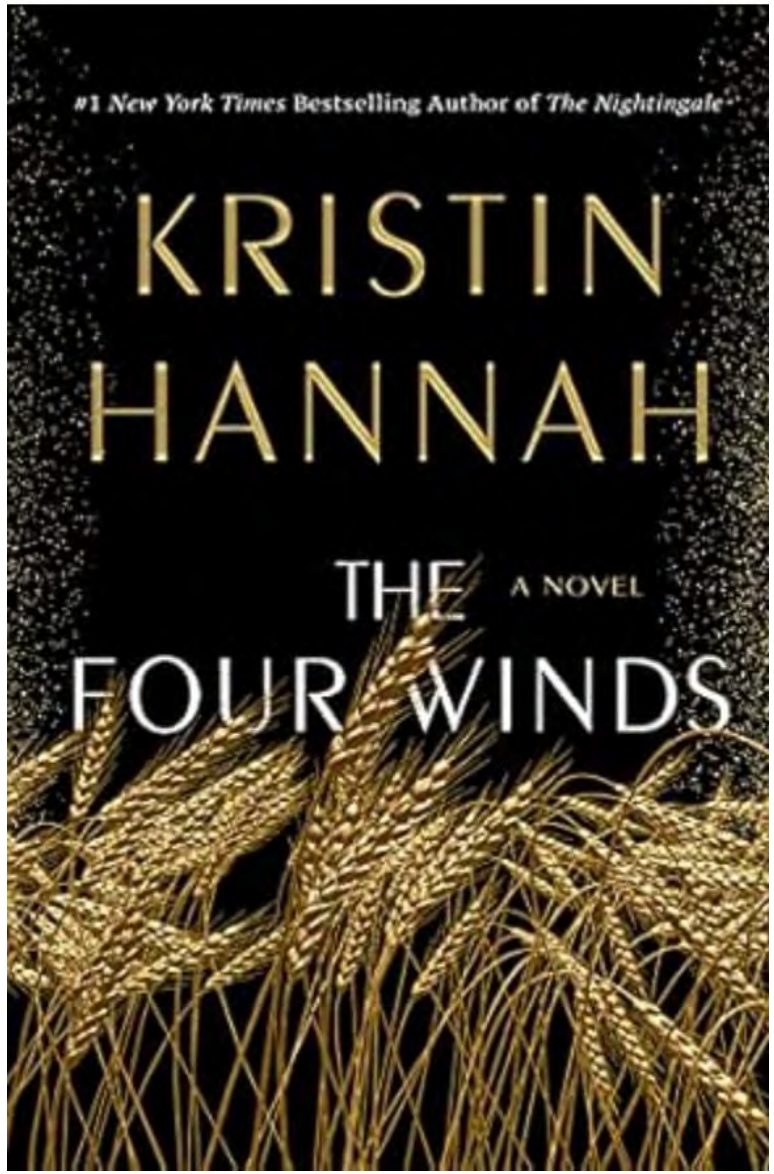
RESEARCH ON BOOK CLUBS CONDUCTED IN OUR LAB HAVE INCLUDED

- Groups lasted 8 weeks with testing pre and post.
- Half of the sessions are on Zoom and half were in person. Group meetings were 1 hour.
- Led by a speech-language pathologist or advanced graduate student in speech-language pathology who was well-versed in promoting communication across the ages.
- Focus groups took place approximately 1–3 weeks following the completion of reading discussion activities. Researchers moderated these sessions utilizing neutrally worded questions to ensure group discussion would largely remain within the bounds of the study's objectives.

OUR BOOK CLUBS READ THE FOUR WINDS

- A librarian and experts on aging who met several times to deliberate on the book selection.

- Set in Great Depression, blends coming of age themes and ways that socioeconomic hardship particularly impacts individuals of more advanced age.



PARTICIPANTS

- People from a variety of backgrounds (e.g. different racial groups and students from various states).
- 29 Older adults and 13 college-graduate student age groups
- 14 Older adults who were controls.

RESEARCH FINDINGS (QUANTITATIVE AND QUALITATIVE)

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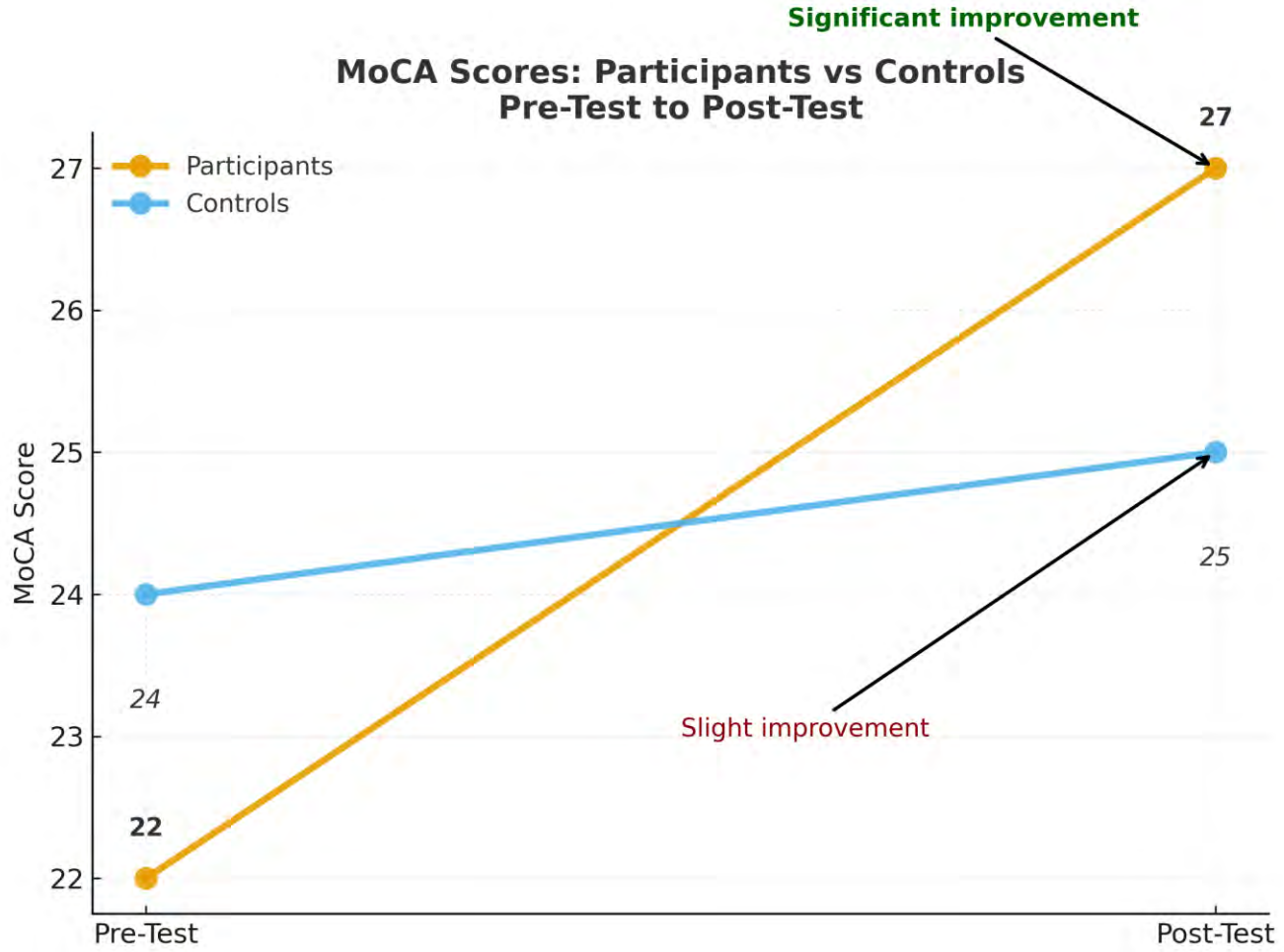
QUANTITATIVE FINDINGS



- Participants increased their MoCA scores by 5 points on average.
- The Control Group increased their MoCA scored by 1 points on average.

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MEASURES OF MOOD, ANXIETY, AND QUALITY OF LIFE

- Scores on the GDS (depression symptoms), DASS21 (depression, anxiety, stress), OPQOL-brief (quality of life), and semantic fluency (naming words in categories) were not found to significantly differ from baseline to post book club intervention.
- Generally, the participants in the present study had high normal scores in mental status and quality of life; therefore, it was difficult to demonstrate improvement on these measures.

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QUALITATIVE FINDINGS

- Analysis of the focus group transcripts yielded several themes that synthesize the experiences and views of both older adults and students

- “I think it would just be great if there were more groups like that of younger and older people. So we could exchange ideas and come to a common ground, per se. And I was really impressed, actually, with the young people, the way they listened to us and understood our point of view, and where we were coming from and what we came through, you know. **I think they got more of an understanding of our generation during those discussions.**

QUALITATIVE FINDINGS

- The majority of older adult participants reported limited interactions with younger generations outside of family members like grandchildren.
- Older adults and students reported benefits such as increased positive emotions
  - Enhanced mutual understanding
  - Reduced biases toward each other
- These outcomes suggest a positive protective effect for mental health.

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CONTRIBUTIONS TO THE FIELD

- Demonstrates the feasibility and formula for implementing an intergenerational book club to increase or maintain cognition.
- Offers insights for community and educational initiatives aiming to bridge generational divides and foster social inclusivity.

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PRACTICAL IMPLICATIONS AND NEXT STEPS

- College courses (e.g. service-learning) where students and older adults discuss literature
- Provide the book club kits to older community groups to replicate benefits.
- Randomized controlled trial/ in-depth qualitative interviews

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DISCUSSION

- The present study addressed two potential preventative strategies for cognitive decline in older adults: social engagement and cognitive stimulation.

- Perry et al. (2022) discuss a hypothetical neuroprotective mechanism of social bridging which refers to social enrichment occurring in the context of expansive networks with casual relationships that cut across or link different social groups beyond the family.

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THANKS!

PLEASE CONTACT US IF YOU'RE INTERESTED IN JOINING A BOOK CLUB

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https://aginglab.org/

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How to Meaningfully Change One's Biological Age and Reduce the Risk of "Age-Related" Cognitive Decline and Dementia: The Power of Food

2025 South Carolina Statewide Aging and Alzheimer's Disease Research Symposium

Columbia, SC 9 October 2025

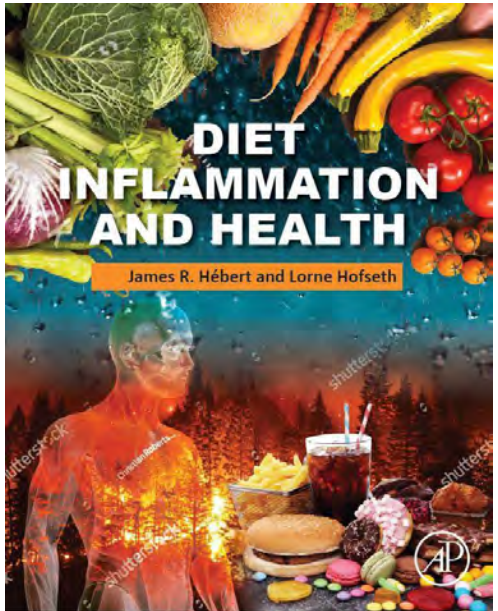
James R. Hébert, MSPH, ScD

Health Sciences Distinguished Professor of Epidemiology
Director, Cancer Prevention and Control Program

South Carolina Statewide
Cancer Prevention & Control Program

ClinTrUSC

Center for Clinical and Translational Research
University of South Carolina



REMEDY

SOUTH CAROLINA CPCRN
South Carolina Cancer Prevention and Control Research Network

President, Scientific Director Chair of Nutrition of:

CHI
CONNECTING HEALTH INNOVATIONS

Disclosures

1. I own controlling interest in Connecting Health Innovations LLC (CHI), a Columbia (SC)-based company that has licensed the right to my invention of the dietary inflammatory index (DII®) from the University of South Carolina to develop computer and smart phone applications for patient counselling and dietary intervention in clinical settings. The company also has designed other products that can be used to assist individuals in lowering their diet-associated inflammation to improve health and well-being and to decrease risk of cardiovascular diseases, cancer, type 2 diabetes (and other chronic diseases).
2. I receive extramural grant support from the NCI, NHLBI, NIDDK, NIMHD, NIGMS, DoD, and the CDC.
3. I serve as a member of the National Institutes of Health (NIH) Nutrition Research Thought Leader Panel for the NIH Nutrition Research Task Force (NRTF), which is charged with providing visionary input in prioritizing gaps and opportunities for strategic planning of nutrition research at the NIH.

Quality of Life Research
https://doi.org/10.1007/s11136-021-02809-1

COMMENTARY

Focus on disability-free life expectancy: implications for health-related quality of life

Ashley E. Galvin[1,2] · Daniela B. Friedman[1,3,4] · James R. Hébert[1,5]

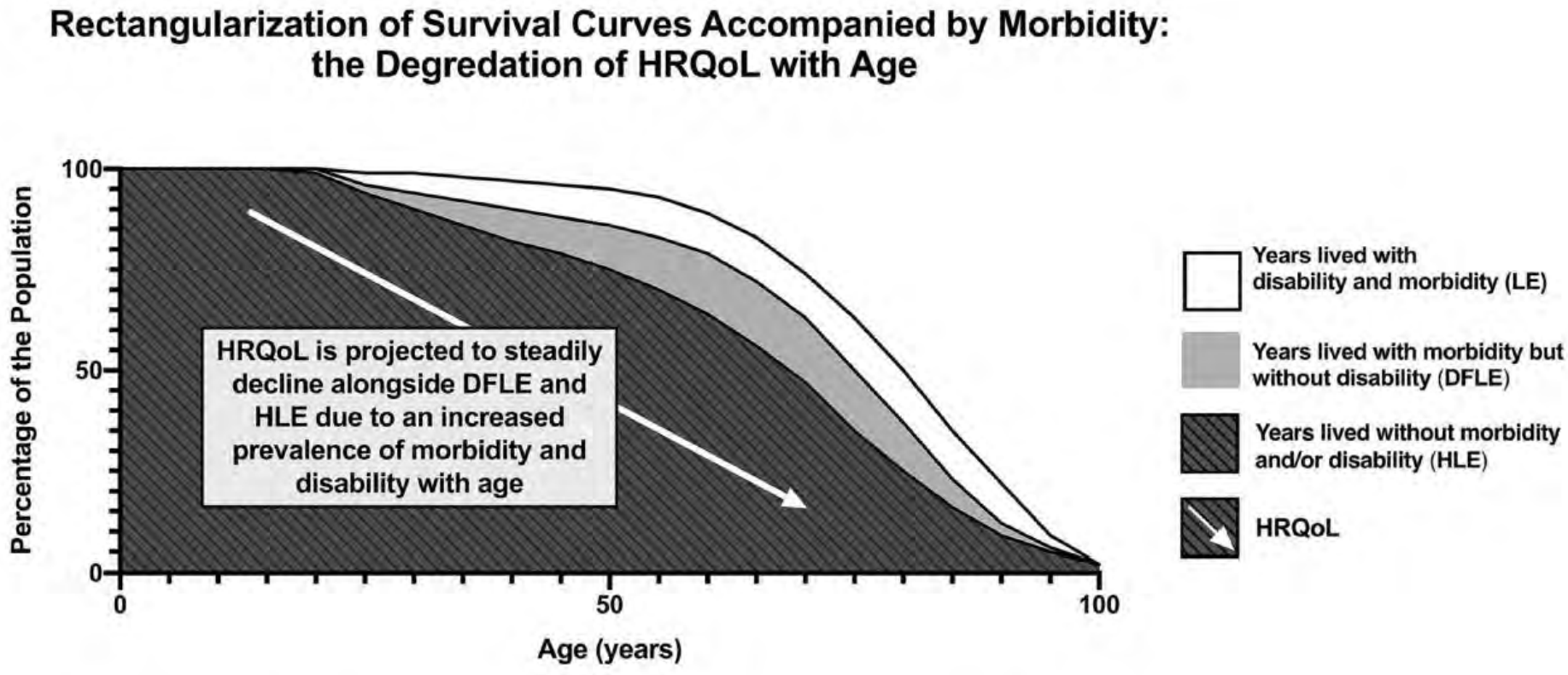


Fig. 1 Rectangularization of survival curves accompanied by morbidity: the degradation of HRQoL with age

Important terms

Inflammaging is low-grade inflammation associated with aging), and

Meta-inflammation is low-grade inflammation associated with overnutrition (e.g., **eating SAD**)

Both are of particular concern as the population ages and the obesity epidemic rages.

Telomeres are an important indicator of Aging and, therefore, should be part of the story.

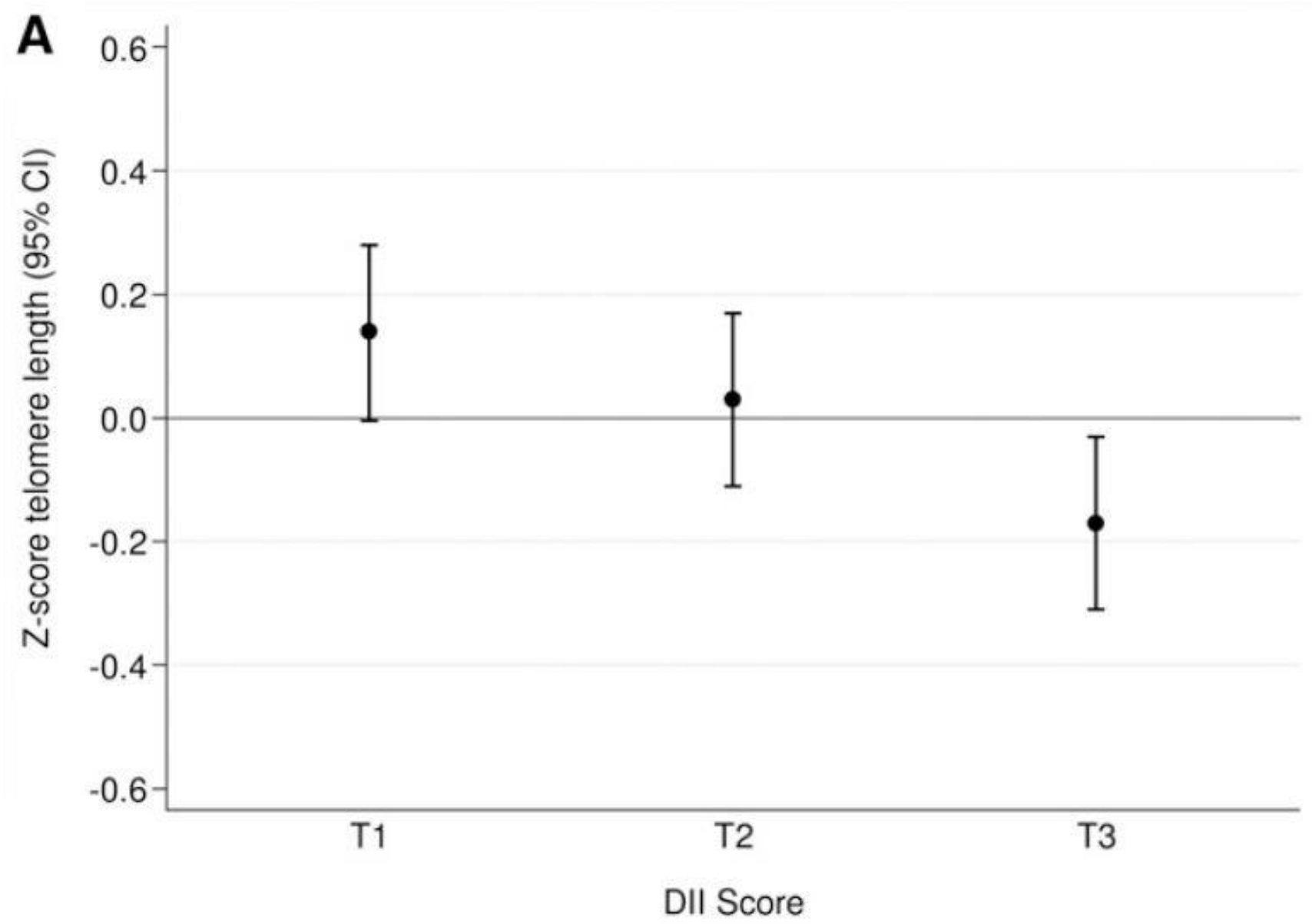
Dietary inflammatory index and telomere length in subjects with a high cardiovascular disease risk from the PREDIMED-NAVARRA study: cross-sectional and longitudinal analyses over 5 y[1]

Sonia García-Calzón,[2,6] *Guillermo Zalba,*[3,6] *Miguel Ruiz-Canela,*[4,6,7] *Nitin Shivappa,*[8,9] *James R Hébert,*[8,9] *J Alfredo Martínez,*[2,5,6,7] *Montserrat Fitó,*[7,10] *Enrique Gómez-Gracia,*[11] *Miguel A Martínez-González,*[4,6,7] *and Amelia Marti*[2,6,7]*

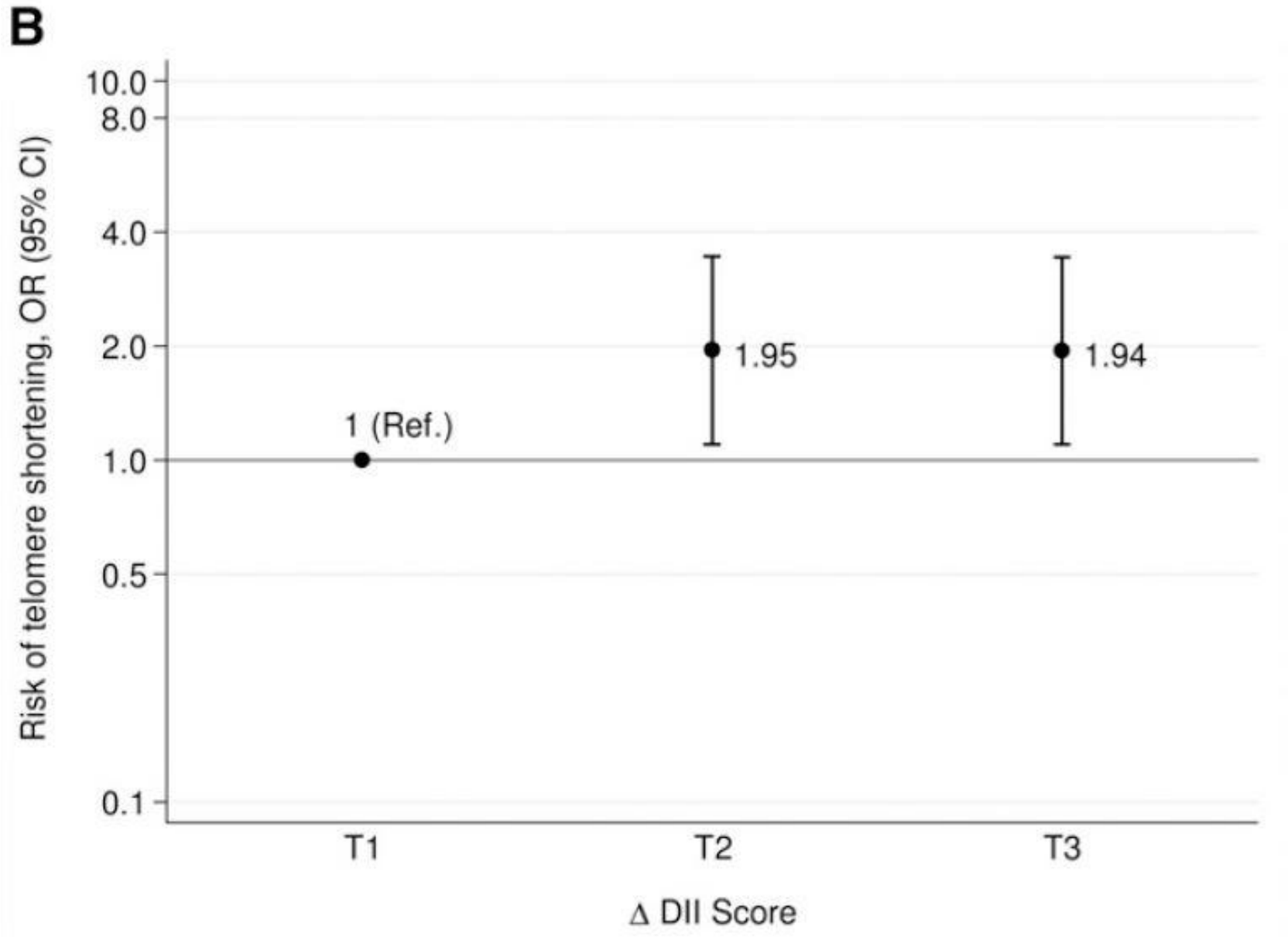
Departments of [2]Nutrition, Food Science and Physiology, [3]Biochemistry and Genetics, and [4]Preventive Medicine and Public Health and [5]Centre for Nutrition Research, University of Navarra, Pamplona, Spain; [6]Navarra Institute for Health Research, Pamplona, Spain; [7]Center of Biomedical Research in Physiopathology of Obesity and Nutrition (CIBEROBN), Institute of Health Carlos III, Madrid, Spain; [8]Cancer Prevention and Control Program and [9]Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC; [10]Cardiovascular Risk and Nutrition Research Group (Regicor Study Group), Barcelona, Spain; and [11]Department of Preventive Medicine, University of Malaga, Malaga, Spain

Am J Clin Nutr 2015;102:897–904. Printed in USA.

So that you can see this clearly, this is what the association between DII score and telomere length looked like at baseline ↓.



This is what it looked like after 5 years in the intervention group



We have published 4 additional papers with similar results on telomere length and diet-associated inflammation:

1. Lecorguillé M, Navarro P, Chen LW, Murrin C, Viljoen K, Mehegan J, Shivappa N, Hébert JR, Kelleher CC, Suderman M, Phillips CM. Maternal and Paternal Dietary Quality and Dietary Inflammation Associations with Offspring DNA Methylation and Epigenetic Biomarkers of Aging in the Lifeways Cross-Generation Study. J Nutr 2023;153(4):1075-88.
2. Meinila J, Perala MM, Kautiainen H, Mannisto S, Kanerva N, Shivappa N, Hebert JR, Iozzo P, Guzzardi MA, Eriksson JG. Healthy diets and telomere length and attrition during a 10-year follow-up. Eur J Clin Nutr 2019;73(10):1352-60.
3. De Meyer T, Bekaert S, De Buyzere ML, De Bacquer DD, Langlois MR, Shivappa N, Hebert JR, Gillebert TC, Rietzschel ER, Huybrechts I. Leukocyte telomere length and diet in the apparently healthy, middle-aged Asklepios population. Sci Rep 2018;8(1):6540.
4. Shivappa N, Wirth MD, Hurley TG, Hebert JR. Association between the Dietary Inflammatory Index (DII) and telomere length and C-reactive protein from the National Health and Nutrition Examination Survey-1999-2002. Mol Nutr Food Res 2016;61(4):10.1002/mnfr.201600630.

nutrients

MDPI

Article

Association between the Inflammatory Potential of the Diet and Biological Aging: A Cross-Sectional Analysis of 4510 Adults from the Moli-Sani Study Cohort

Claudia F. Martínez [1,2], Simona Esposito [1], Augusto Di Castelnuovo [3], Simona Costanzo [1], Emilia Ruggiero [1], Amalia De Curtis [1], Mariarosaria Persichillo [1], James R. Hébert [4,5], Chiara Cerletti [1], Maria Benedetta Donati [1], Giovanni de Gaetano [1], Licia Iacoviello [1,6,*], Alessandro Gialluisi [1] and Marialaura Bonaccio [1,†] on behalf of the Moli-sani Study Investigators

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3 Mediterranea Cardiocentro, 80122 Napoli, Italy
4 Cancer Prevention and Control Program and Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC 29208, USA
5 Department of Nutrition, Connecting Health Innovations LLC, Columbia, SC 29201, USA
6 Department of Medicine and Surgery, Research Center in Epidemiology and Preventive Medicine (EPIMED), University of Insubria, 21100 Varese-Como, Italy
* Correspondence: licia.iacoviello@moli-sani.org
† Moli-sani Study investigators; list available at https://www.moli-sani.org/?page_id=173.

The Energy-adjusted Dietary Inflammatory Index (E-DII^{TM}) was used to quantify the inflammatory potential of the diet. A deep neural network approach based on circulating biomarkers was used to compute BA, and the resulting Δage (BA-CA) was fit as the dependent variable. In 4,510 participants (men 52.0%), the mean of CA (SD) was 55.6 y (±11.6), BA 54.8 y (±8.6), and Δage −0.77 (±7.7). In a multivariable-adjusted analysis, an increase in E-DII scores led to an increase in Δage (β = 0.22; 95%CI 0.05, 0.38). **We found interaction for E-DII by BMI.**

What is the range of effect sizes we might see?

Based on the hundreds of papers that we and others have written on diet-associated inflammation, it is conceivable that there is up to a 50-year discrepancy in biological age between someone eating a SAD and living a sedentary lifestyle vs. eating a low-DII and getting lots of physical activity.

Results on Aging are consistent with results on Cognition & dementia:

1. Mossavar-Rahmani Y, Hyun N, Hakun JG, Katz MJ, Pavlovic JM, Zetterberg H, Wang Z, Yang JB, Wylie-Rosett J, Hebert JR, Sliwinski MJ, Shaw PA. The effects of the Multicultural Healthy Diet on cognitive decline & Alzheimer's disease risk: A randomized controlled trial in middle-aged adults. Am J Clin Nutr 2025;122(1):48-59.
2. Mohseni M, Shivappa N, Shojaei M, Bagherniya M, Mohammadi H, Hasanzadeh A, Hébert JR, Askari G, Sahebkar A. The Association of Dietary Inflammatory Index and Cognitive Function in Iranian Elders. Recent Adv Food Nutr Agric 2024;15(1):59-73.
3. Zabetian-Targhi F, Srikanth VK, Smith KJ, Oddy Ph DW, Beare R, Moran C, Wang W, Shivappa N, Hébert JR, Breslin M, van Weel JM, Callisaya ML. Associations Between the Dietary Inflammatory Index, Brain Volume, Small Vessel Disease, and Global Cognitive Function. Journal of the Academy of Nutrition and Dietetics 2021;121(5):915-24.e3.
4. Jayanama K, Theou O, Godin J, Cahill L, Shivappa N, Hébert JR, Wirth MD, Park YM, Fung TT, Rockwood K. Relationship between diet quality scores and the risk of frailty and mortality in adults across a wide age spectrum. BMC Med 2021;19(1):64.
5. Cervo MMC, Scott D, Seibel MJ, Cumming RG, Naganathan V, Blyth FM, Le Couteur DG, Handelsman DJ, Ribeiro RV, Waite LM, Shivappa N, Hebert JR, Hirani V. Proinflammatory Diet Increases Circulating Inflammatory Biomarkers and Falls Risk in Community-Dwelling Older Men. J Nutr 2020;150(2):373-81.
6. Shin D, Kwon SC, Kim MH, Lee KW, Choi SY, Shivappa N, Hebert JR, Chung HK. Inflammatory potential of diet is associated with cognitive function in an older adult Korean population. Nutrition 2018;55-56:56-62.
7. Frith E, Shivappa N, Mann JR, Hebert JR, Wirth MD, Loprinzi PD. Dietary inflammatory index and memory function: population-based national sample of elderly Americans. Br J Nutr 2018;119(5):552-8.
8. Kesse-Guyot E, Assmann KE, Andreeva VA, Touvier M, Neufcourt L, Shivappa N, Hebert JR, Wirth MD, Hercberg S, Galan P, Julia C. Long-term association between the dietary inflammatory index and cognitive functioning: findings from the SU.VI.MAX study. Eur J Nutr 2017;56(4):1647-55.
9. Hayden KM, Beavers DP, Steck SE, Hebert JR, Tabung FK, Shivappa N, Casanova R, Manson JE, Padula CB, Salmoirago-Blotcher E, Snetselaar LG, Zaslavsky O, Rapp SR. The association between an inflammatory diet and global cognitive function and incident dementia in older women: The Women's Health Initiative Memory Study. Alzheimers Dement 2017;13(11):1187-96.
10. Shivappa N, Blair CK, Prizment AE, Jacobs DR, Jr., Steck SE, Hebert JR. Association between inflammatory potential of diet and mortality in the Iowa Women's Health study. Eur J Nutr 2016;55(4):1491-502.

ELSEVIER

Alzheimer's & Dementia 13 (2017) 1187-1196

Alzheimer's & Dementia

Featured Article

The association between an inflammatory diet and global cognitive function and incident dementia in older women: The Women's Health Initiative Memory Study

Kathleen M. Hayden[a,*], Daniel P. Beavers[b], Susan E. Steck[c], James R. Hebert[c,d], Fred K. Tabung[e], Nitin Shivappa[c,d], Ramon Casanova[b], JoAnn E. Manson[f], Claudia B. Padula[g], Elena Salmoirago-Blotcher[h], Linda G. Snetselaar[i], Oleg Zaslavsky[j], Stephen R. Rapp[a,k]

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[h]*Centers for Behavioral and Preventive Medicine, The Miriam Hospital; Departments of Medicine and Epidemiology, Warren Alpert School of Medicine and School of Public Health, Brown University, Providence, RI, USA*
[i]*Department of Epidemiology, University of Iowa College of Public Health, Iowa City, IA, USA*
[j]*Department of Behavioral Nursing and Health Informatics, University of Washington School of Nursing, Seattle, WA, USA*
[k]*Department of Psychiatry, Wake Forest School of Medicine, Winston-Salem, NC, USA*

Importantly, there are 3 meta-analyses published on the DII and cognition-related outcomes (NB: We were not authors on any of these):

1. **Fang B, Wang Z, Nan G. Dietary inflammatory potential and the risk of cognitive impairment: A meta-analysis of prospective cohort studies. J Nutr Health Aging 2025;29(2):e100428**.
2. **Ding T, Aimaiti M, Cui S, Shen J, Lu M, Wang L, Bian D. Meta-analysis of the association between dietary inflammatory index and cognitive health. Front Nutr 2023;10:e1104255.**
3. **Jia Y, Yan S, Sun M, Yang Y, Wang L, Wu C, Li P. Association between dietary inflammatory index and cognitive impairment: A meta-analysis. Front Aging Neurosci 2022;14:e1007629.**

What kind of effect sizes do we see?

Across quantiles of DII / E-DII scores:

- 34% increased risk of Cognitive Impairment (95% CI = 1.15-1.55) based on 266k participants.
- 34% increased risk of Alzheimer's Disease (95% CI = 1.21-1.49).
- 63% increased risk of Global Function Impairment (95% CI = 1.36-1.96).
- 18% increase in Verbal Fluency Impairment per unit DII score increase (95% CI = 0.08-0.42).
- 46% increased risk of cognitive impairment (95%CI = 1.26, 1.69).

What does all this mean ?

There is ≈ doubling of risk for each 2.5 to 5.0 DII/ E-DII points. This is ≈ ¼ to ½ the difference between the SAD and:

- **The average of recipes in Greek Revival**
  [Moore-Pastides P. Greek Revival: Cooking for Life. Columbia, SC: University of South Carolina Press; 2010.]
- **The best (least pro-inflammatory) diets reviewed in US News & World Report**
  [Turner-McGrievy G, Wirth MD, Hill KL, Dear ER, Hébert JR. Examining commonalities and differences in food groups, nutrients, and diet quality among popular diets. Clin Nutr ESPEN 2021;41:377-85.]

Summary and Challenges for the Future

- **Diet exerts a huge effect on biological aging (BA), cognition, and dementia.**
- **More studies are needed to quantify BA.**
- **Rather than constrain diet to narrow ranges of exposure, we need to think more expansively and apply this both in clinical medicine and in public health.**
- **Combining diet with Physical Activity is Crucial – especially as people age**
- **As in the psychological literature, being healthy is considered an aberration in this field.**
- **Why do we continue to settle for suboptimal outcomes?**

Take Brain Health to Heart

Karilyn Tremblay, MPH

SC Department of Public Health (DPH)

Building Our Largest Dementia (BOLD)

- **DPH was awarded the 5-year CDC BOLD Grant Funding (2023-2028)**
  - Karilyn Tremblay, DPH BOLD Program Manager, bold@dph.sc.gov

- **Focus Areas**: Risk reduction, early detection, caregiver support, and prevention of hospitalizations.

- **BOLD Infrastructure for Alzheimer's Act**: Passed into law in December 2018 to create a national public health infrastructure addressing Alzheimer's disease and related dementias (ADRD). The BOLD Reauthorization Act was signed into law in December 2024.

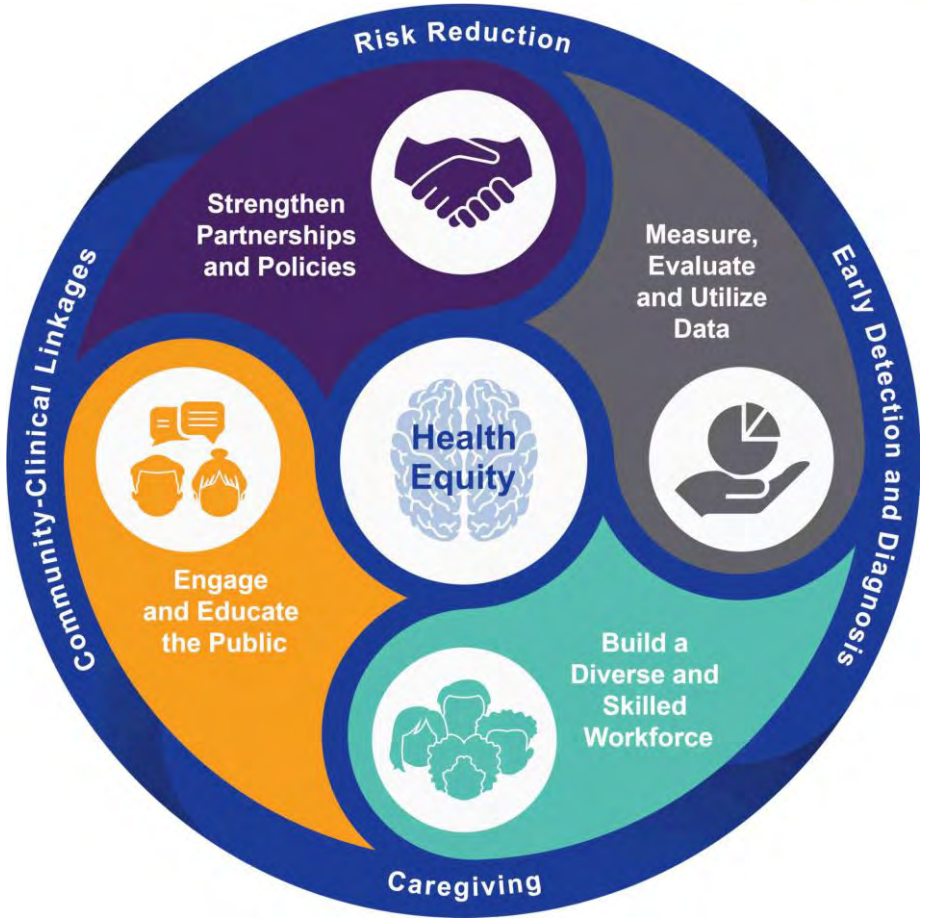
Healthy Brain Initiative (HBI)

The framework of the HBI Road Map includes the 4 Essential Public Health Services:

- Strengthen partnerships, and policies
- Measure, evaluate, and utilize data
- Build a diverse and skilled workforce
- Engage and educate the public

HBI Road Map Priority Areas:

- Risk Reduction
- Early Detection and Diagnosis
- Caregiving
- Community-Clinical Linkages



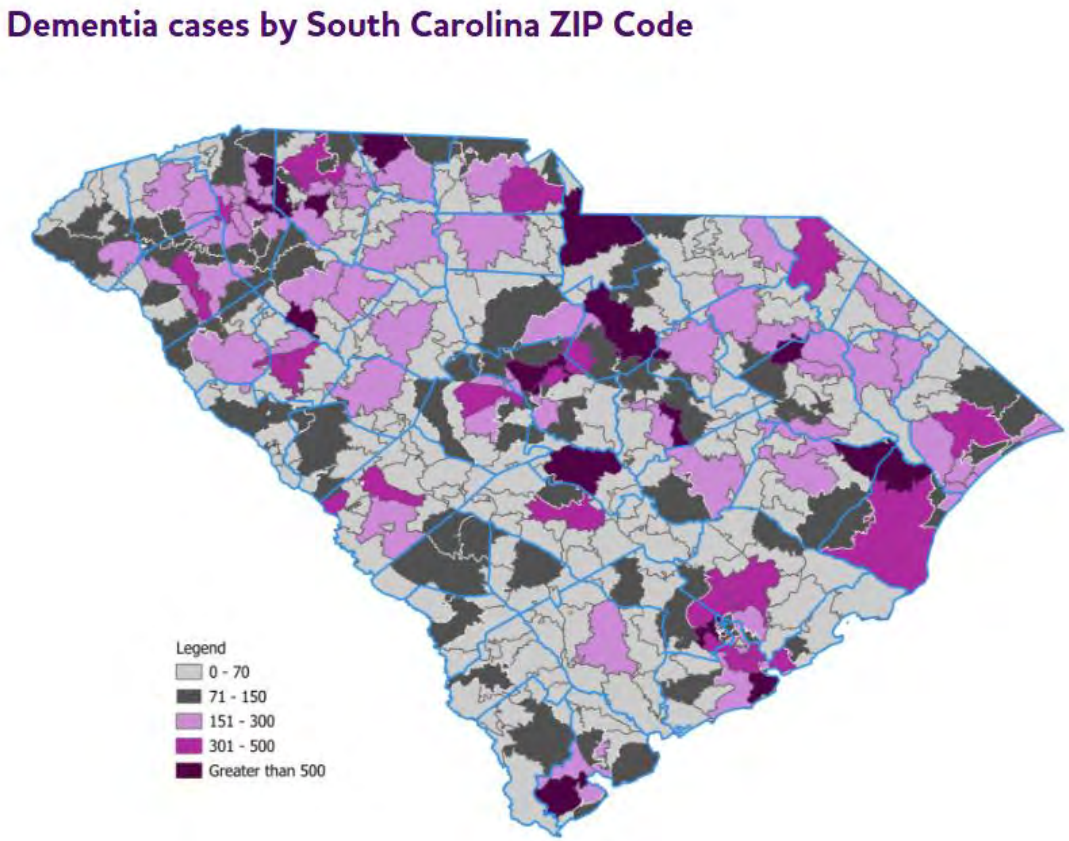
Source: Alzheimer's Association – HBI Road Map Conceptual Framework

Why use the HBI Roadmap in SC?

377,143 cases of ADRD reported to the Alzheimer's Registry (since 1988)

125,538 South Carolinians living with a diagnosis of ADRD (2022)

61% of adults ages 65+ have two or more chronic conditions



Source: Alzheimer's Association – Alzheimer's in South Carolina - Map Retrieved 2/27/2025
Source: Alzheimers_Registry_Report_2023.pdf
Source for Chronic Conditions: Archives of Neurology, 2003; Vol. 60, 119- 1122
State Health Assessment | Live Healthy South Carolina

State of the Science on Risk Factors

10

factors with the STRONGEST EVIDENCE

Risk Factors	Evidence Level for: Cognitive Decline	Dementia
Formal Education (+)	STRONG	STRONG
Traumatic Brain Injury	STRONG	STRONG
Midlife Hypertension	STRONG	MODERATE
Midlife Obesity	STRONG	MODERATE
Diabetes	STRONG	MODERATE
Physical Activity (+)	STRONG	MODERATE
Smoking	STRONG	MODERATE
Sleep Disorders/Poor Sleep	STRONG	MODERATE
Balanced Nutrition (+)	MODERATE	Lower
Cognitive Engagement (+)	MODERATE	Lower

Risk Factors	Evidence Level for: Cognitive Decline	Dementia
Air Pollution	Lower	Lower
Social Isolation	Lower	Unclear
Depression	Lower	Unclear
Hearing Loss	Lower	Unclear
Moderate Alcohol Use (+)	Lower	Unclear
Hyperlipidemia	Unclear	Unclear
Alcohol Abuse	Unclear	Unclear
Substance Abuse	Unclear	Unclear

(+) Indicates protective factor

EVIDENCE LEVELS

STRONG

Consistent evidence of a causal relationship, including intervention studies suggesting modification of risk

MODERATE

Some evidence (reproducible in multiple studies) of either a causal relationship or positive effect of interventions

LOWER

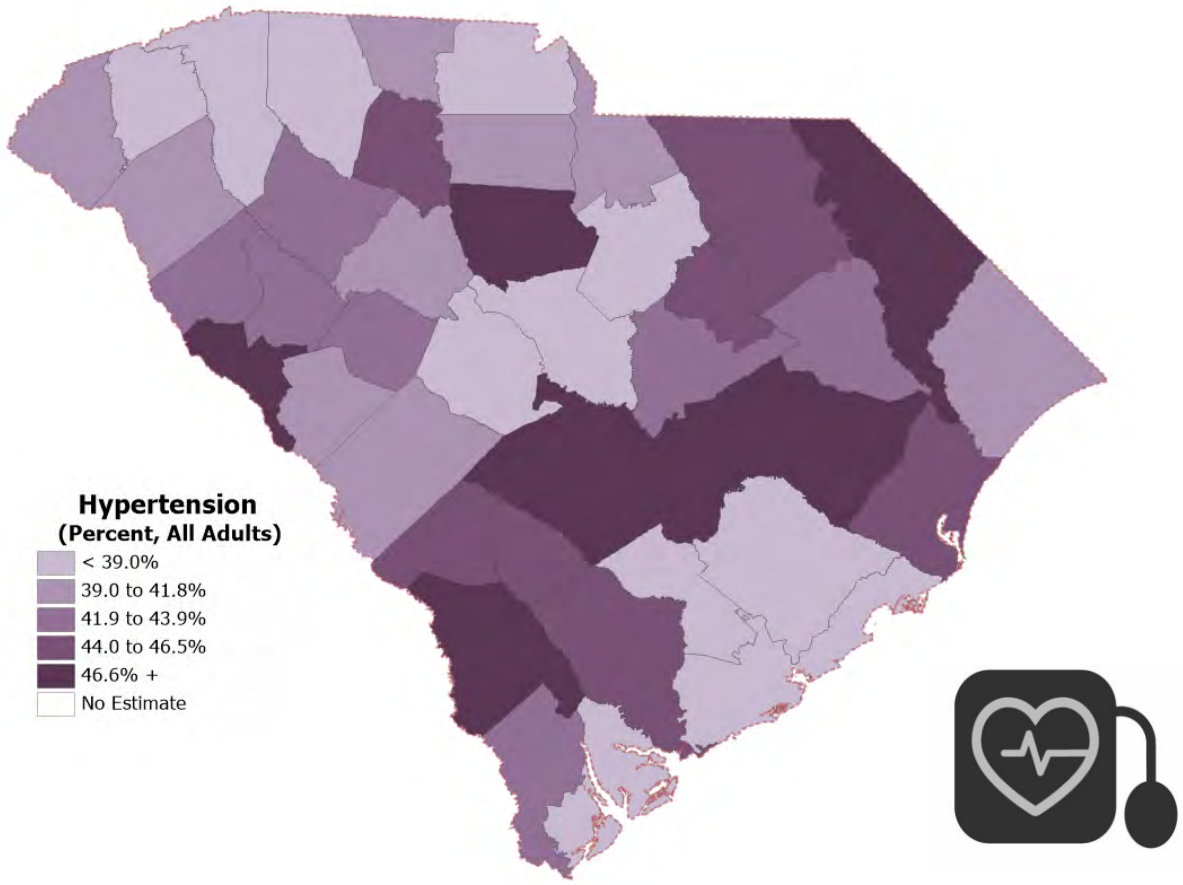
Some relationship, but studies are limited in number, scope and/or strength - and/or have some contradictory findings

UNCLEAR

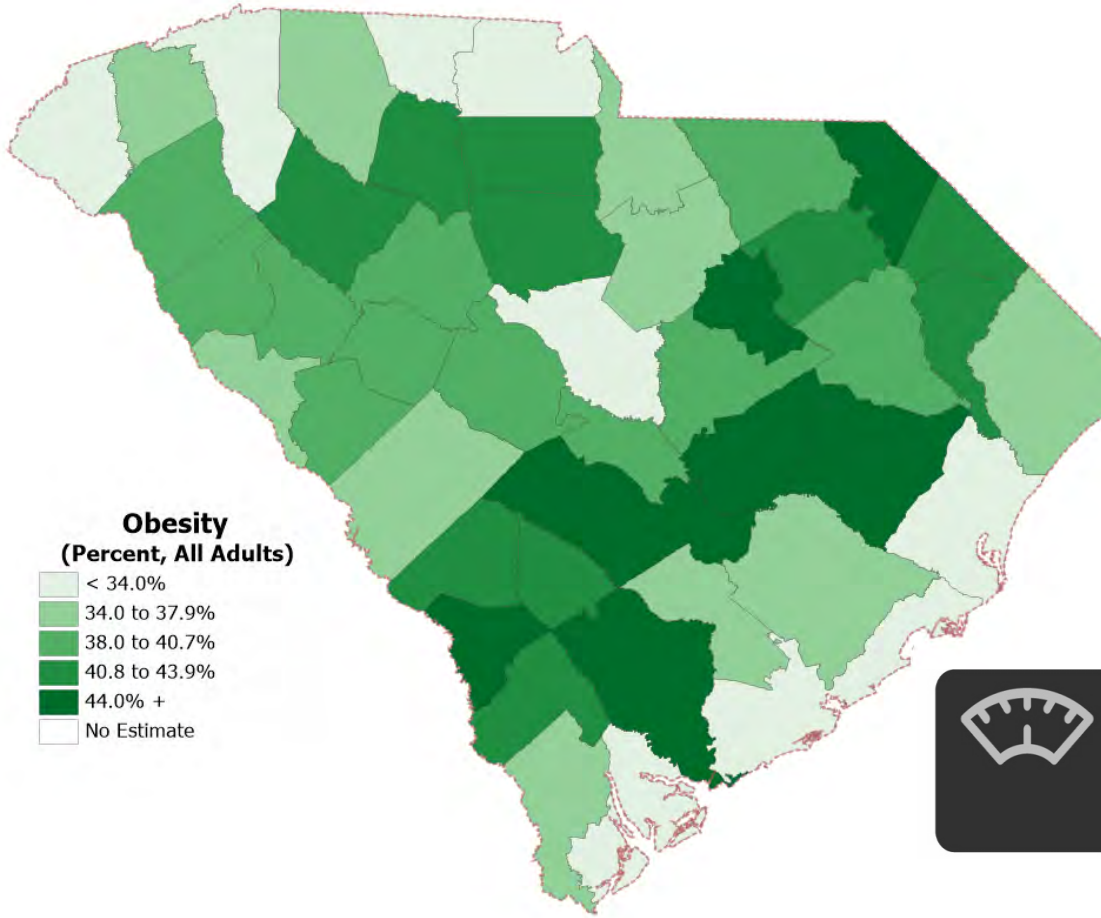
Emerging areas of research and/or areas with currently unclear relationships

2024 – Lancet Commission on Dementia - Hope for Prevention, Intervention, and Care

Control Your Blood Pressure



Maintain a Healthy Weight

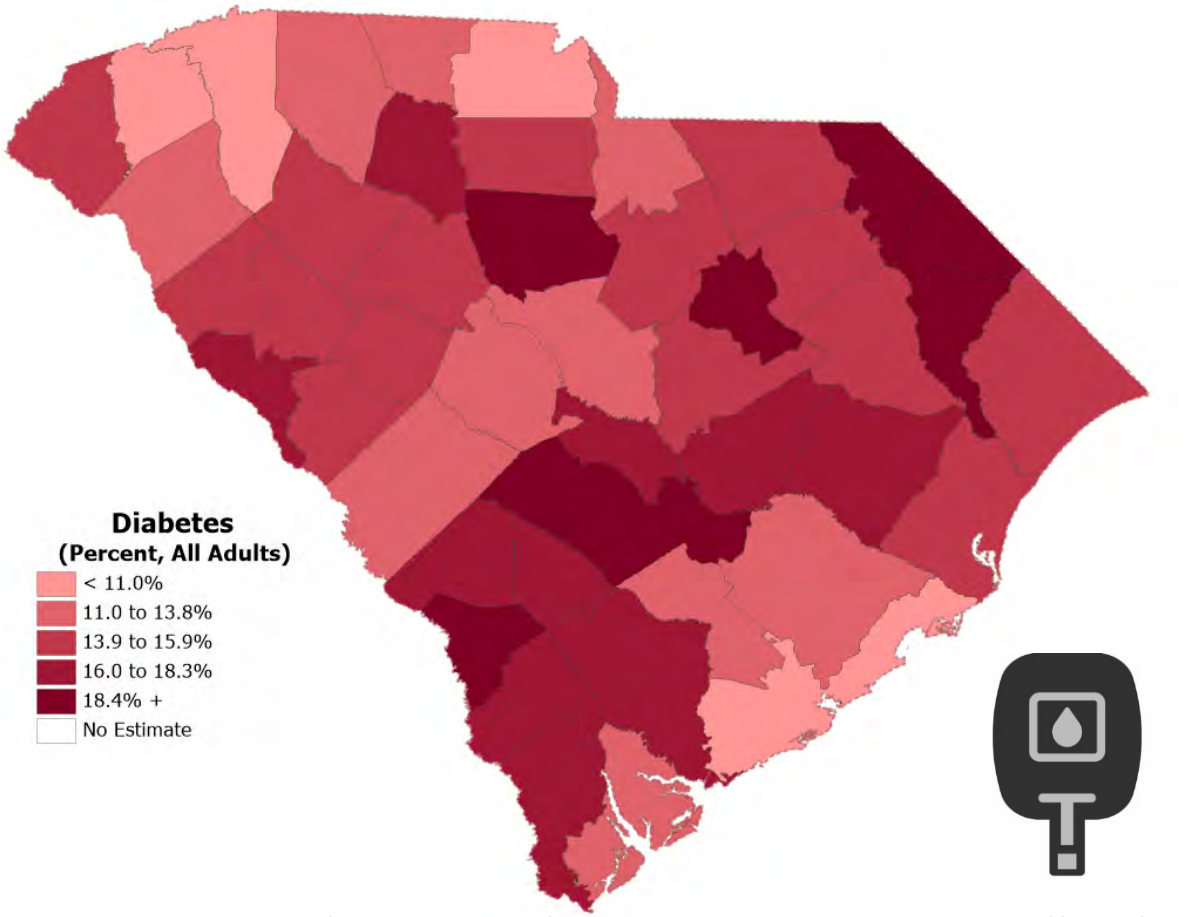


Medications can help lower high blood pressure.

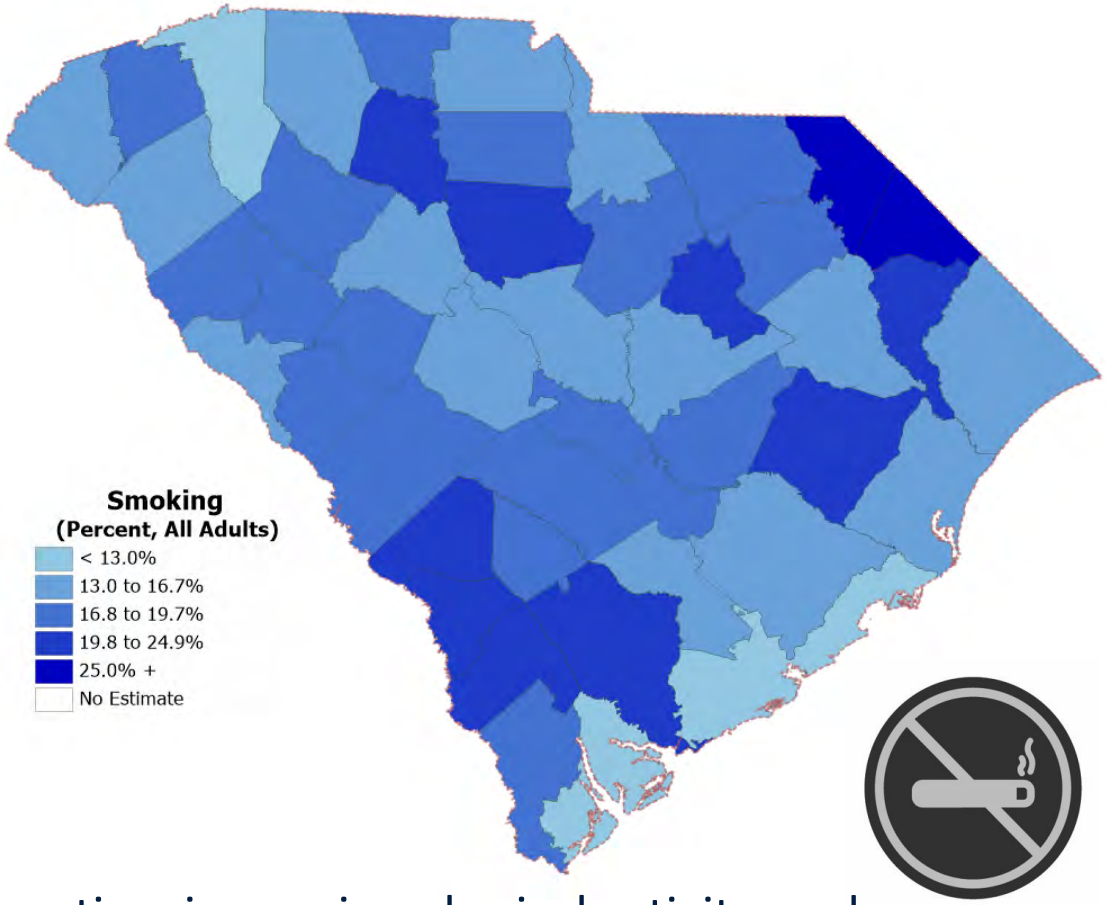
Start healthy habits like eating right and physical activity.

Work with a health care provider and discuss a healthy diet.

Prevent Diabetes



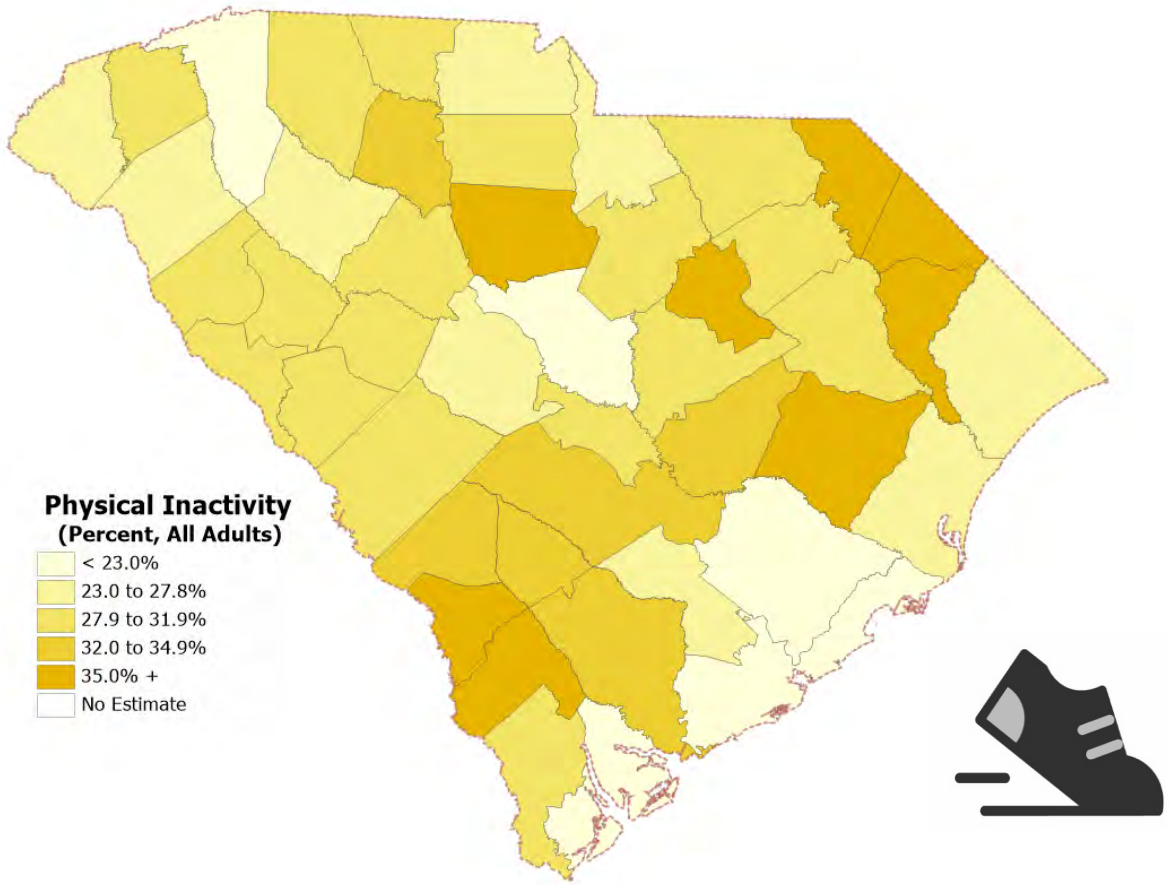
Quit Smoking



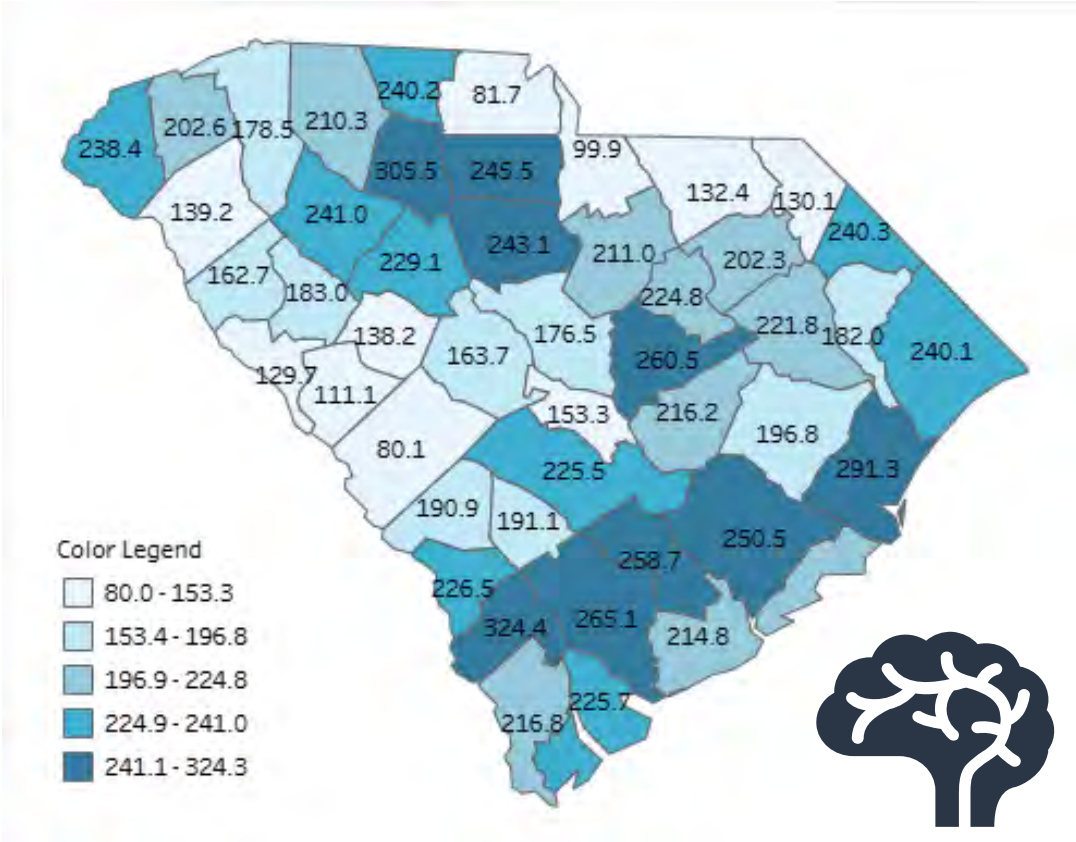
Type 2 diabetes can be prevented or controlled by healthier eating, increasing physical activity, and medication, if necessary.

Quitting smoking can lower the risk of cognitive decline back to levels similar to those who have not smoked. It's never too late to stop.

Get Moving



Prevent TBI

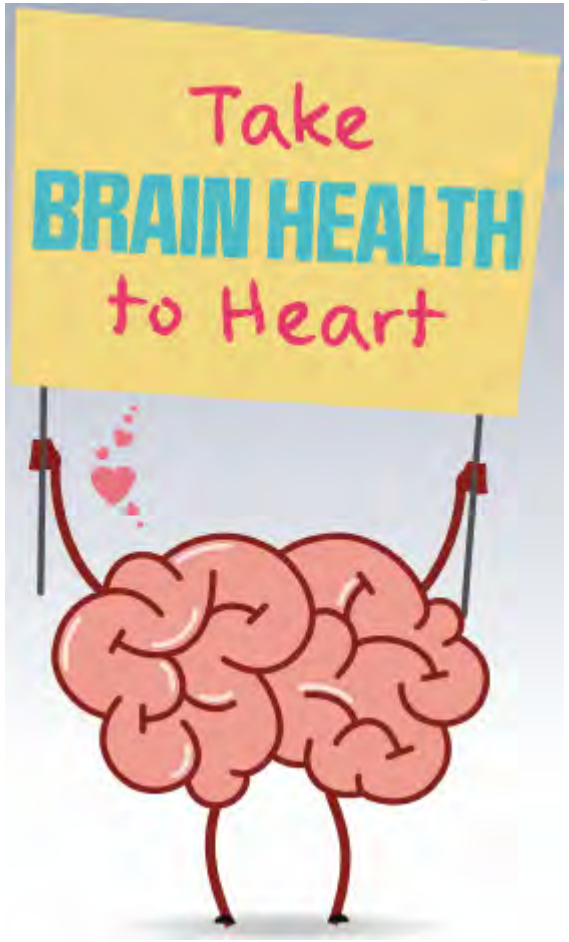


Engage in regular physical activity to increase blood flow to the brain and body.
Increase daily activities of walking, dancing, gardening, etc.
Wear a helmet especially when riding a bike or motorcycle.
Use seat belts and pay attention to traffic safety signs.

ALZHEIMER'S ASSOCIATION

Take Brain Health to Heart Campaign

- Raise **awareness** about the connection between **brain and heart health**
- Highlight **shared risk factors** for brain and heart health, like diet, physical activity, nutrition, and tobacco use
- Provides **tools and resources** to promote healthy living and brain injury prevention



What's good for your heart is also good for your brain

The Lifespan Approach

- Previously when working on **dementia programs**, your focus might be with seniors or older adults
- Risk reduction efforts need to find a **younger audience**
- Healthy Aging takes a **lifespan approach** so that all ages can have a dementia risk reduction plan
- Make connections between the current chronic disease prevention programs and **Brain Health**

DPH Internal Partners

- Nutrition, Physical Activity, & Obesity Prevention Services
- Heart Disease and Stroke - Check Your Blood Pressure
- Manage Diabetes Learn the Diabetes ABCs
- Oral Health Essential Programs and Resources
- Injury, Tobacco, & Substance Abuse Prevention
  - SC Tobacco Quitline (1-800-QUIT-NOW) Tobacco Cessation
  - Injury Prevention Traumatic Brain Injury
- DPH has Strong Regional Partners - Community Health Workers

DPH External Partners

- BOLD Public Health | Alzheimer's Disease Program | CDC
- Alzheimer’s Association | South Carolina Chapter
- South Carolina Department on Aging (SCDOA)
- Alzheimer’s Resource Coordination Center (ARCC)
- Alzheimer’s Disease Registry | Office for the Study of Aging
- South Carolina Alzheimer’s Disease Research Center (SC-ADRC)

Take Brain Health to Heart Survey

Purpose of the Survey

- Gather feedback on educational materials for brain and heart health

Key Feedback Goals

- Helpfulness
- Memorability
- Motivational Effect

DPH.SC.GOV/BRAINHEALTH

The BOLD grant funding awarded to the SC Department of Public Health supported the development of this presentation. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by Centers for Disease Control and Prevention and the U.S. Department of Health and Human Services (HHS), or the U.S. Government.

Risk Reduction Resources:

- Alzheimer's Public Health News
- Addressing Social Determinants of Health and Dementia Risk
- Getting Public Health to Address Dementia Risk: A Center of Excellence Conversation
- Science Summaries on the Modifiable Risk Factors for Dementia
- Summaries for the Social Determinants of Health (SDOH) related to dementia risk

General Resources:

- 10 Healthy Habits for Your Brain
- Public Health Approach to Alzheimer's
- Alzheimer's and Dementia: A Public Health Issue
- 24/7 Helpline: 800.272.3900
- What is Dementia? Symptoms, Causes & Treatment
- 10 Early Signs and Symptoms of Alzheimer's and Dementia

Student Research Poster Award Winners

1. **Most Outstanding Undergraduate Poster**
   Aurora Drye – Furman University
   The Associations of Tobacco and Alcohol in Pre-Clinical Neurodegeneration: A cross-sectional analysis

2. **Most Outstanding Graduate Poster**
   Kade Horacek – University of South Carolina
   Narrower Retinal Vessels Reflect Systemic Vascular Dysfunction in High Perfusion Brain Regions

3. **Most Outstanding Postdoctoral Fellow Poster**
   Fanghui Shi – University of South Carolina
   Genome-Wide Associated Variants of Neurocognitive Disorder Among People with and without HIV in the All of Us Research Program

4. **Most Creative Poster**
   Shelby A. Payne – Medical University of South Carolina
   The Auditory Nerve Glial Transition Zone: A Novel Site of Age-Related Neuroimmune Dysfunction

5. **Most Interdisciplinary Team Science Poster**
   Jeffrey Woodward – University of South Carolina School of Medicine, Greenville
   Barriers and Facilitators to Inclusion of People with Dementia in Research

UNIVERSITY OF South Carolina

South Carolina Alzheimer's Disease Research Center

2025 STATEWIDE AGING AND ALZHEIMER'S DISEASE RESEARCH SYMPOSIUM

Welcome to Day 2!

First Panel to Begin at 9:00 AM

CLEMSON® UNIVERSITY INSTITUTE FOR ENGAGED AGING

UNIVERSITY OF South Carolina

MUSC Medical University of South Carolina

DIAGNOSING DEMENTIA: NEW FRONTIERS IN EARLY DETECTION, TREATMENT, AND PERSONALIZED CARE

Dr. Dariusz Pytel

Dr. Angela Murphy

Dr. Daping Fan

Dr. John Absher

Dr. Jens Jensen

Panel Moderated by Dr. Qun Lu

UNIVERSITY OF South Carolina

Biomarkers in Action: SC-ADRC Biomarker Core Contributions to Early Detection of AD/ADRDs; Progress and Infrastructure Updates

2025 Statewide Aging and Alzheimer's Disease Research Symposium
October 9-10, 2025
Pastides Alumni Center
Columbia, SC

SC-ADRC Molecular and Genomic Biomarker Core (MGBC)

Feng Ding (Director), Clemson University

Melissa Moss, University of South Carolina (USC)

Chang Liu, University of Massachusetts Amherst (UMass)

Darek Pytel, Medical University of South Carolina (MUSC)

South Carolina Alzheimer's Disease Research Center

A statewide initiative of

MUSC Medical University of South Carolina | CLEMSON UNIVERSITY | UNIVERSITY OF South Carolina

Role of the MGBC

Our primary goal is to support investigators in testing well-established and validated biomarkers, and secondarily, to utilize cutting-edge technology to advance AD/ADRD studies and develop new analysis and detection approaches

The specific aims are:

1. **Provide longitudinal well-established biomarker data from a wide range of subjects to facilitate translational and clinical AD/ADRD research.** Measure, store, and share well-established AD and ADRD-related key biomarker data (e.g., Ab 40/42, Tau, p-Tau 217, NFL, α-synuclein). Incorporate genomic data (e.g. whole genome sequencing) to track disease risk and progression in participants over time.

2. **Streamline sample/data management and promote collaborations by coordinating with other SC-ADRC Cores.** Standardize protocols (acquisition, processing, storage) to ensure reproducibility across different research settings. Develop a database to integrate biomarker, clinical and imaging data, enabling multimodal deep learning for improved predictive modeling. Collaborate with Clinical, Neuropathology, and Data Management and Statistical Cores to share resources among SC-ADRC investigators and external research consortia. Collaboration with the Outreach, Recruitment, and Engagement Core, to raise biomarker awareness and encourage community participation in research.

3. **Expand AI-driven data analysis and Biosensor Technology Support.** Development of predictive AI modeling which includes multi-modal datasets that combine protein, genetic, and imaging data to enhance diagnostics. Validating novel biomarkers and biosensing approaches. Applying novel biosensors with ultrasensitive detection limits into point-of-care testing (POCT).

MGBC Equipment

MEDICAL UNIVERSITY OF SOUTH CAROLINA

Automated immunoassay platform
- Simoa Quanterix HD-X Analyzer

High-Throughput Cellular Screening System
- FLIPR Penta

Sequencing
- Hamilton liquid handler
- QIAcube HT instruments
- Viaflow,
- Tape Station
- PCR thermal cyclers,
- Illumina NextSeq550Dx
- Illumina NovaSeq6000

CLEMSON UNIVERSITY

Palmetto Cluster: The Palmetto Cluster is a 15.42 TFlop Dell PowerEdge 1950 server with 257 nodes, 8 cores, an Intel Xeon E5345 2.33 GHz x 2 processor, and 12 GB of memory.

UNIVERSITY OF SOUTH CAROLINA

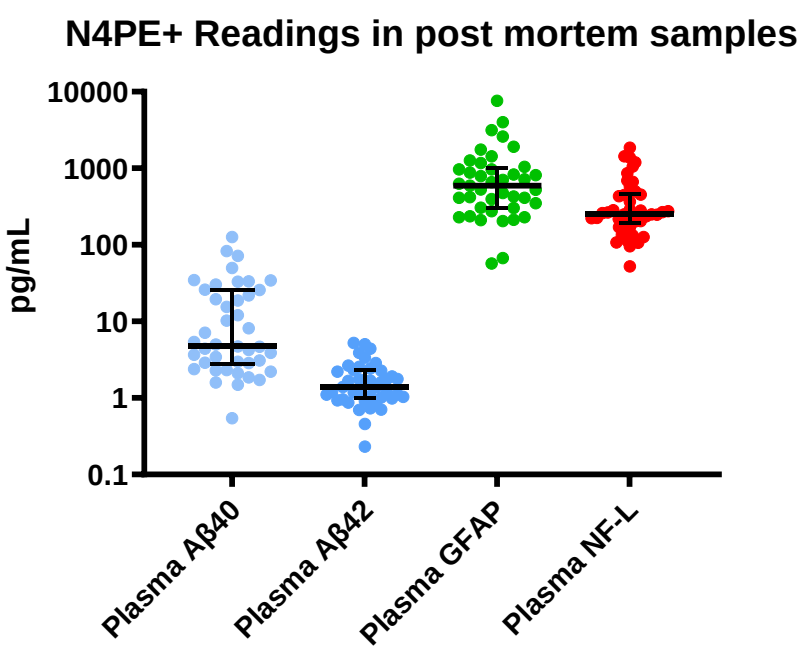
Nanopore Analysis
- Probe station with Warner Instruments amplifiers and interfaces for low-current nanopore measurements set up with Faraday cages in a low-noise environment.
- Elements miniaturized nanopore reader
- Northern Nanopore Instruments Spark-E2 nanopore fabrication unit

Microfluidics
- Lead Fluid Laboratory programmable precision syringe pump
- NMN-21 Three-axis micromanipulator
- Caltex BX3 HD Digital HD video microscope
- Class-100/1000 cleanroom

Molecular Characterization
- Opentrons OT-2 liquid handling robot for ELISA and multiplex assays
- Bruker Ultraflex III MALDI-TOF/TOF mass spectrometer
- Thermo Scientific LTQ Orbitrap XLTM Hybrid FT mass spectrometer
- Agilient 8453 UV-Vis
- Implen NanoPhotometer N60 UV/Vis spectrophotometer for nano volume

Purification
- Bio-Rad NGC Quest Plus Chromatography System

Progress Report



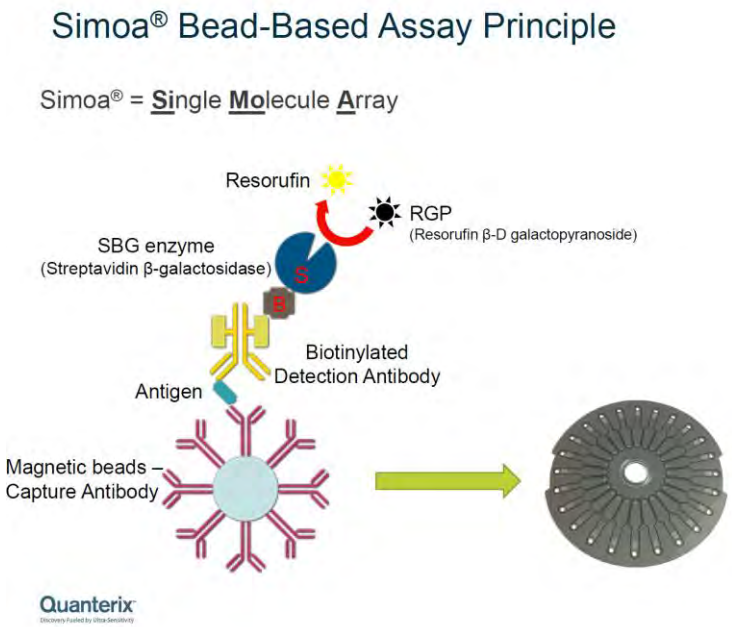
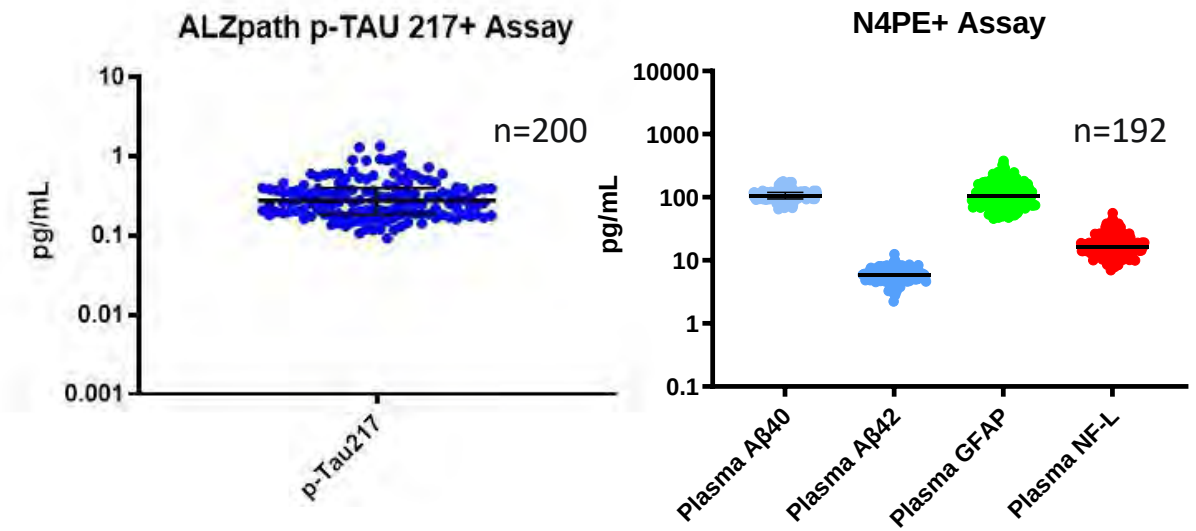


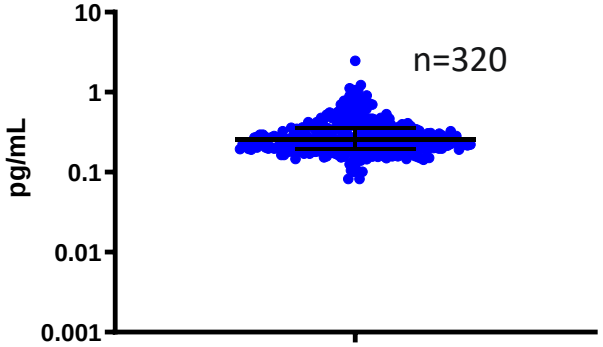
Fig. Endogenous sample reading: concentrations (pg/ml) were determined for EDTA plasma (n=43) from post-mortem AD/ADRD donors using the Simoa Human Neurology 4-Plex E (N4PE+) Advantage Plus Assay (Aβ40, Aβ 42, GFAP, NF-L) on the HD-X Quanterix platform. Bars depict median with interquartile range.

Imaging, Aging, Memory (IAM) Study
MUSC

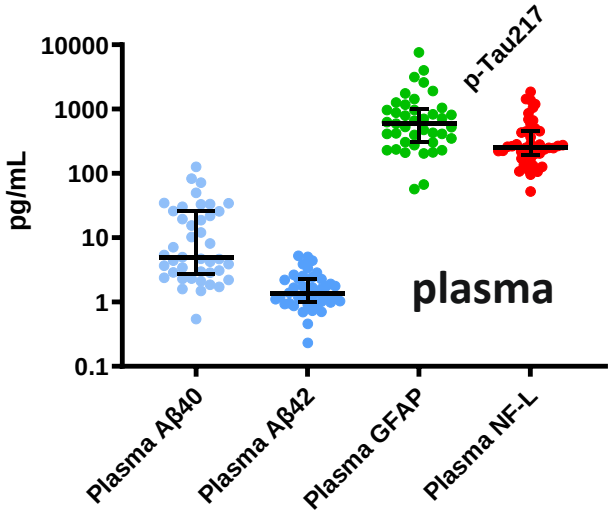
The Aging Brain Cohort (ABC) Study
USC

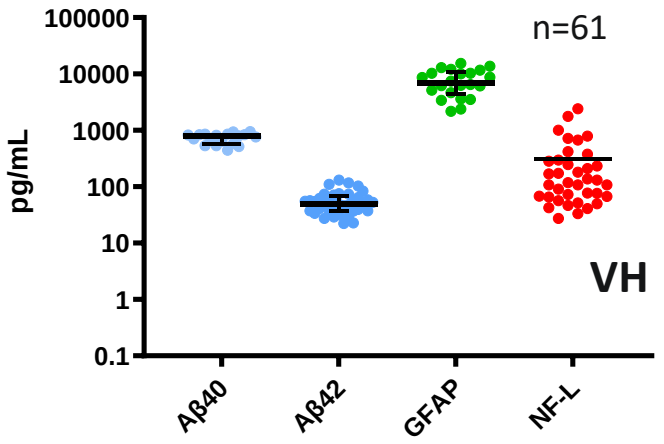
Post-mortem Study
MUSC





Endogenous sample reading: concentrations (pg/ml) were determined for samples using the Simoa Human Neurology 4-Plex E (N4PE+) Advantage Plus Assay (Aβ40, Aβ 42, GFAP, NF-L) or ALZpath p-Tau 217 Advantage Plus Assay on the HD-X Quanterix platform. Bars depict median with interquartile range.





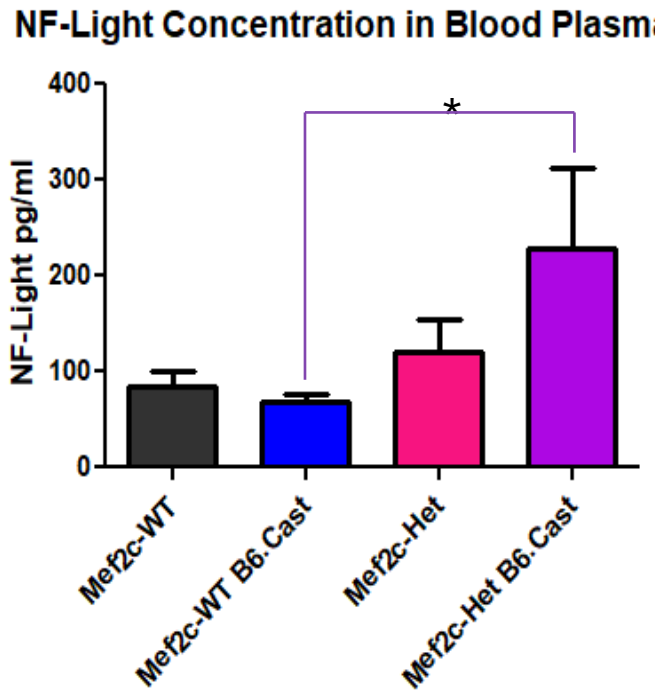
Blood Collection

Centrifugation

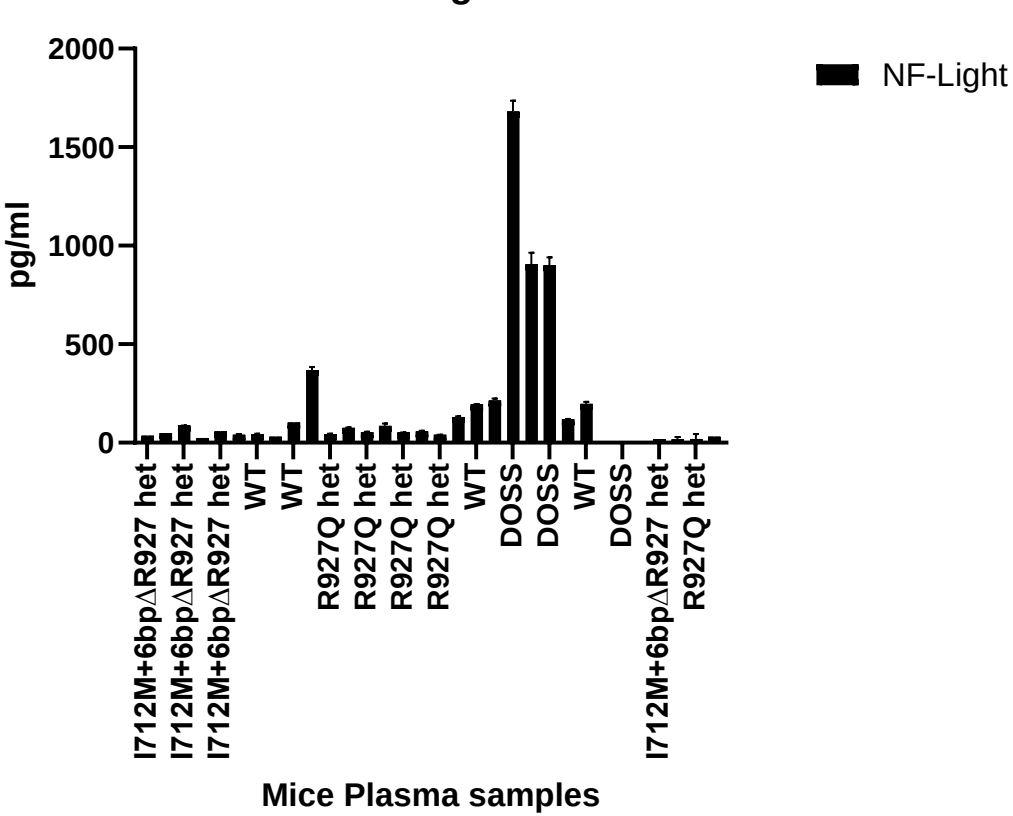
Load plasma into Quanterix HD-X

Hearing & Dietary Study
MUSC

Mouse/Rat study
BD-Tau

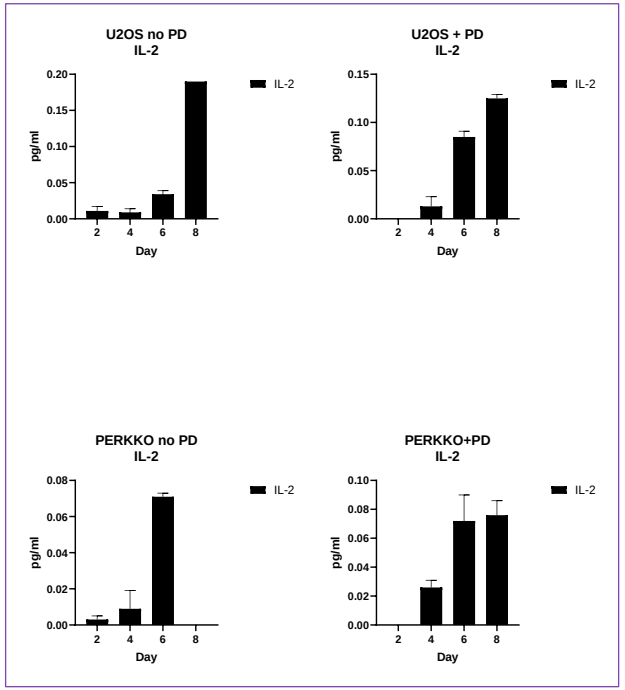


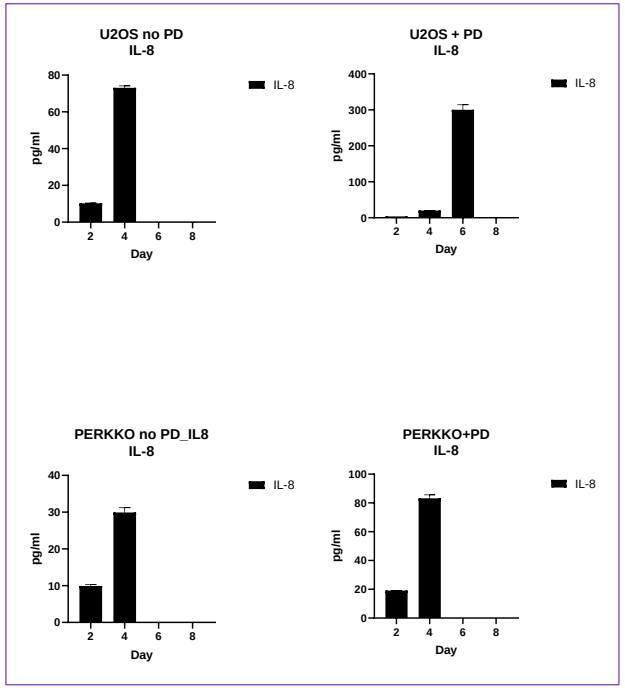
Mef2c-WT n=6
Mef2c-WT B6.Cast n=7
Mef2c-Het n= 5
Mef2c-Het B6.Cast n= 5

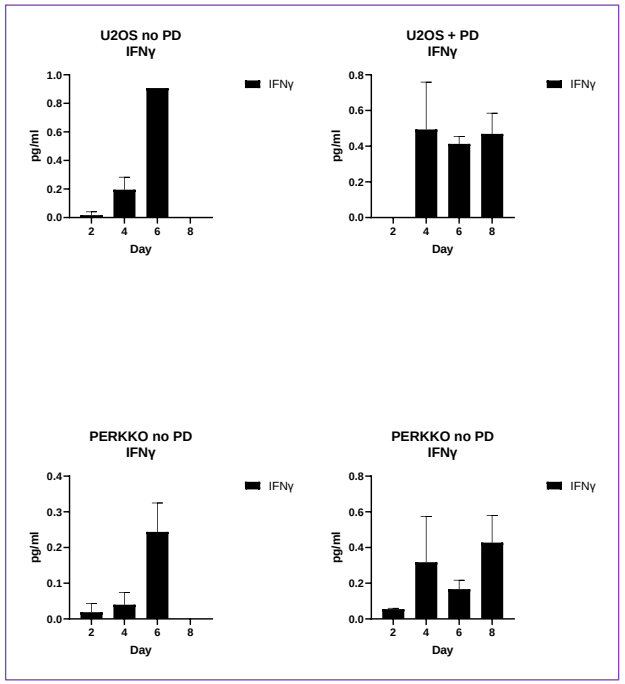


Cell lines ER-stress study

C4PC assay







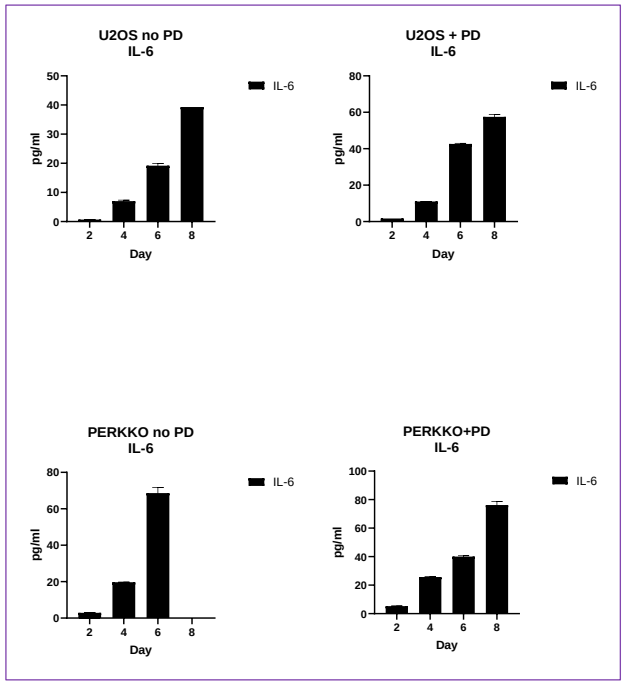


Figure. Endogenous sample readings. Concentrations (pg/ml) were determined for supernatants from U2OS or PERK KO cells treated for 2, 4, 6, or 8 days with or without palbociclib (PD0332991), a selective ATP-competitive inhibitor of CDK4/6. Measurements were performed using the Simoa Cytokine 4-Plex C (C4PC) Advantage PLUS Assay (A) IL-2, (B) IL-4, (C) IL-8 and (D) IFNγ on the HD-X Quanterix platform.

Quanterix®

PRODUCT ROADMAP

Products are in development and launch dates are subject to change without notice

	2025 Q1	2025 Q2	2025 Q3	2025 Q4	2026
 **HD-X**	IL-12p70 ✓ IL-22 ✓ IL-1b ✓ IL-10 ✓	Alpha-Synuclein (total)	pTau-205 pTau-212 MouseAb40/42 IL-11 YKL-40	IL-18 ApoE IL-17F Mouse GFAP	TDP-43*Adv+
 **SR-X** *All SR-X kits will be Advantage Plus*	pTau-181 ✓	N4PE ✓ N2PA ✓ GFAP ✓ N2PB ✓ N4PD ✓ C4PA	C4PB PSD-95 SNAP-25	IL-22 IL-12p70 Alpha-Synuclein (total)	

✓ *Indicates Launched*

Version 7_6.26.25

Mapping the Tau Cascade

New Insights from p-Tau 205 and p-Tau 212 for Disease Staging and Monitoring

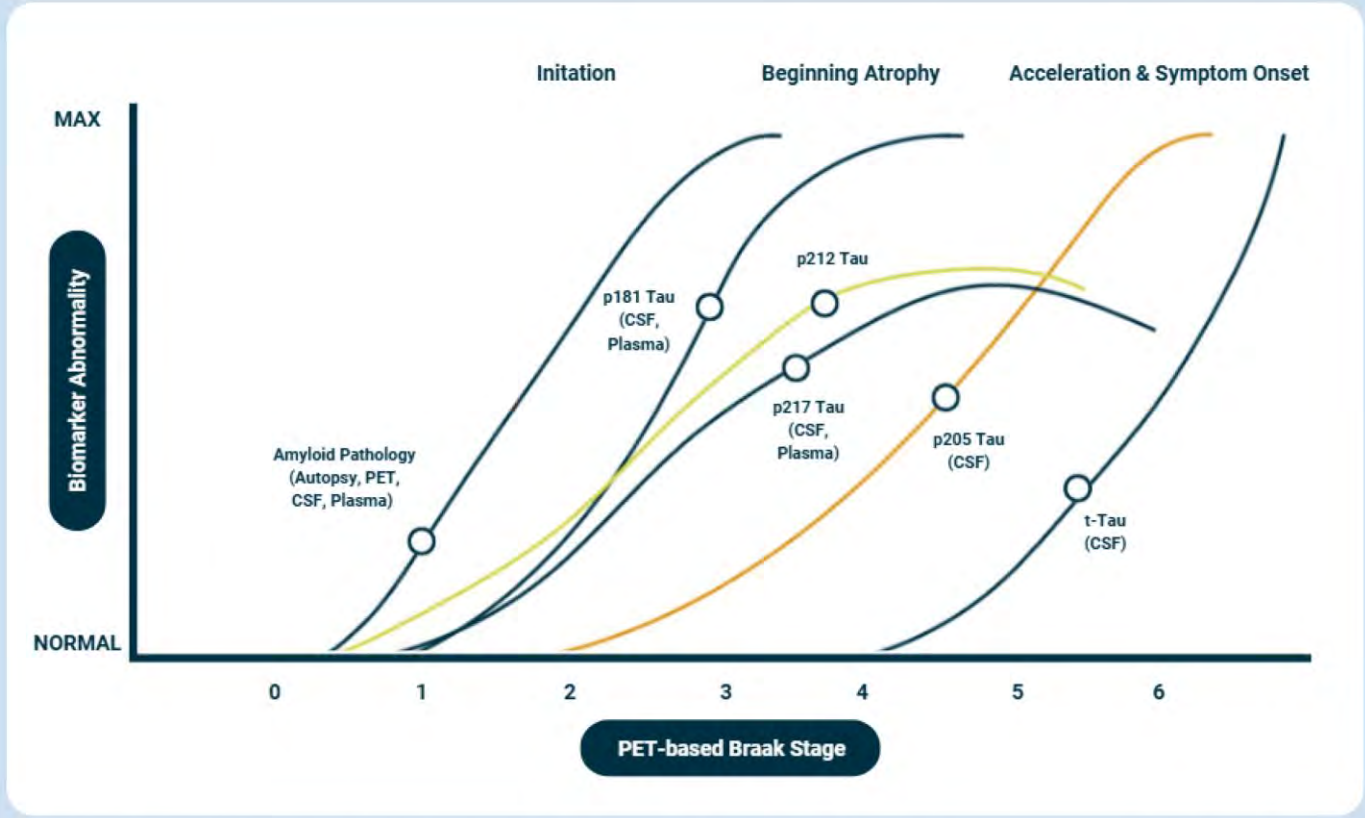


Figure 1. The evolving biomarker landscape in parallel with disease biology. Together, these markers refine our ability to stage pathology, align biomarker strategy to therapeutic mechanism, and monitor Alzheimer's progression with greater fidelity.

Enabling Therapeutic Discovery and Response Monitoring

The expanded tau biomarker portfolio supports therapeutic development strategies from early detection through late-stage intervention.

p-Tau 205 is especially well-suited for evaluating tau aggregation inhibitors and tracking downstream tangle resolution.

p-Tau 212 offers a pharmacodynamic lens into earlier intervention points, particularly for therapies targeting soluble tau species.

Next Steps

- Test remaining 200 Brain Bank samples (Plasma, CSF, VH - N4PE+, p-Tau217 Assays, WGS/WES)
- SPARK – ADRC Neurodegenerative biomarkers and cognitive training effect study (N4PE+, p-Tau217, BDNF), Clemson University
- Cognition, and mental health in long COVID study (N4PE+, p-Tau217), MUSC
- 100 Clinical Core participants will be recruited each year, and samples will be analyzed on the HD-X
- U01 submission
  - PAR-23-258: Analytical and Clinical Validation of Biomarkers for Alzheimer's Disease (AD) and AD-Related Dementias (ADRD) (U01 Clinical Trial Optional)

    Due Date: February, 2026

R03 (PI: J. McQuail) USC
R01 (MPI: J. Anker, S. Carroll, D. Pytel) Clemson, MUSC
R01 (MPI: F. Fan, D. Pytel) August University, MUSC

The Post and Courier
FOUNDED 1803 WINNER OF THE PULITZER PRIZE

SC patients with suspected Alzheimer's disease might soon get a blood test for answers

Dr. Steve Carroll (left) and Dr. Dariusz Pytel stand beside the Quanterix HD-X, which they'll use for Alzheimer's disease testing and research, at The Medical University of South Carolina,

Contact Us:

Scan the QR code to request a quote for our Quanterix HD-X services.

South Carolina Alzheimer's Disease Research Center

A statewide initiative of

MUSC Medical University of South Carolina

CLEMSON UNIVERSITY

UNIVERSITY OF South Carolina

Developing and testing innovative preventive and therapeutic strategies for mixed Alzheimer's disease and vascular dementia

Angela Murphy, PhD, Professor, USC SOM

Daping Fan, MD, PhD, Professor, USC SOM

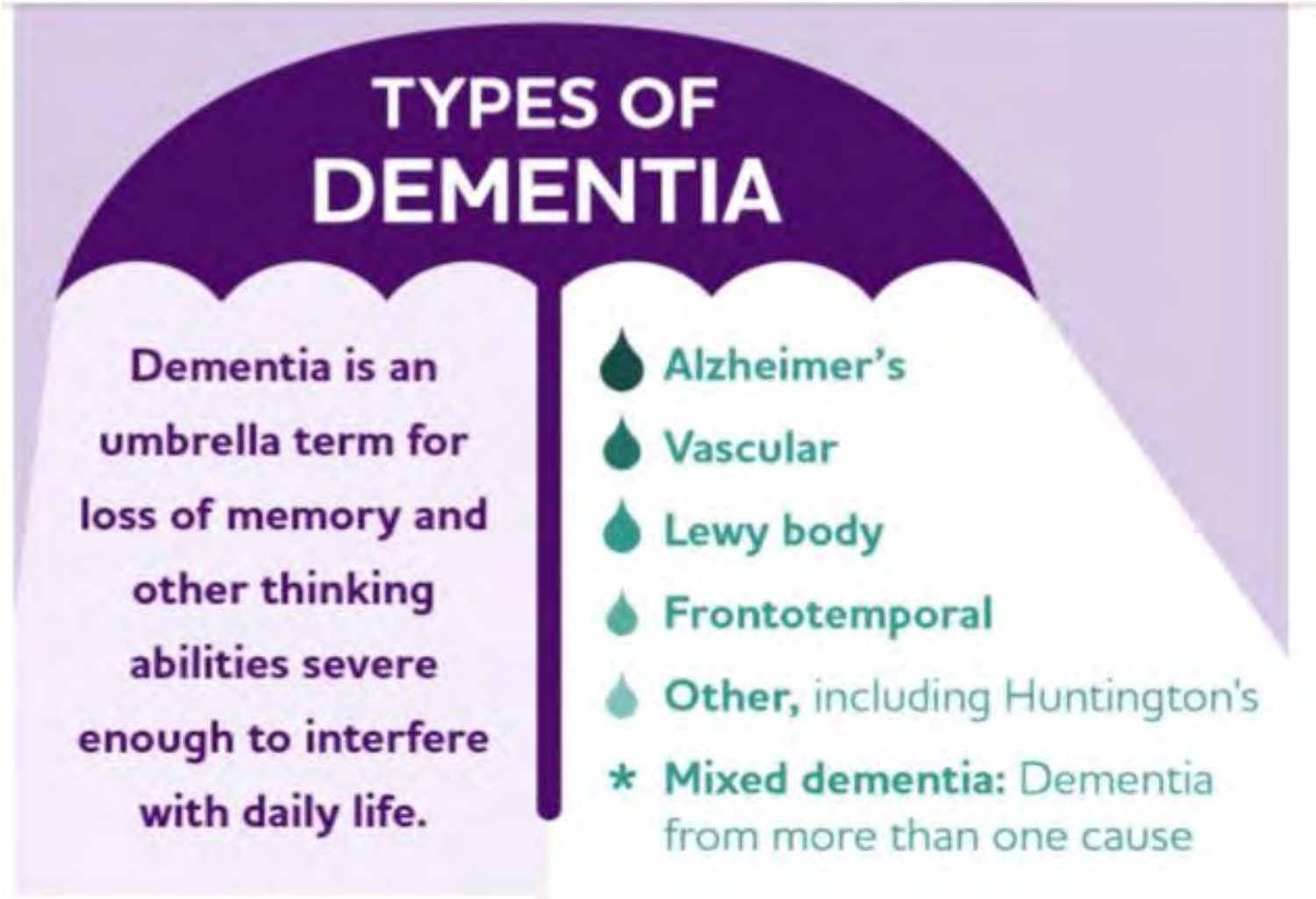
Disclosure

I am the Founder and CEO of AcePre LLC

Outline

- Background: Mixed Alzheimer's disease and vascular dementia
  - ***The pathophysiology of mixed Alzheimer's disease and vascular dementia***. Sarhan M, Wohlfeld C, Perry-Mills A, Meyers J, Fadel J, Murphy EA, Bonilha L, Fan D. *Theranostics*. 2025 Sep 3;15(18):9793-9818.
- Ongoing projects (preliminary data)
  - Novel mouse models for mixed AD/VaD
  - Human iPSC-derived brain organoids for modeling of mixed AD/VaD
  - Low-dose phytochemical cocktails for the prevention and treatment of mixed AD/VaD
- Acknowledgements

Background: Mixed AD/VaD



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Co-Director & Registry Manager

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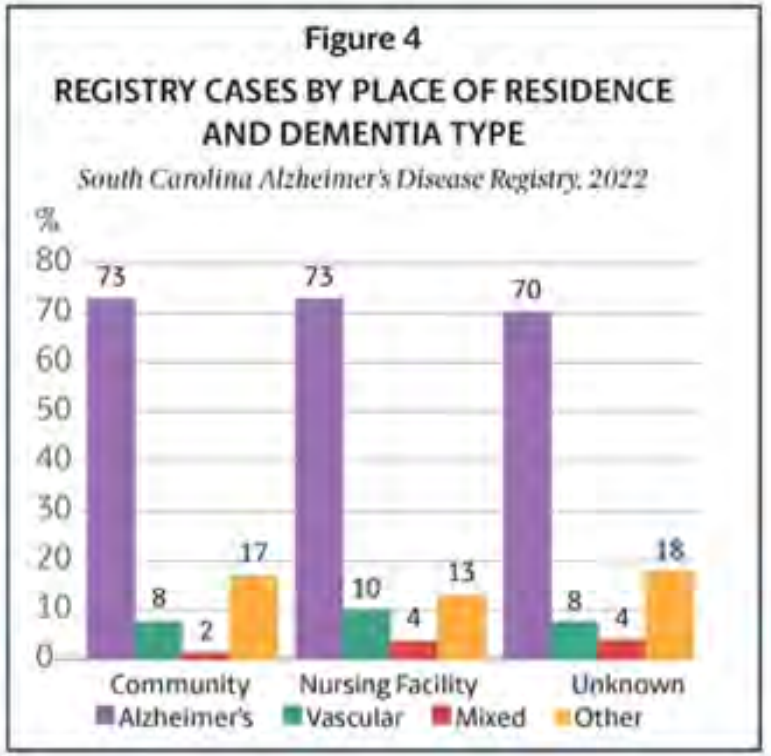
Co-Director & Dementia Dialogues® Manager

2022 Registry Data Report

South Carolina Population Prevalence of ADRD

- In 2022, the Registry maintained information on 125,538 individuals living with ADRD.
- Based on the Registry and 2022 population estimates from the United States Census:
  - 11% of South Carolinians age 65 or over have ADRD;
  - 55% of South Carolinians age 85 or over have ADRD;
  - ADRD prevalence rates vary notably among SC counties; and
  - African Americans are at notably higher risk of an ADRD diagnosis than are non-Hispanic whites. At ages 65 and older, for example, **African American South Carolinians are 32% more likely to have ADRD as are non-Hispanic whites.**

The prevalence of mixed Alzheimer's disease and vascular dementia is often significantly underestimated.



State of the Heart

HEART DISEASE IN SOUTH CAROLINA

BURDEN OF DISEASE:

About **680,000** Americans die each year from heart disease. Heart disease is a leading cause of death and disability in the United States.[1] The most common form of heart disease in the United States is coronary heart disease, which can lead to heart attack.[2]

Heart disease was the leading cause of death in South Carolina in 2023.

During 2023, **12,274** South Carolinians died from heart disease.

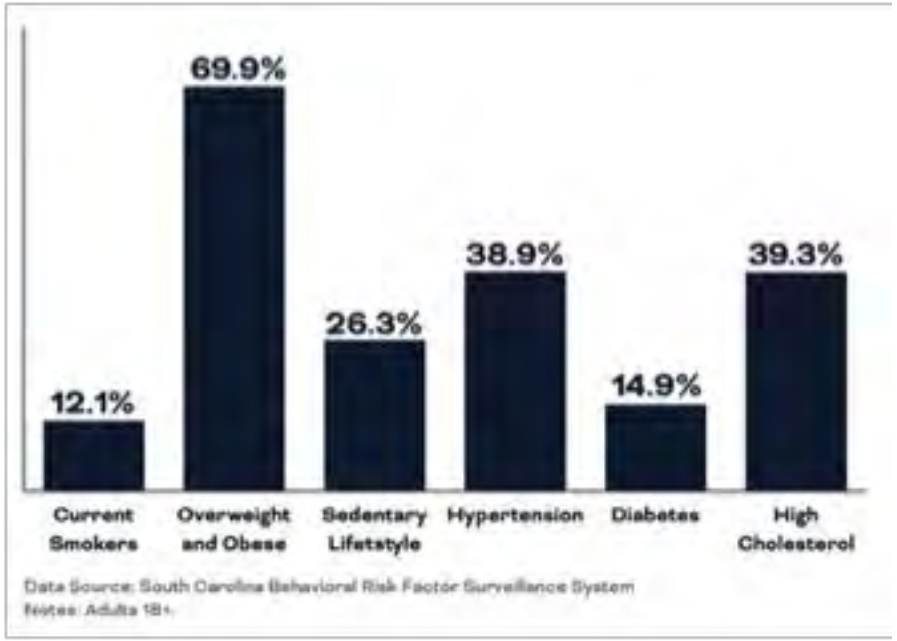
Heart disease accounted for **59,399** hospitalizations in South Carolina during 2023, with total hospitalization charges of more than **$5.9 billion**.

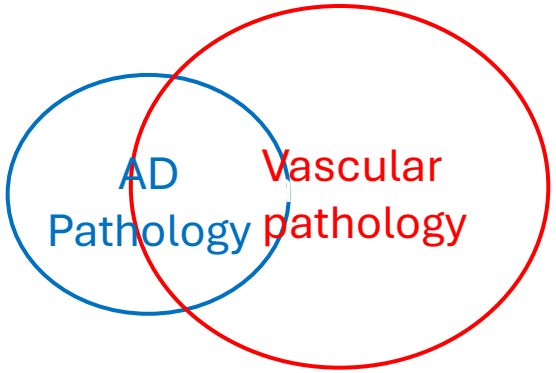
Stroke

IN SOUTH CAROLINA

BURDEN OF DISEASE FOR SOUTH CAROLINIANS:

- Stroke is a leading cause of serious, long-term disability in the United States.
- According to 2023 national data, South Carolina had the **twelfth highest** stroke death rate in the nation and is part of the "Stroke Belt," a group of Southeastern states with high stroke death rates.
- Stroke was the fourth leading cause of death in South Carolina, resulting in **2,974** deaths during 2023.
- African Americans are **46 percent** more likely to die from stroke than Caucasians in South Carolina.
- Stroke resulted in **18,777** hospitalizations in South Carolina in 2023. Of these, **65 percent** were less than 65 years old.





Research goals

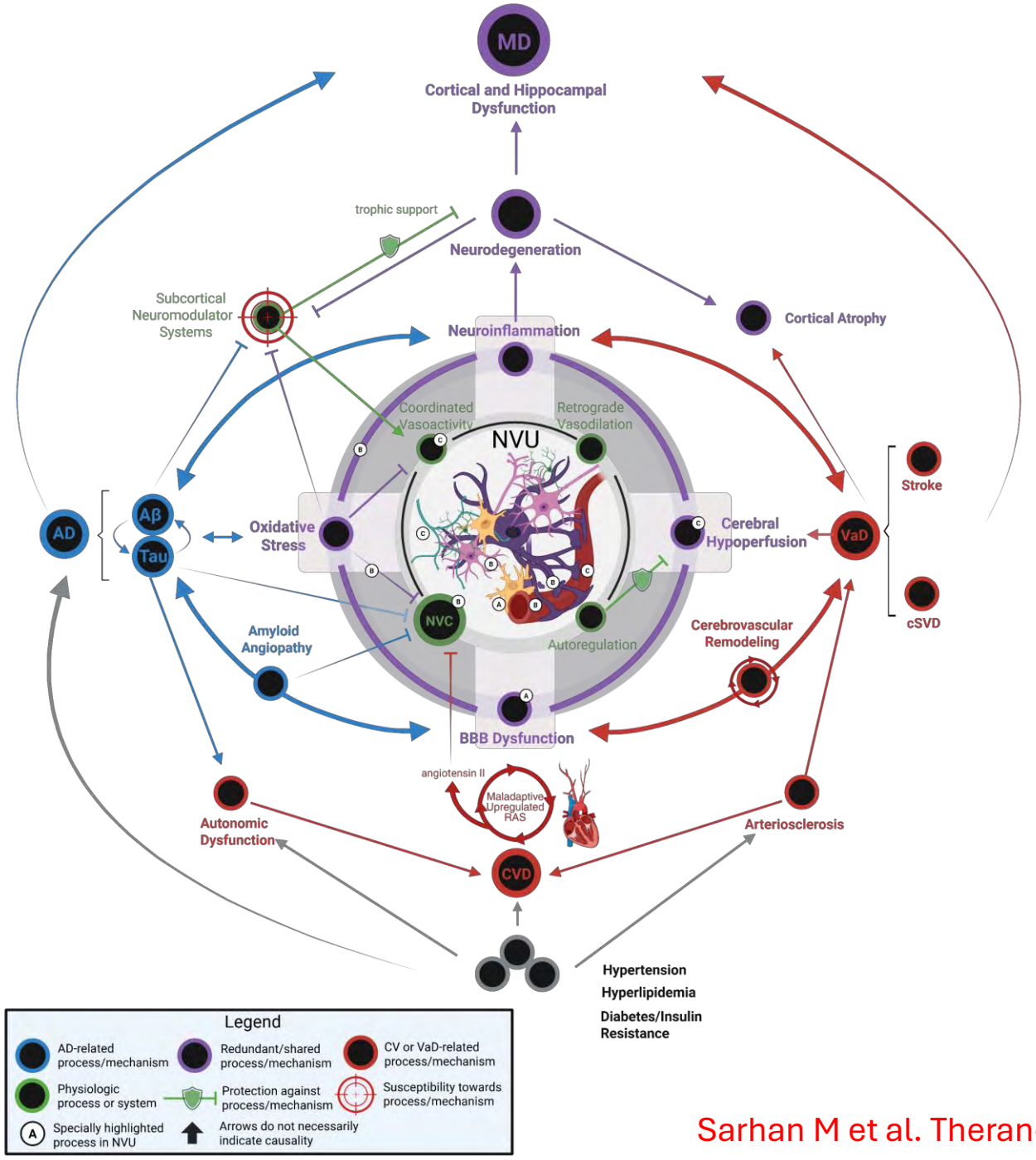
- **Basic research**: Elucidate the pathogenic mechanisms of mixed AD/VaD, particularly how vascular dysfunction accelerates AD progression

  Current stage: **model development**

- **Translational research**: Develop phytochemicals as preventive and therapeutic agents for mixed AD/VaD

  Current stage: ***in vitro* compound screening**

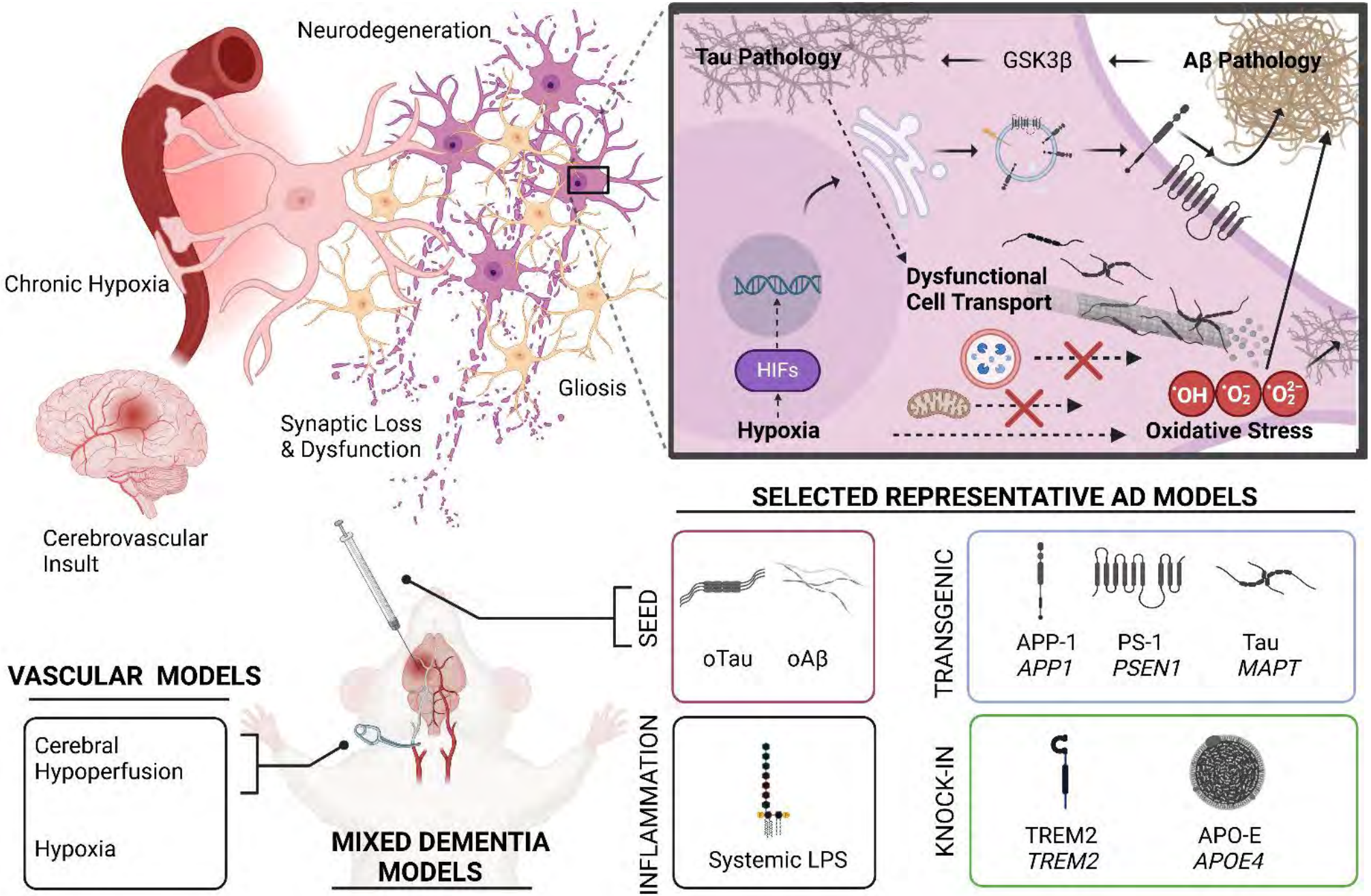
Entangled pathogenic pathways leading to mixed AD/VaD



Our hypothesis: Cerebral microvascular endothelial cell (CMECs) senescence and dysfunction mediate the crosstalk between AD and VaD pathologies; therefore, protection of CMECs is an effective strategy for the prevention and treatment of AD/VaD.

Sarhan M et al. Theranostics, 2025

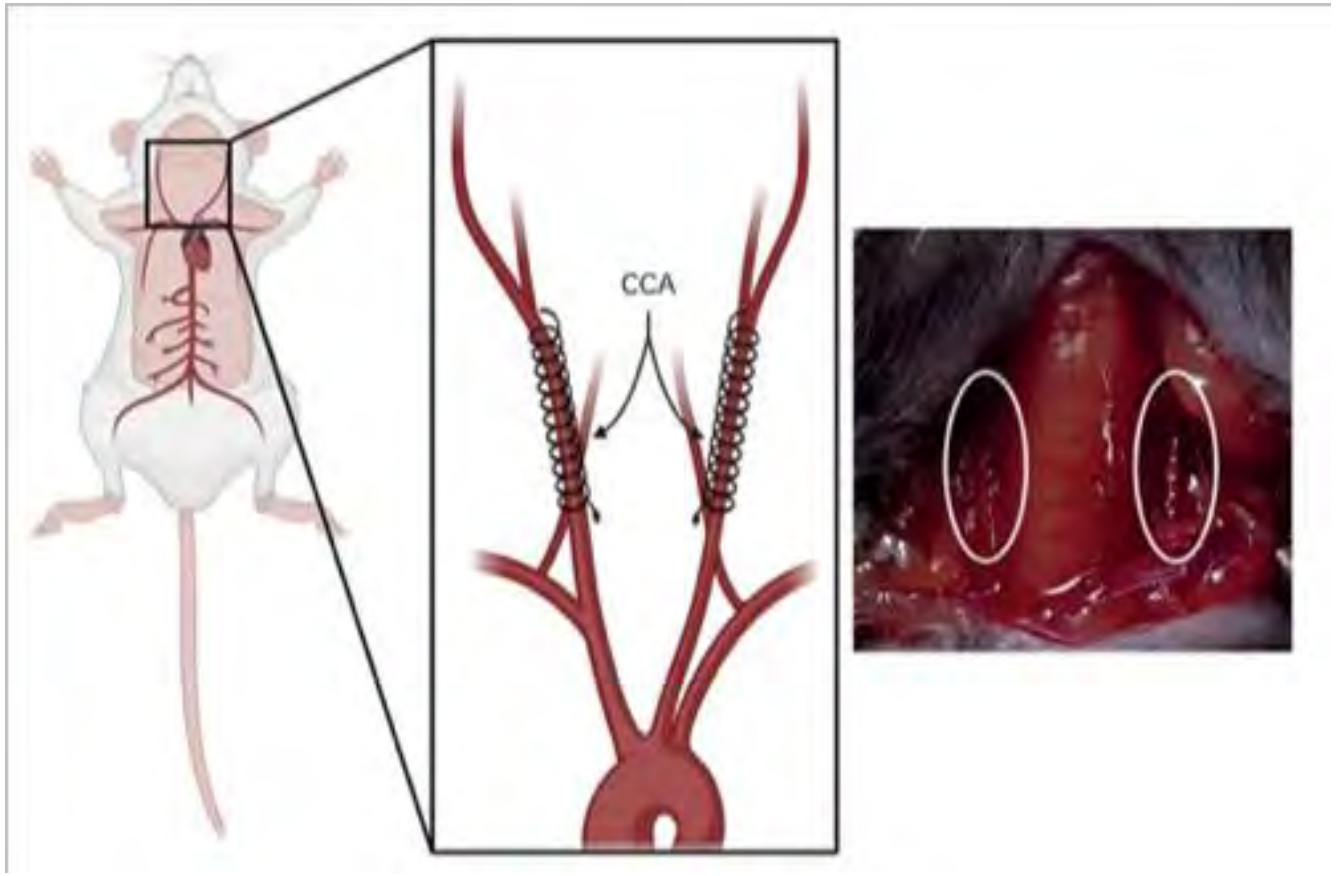
Establish mouse models for mixed AD/VaD

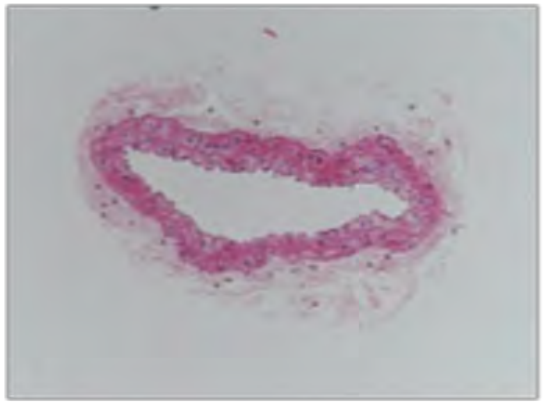


Sarhan M et al. Theranostics, 2025

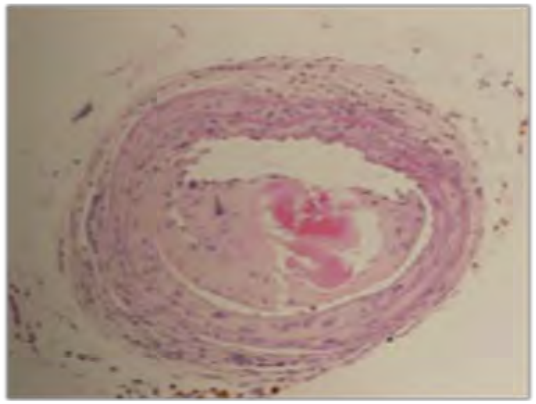
AD/VaD mouse model 1: 3xTg-AD/BCAS

- 3xTg-AD mice: Includes three human genetic mutations, APP Swedish, PSEN1 M146V, and tau P301L, that lead to the formation of both amyloid plaques and tau tangles.
- BCAS: Bilateral common carotid artery stenosis, leads to chronic cerebral hypoperfusion

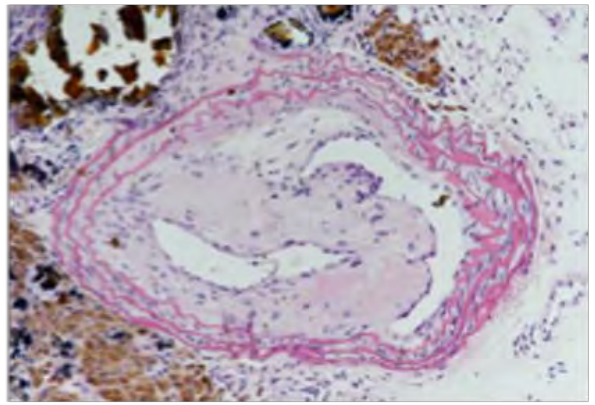




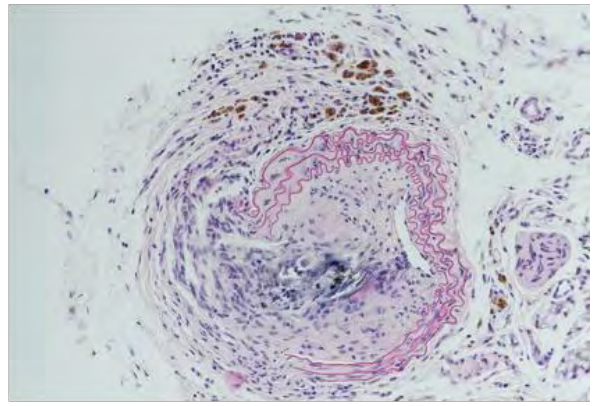
Control



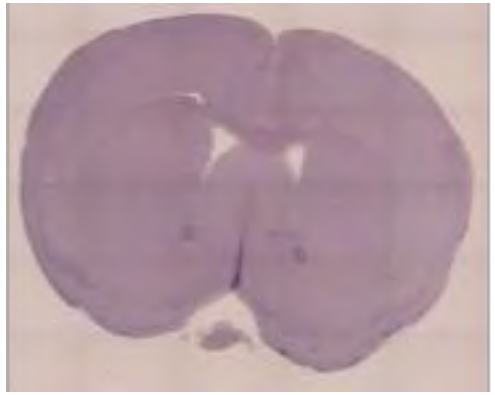
2 months post-BCAS



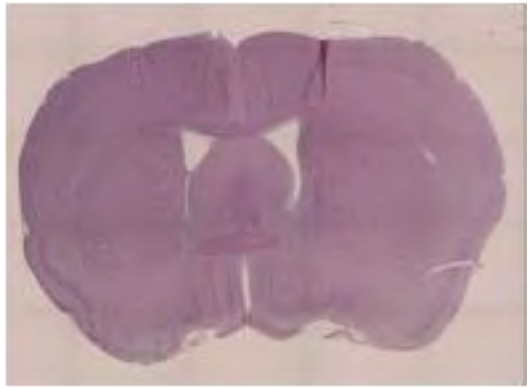
3 months post-BCAS



4 months post-BCAS

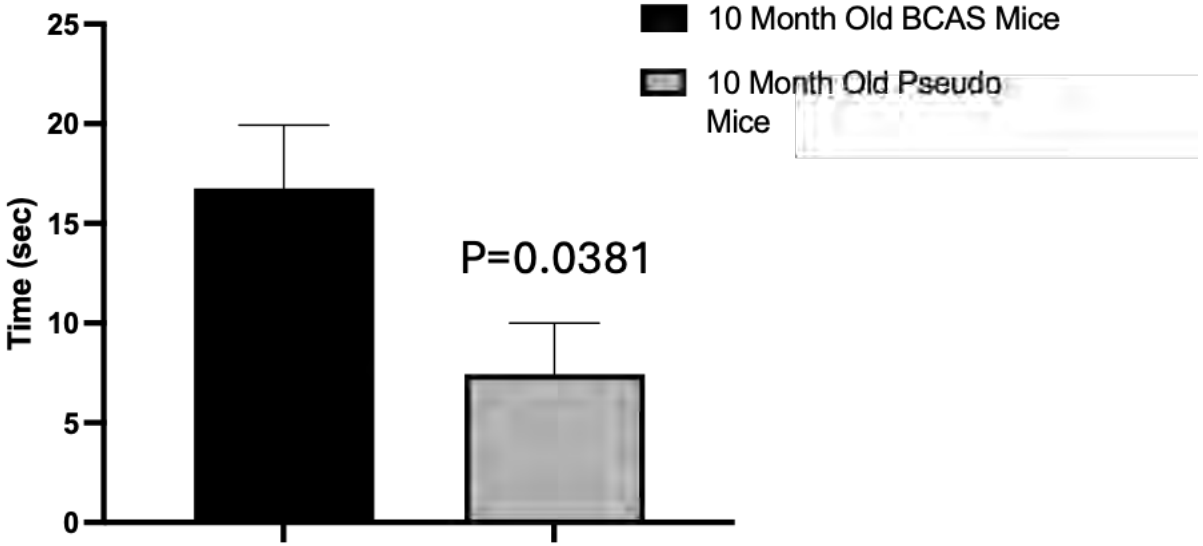


Pseudo



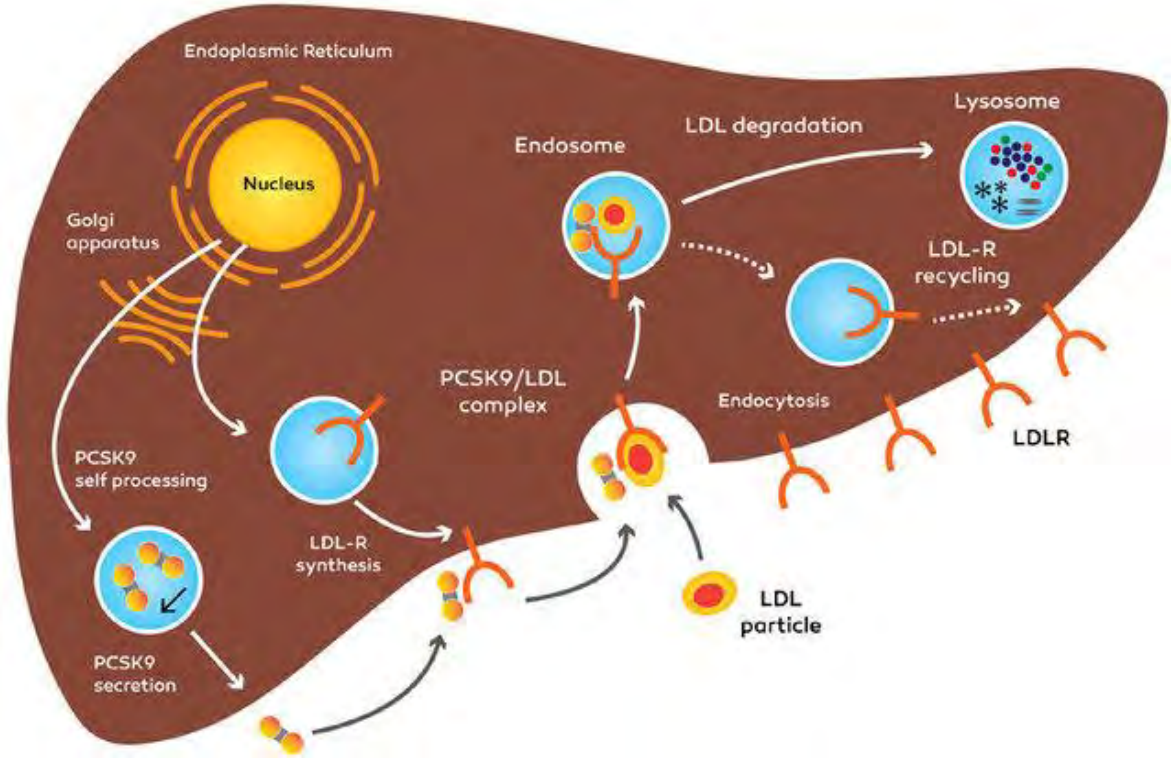
4 months post-BCS

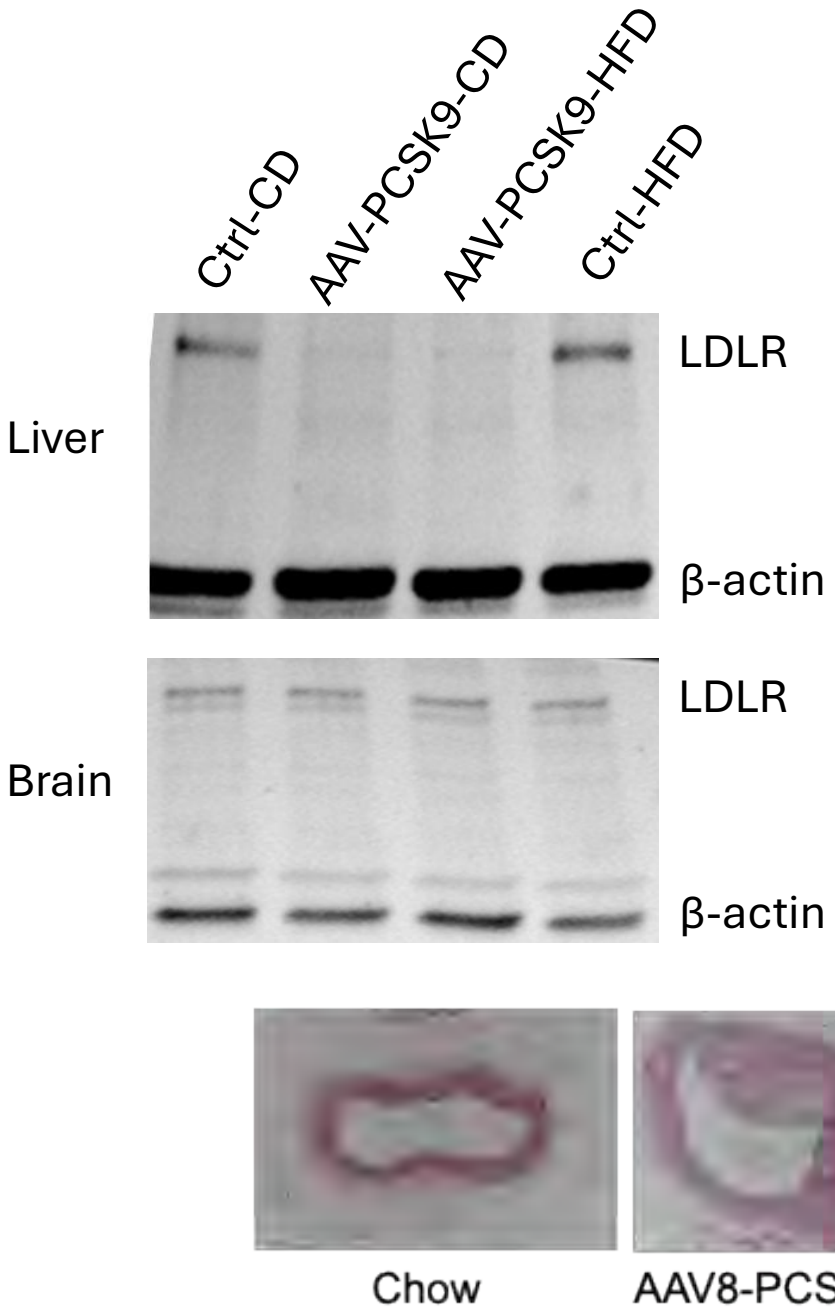
Primary latency in reversal to original target

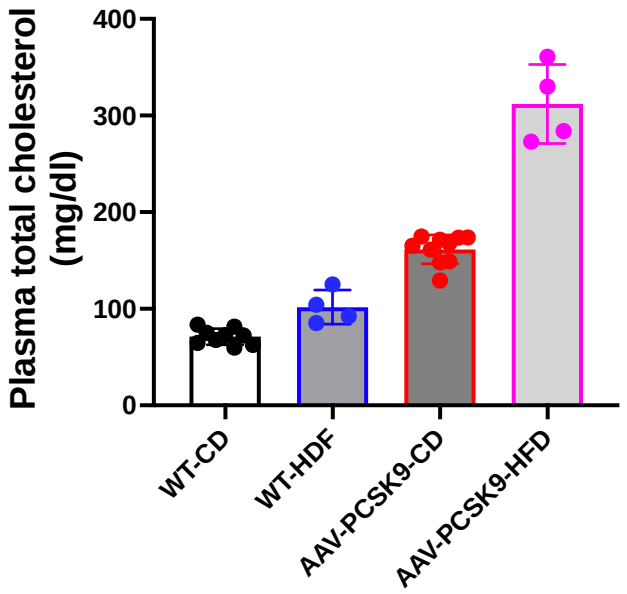


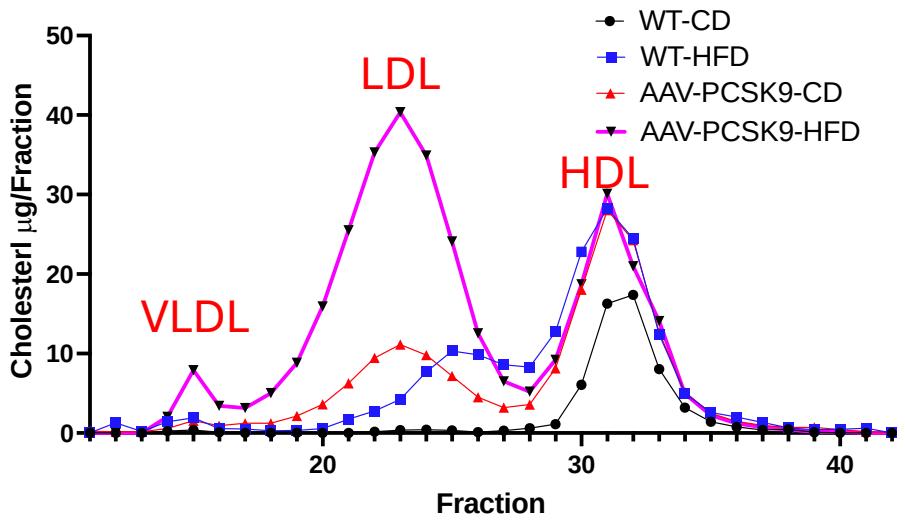
AD/VaD mouse model 2: 3xTg-AD/PCSK9

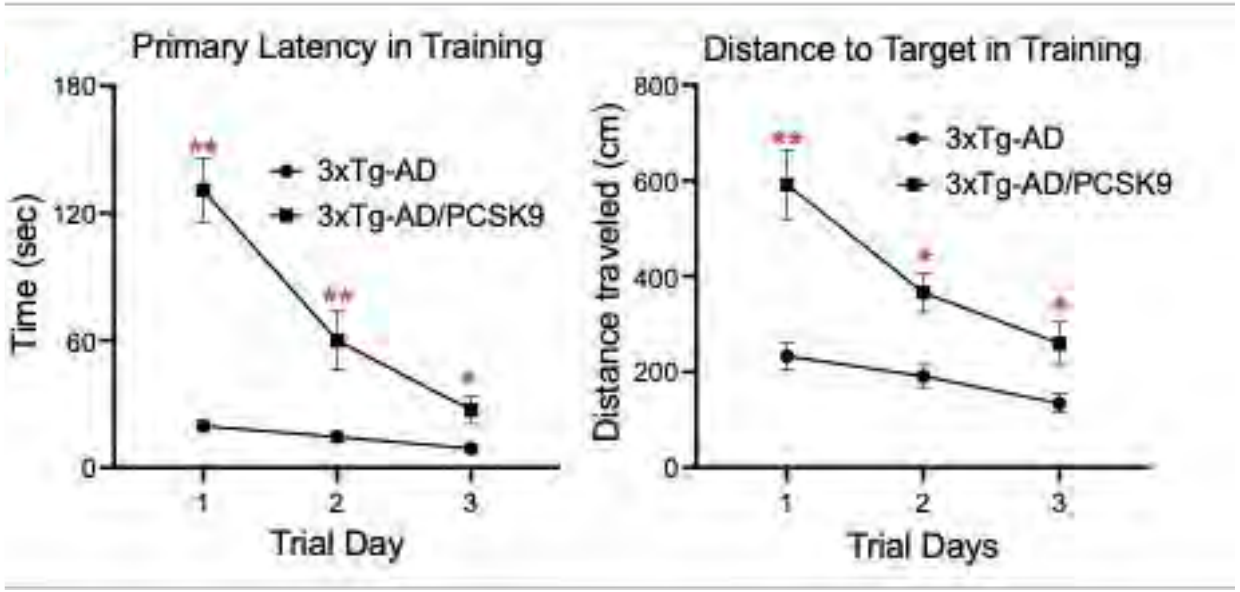
- 3xTg-AD mice
- AAV8-PCSK9 injection
- AAV8 homes to the liver
- Liver LDLR reduction
- Brain LDLR/LRP not compromised
- With or without high-fat diet
- Hyperlipidemia
- Oxidized LDL
- Arteriosclerosis



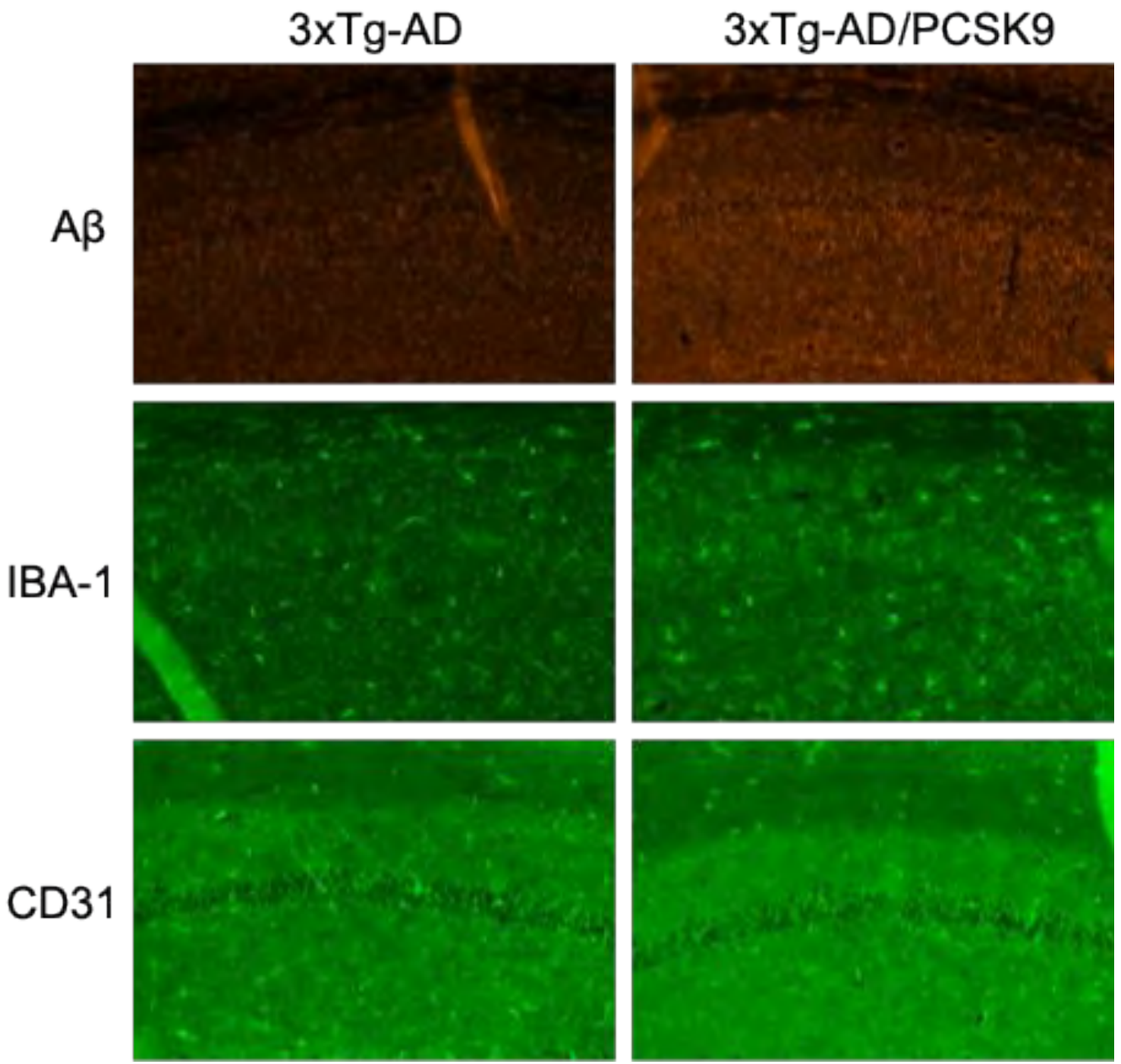

Ctrl-CD
AAV-PCSK9-CD
AAV-PCSK9-HFD
Ctrl-HFD
Liver
LDLR
β-actin
Brain
LDLR
β-actin
Chow
AAV8-PCSK9/HFD


Plasma total cholesterol (mg/dl)
400
300
200
100
0
WT-CD
WT-HDF
AAV-PCSK9-CD
AAV-PCSK9-HFD


WT-CD
WT-HFD
AAV-PCSK9-CD
AAV-PCSK9-HFD
LDL
HDL
VLDL
Cholesterl μg/Fraction
50
40
30
20
10
0
20
30
40
Fraction

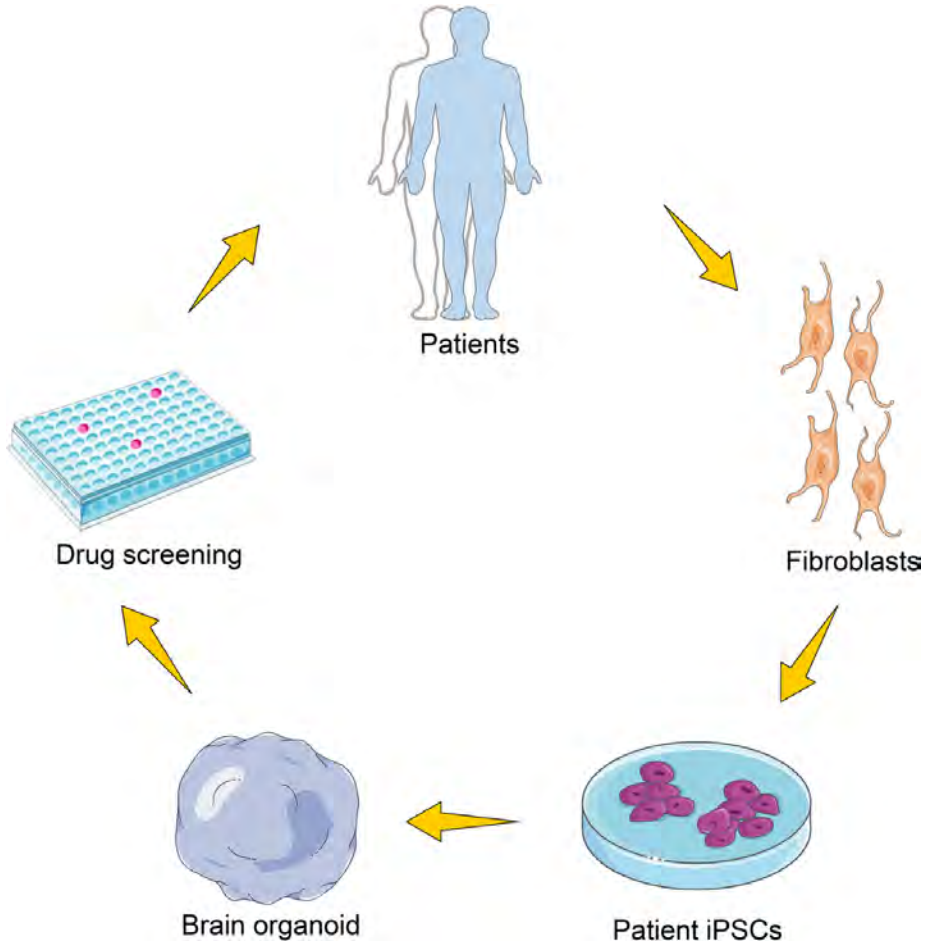

Primary Latency in Training
Time (sec)
180
120
60
0
3xTg-AD
3xTg-AD/PCSK9
1
2
3
Trial Day
Distance to Target in Training
Distance traveled (cm)
800
600
400
200
0
3xTg-AD
3xTg-AD/PCSK9
1
2
3
Trial Days

Hyperlipidemia accelerated Aβ deposition, increased microglia activation, and resulted in rarefaction in 3xTg-AD mice



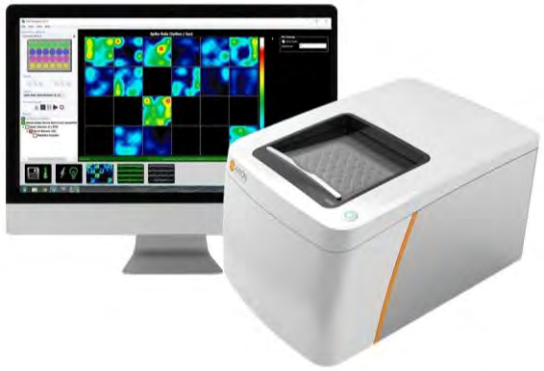
Human iPSC-derived brain organoids

- Small, three-dimensional structures; grown from human induced pluripotent stem cells; mimic features of the human brain
- Model human cells, cell-cell interactions, can be vascularized
- Enable studying human specific pathogenic pathways
- Platform for high-throughput drug screening

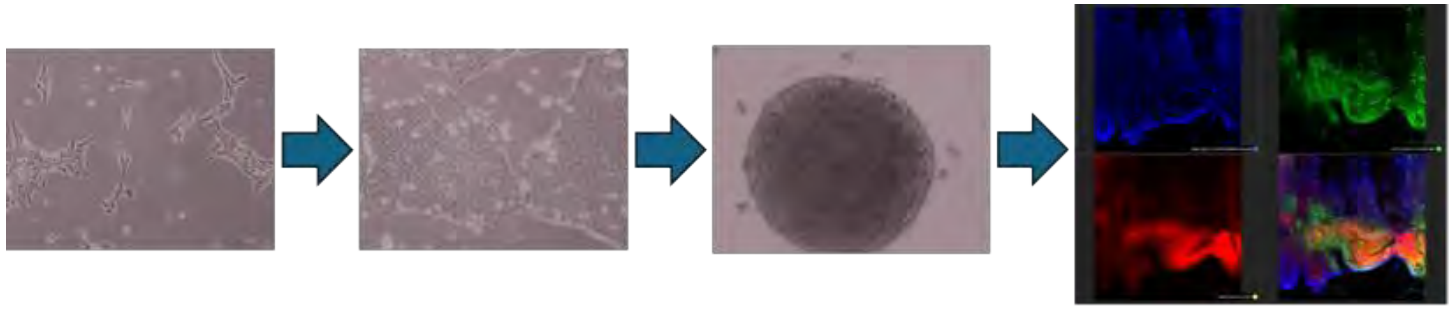


Human iPSC-derived organoid generation and characterization

Celvivo ClinoStar



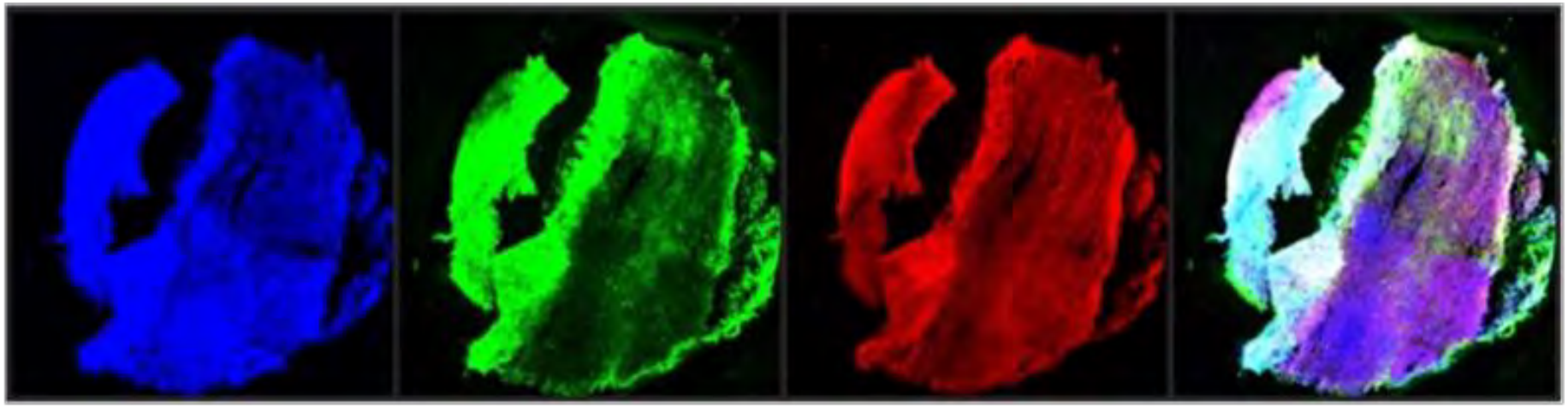
Maestro Edge MEA



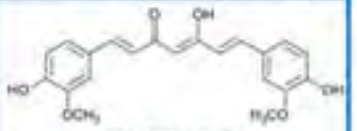
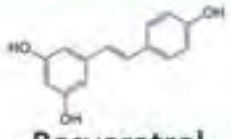
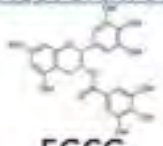
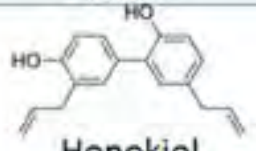
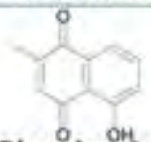
iPSC expansion

EB formation and organoid generation

Blue: DAPI (Nuclei)
Green: TUJ1 (Neurons)
Red: PAX6 (Neural progenitor cells)



Phytochemical screening

Source	Phytochemical
 Turmeric	 Curcumin
 Grapes	 Resveratrol
 Tea	 EGCG
 *Magnolia*	 Honokiol
 *Pumblago*	 Plumbagin

- Goal: To develop phytochemicals and low-dose phytochemical cocktails for AD/VaD prevention and treatment.
- Phytochemicals: Naturally occurring plant compounds; plants' defense arsenal and homeostasis guards.
- Health benefit: Antimicrobial, antioxidant, anti-inflammatory, immune homeostasis, etc.
- Mechanisms: Act on multiple cell types via multi-targets and multi-pathways
- Low water solubility, low bioavailability, (low toxicity?)
- Modern agriculture, food processing, and food choice, cooking methods → we are getting much less active phytochemicals from food than our ancestors.
- Phytochemical stacking: Achieve efficacy synergy while avoiding toxicity superposition.

Phytochemicals with potential benefit against mixed AD/VaD pathogenesis

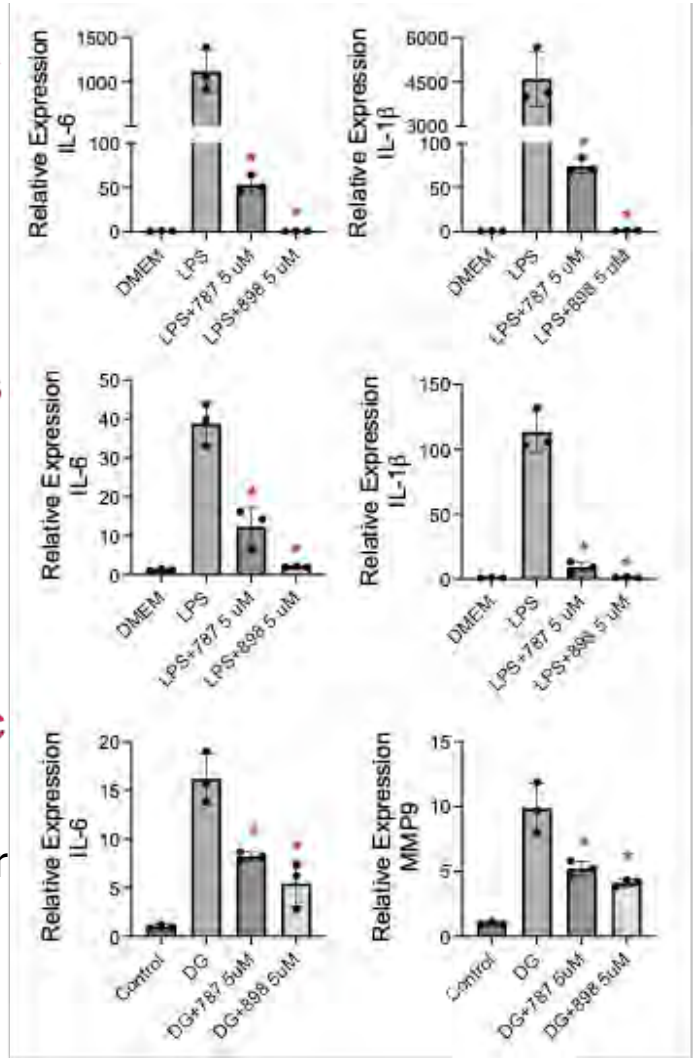
Compound	Antioxidant Effects	Anti-inflammatory Effects	Other MD-Relevant Effects
Resveratrol	Nrf2 ↑ (SOD, catalase, GPx, HO-1)	IKK/NF-κB ↓; SIRT1-p65 deacetylation	↑ non-amyloidogenic APP; ↓ tau-P; ↑ eNOS/NO
Curcumin	Keap1–Nrf2 disruption → HO-1, GSH up	IκB stabilization → NF-κB ↓; microglia ↓	↓ Aβ (BACE1/γ-sec); ↓ tau-P (GSK-3β/PP2A); ↑ eNOS activity
EGCG	SOD ↑; MDA ↓	NF-κB, microglia ↓; PKC modulation	↓ Aβ aggregation (BACE1/γ-sec); ↑ sAPPα; ↑ PI3K/Akt/eNOS → vasodilation
Quercetin	Nrf2/ARE activation; ROS ↓;lipid peroxides ↓	IκBα stabilization → NF-κB ↓; COX-2 ↓	Aβ & tau aggregation ↓; AChE inhibition; improves cell survival & behavior
Xanthohumol (XN)	Direct ROS scavenging; Nrf2 ↑; MDA ↓	NF-κB, NF-AT, AP-1 ↓	↓ Aβ plaques (BACE1, cholinesterase); ↓ tau-P; limits VSMC proliferation
Luteolin	ROS ↓; SOD & catalase ↑; HO-1, NQO1 ↑	IκBα stabilization; JNK/AP-1 ↓	↓ Aβ & tau pathology; improves memory in TBI & AD models
Berbamine HCl	Nrf2 ↑ (PC12); ORAC/SOAC activity	Cytokines ↓ (LPS/CoV models); autophagy ↑	↓ Aβ aggregation & NFTs; improves spatial memory
Huperzine A	nAChR–NF-κB inhibition; ROS ↓	AChE ↓ → NF-κB ↓	↑ non-amyloidogenic APP; ↓ tau-P; ↑ CBF; ↓ infarct size
N-Acetylcysteine	GSH precursor; peroxynitrite scavenging	IKK/NF-κB ↓; iNOS/NO ↓	↓ Aβ toxicity; ↑ neuronal survival; ↓ oxidative stress & infarct size
Octyl Gallate (OG)	ROS scavenging (in vitro)	Cytokines ↓	Potential vascular protection; data still preliminary
Britannin	ROS generation ↓ (cell models)	NF-κB p65 & NLRP3 ↓	Early Aβ/tau inflammation ↓; needs further validation
Sulforaphane (SFN)	Nrf2–ARE activation → ↑ HO-1, NQO1, SOD, GPx; ↓ ROS, MDA; preserves BBB integrity	Reduces oxidative-stress driven inflammation; lowers apoptosis markers	↓ Aβ (BACE1/PS-1 ↓);↓ Tau protein expression; ↓ infarct volume in ischemia; improves cognition in AD and VCI models

Phytochemical screening: anti-inflammatory activity and endothelial cell protection

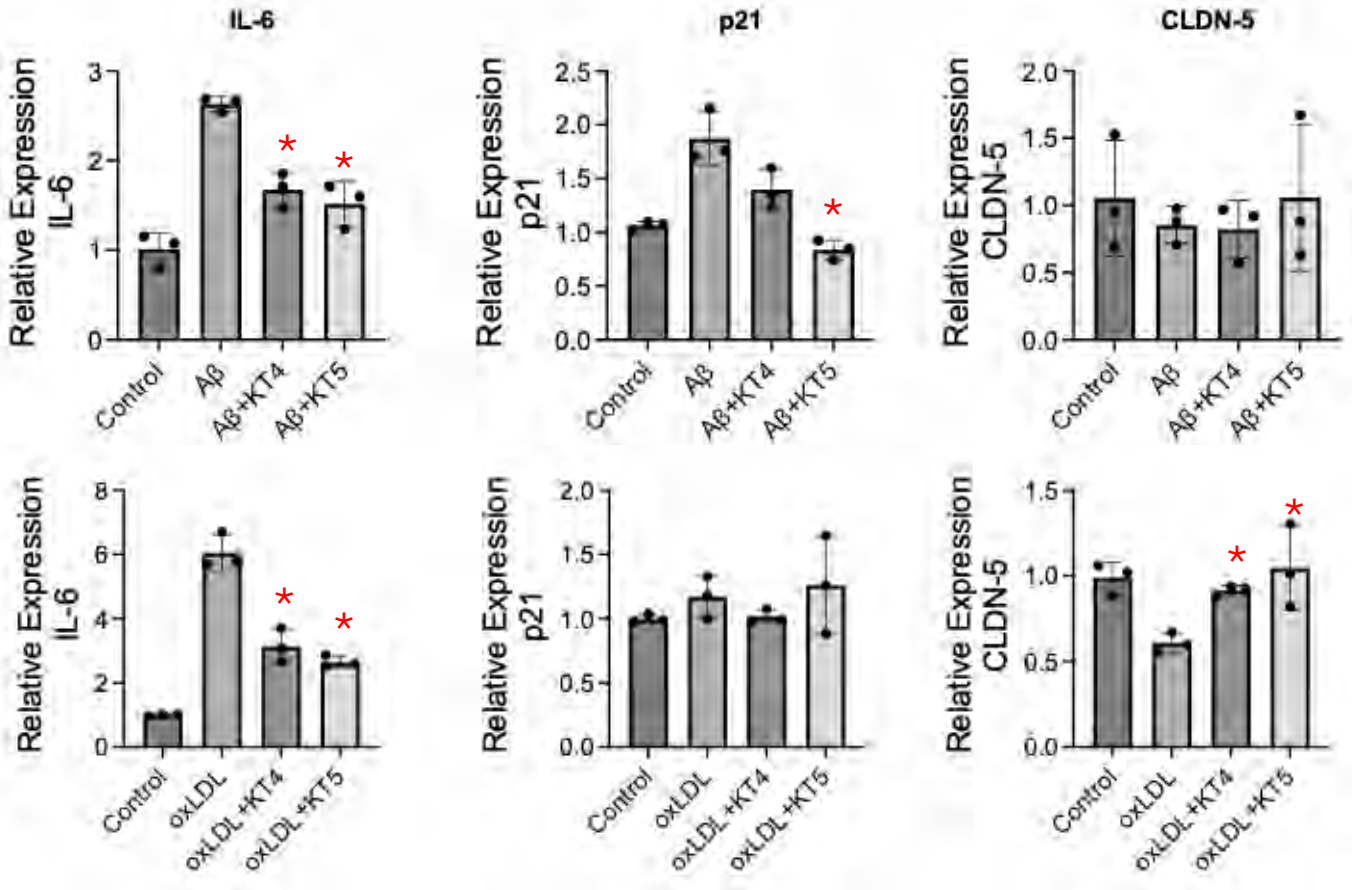
Mouse primary macrophages

Mouse primary microglia

Human cerebral microvascular endothelial cells



Human cerebral microvascular endothelial cells (hCMECs)



Kantrum-4 (KT4) and KT5 @ 2 μM

Future directions

- Further characterize the mouse models through IHC, high-parameter flow cytometry, scRNA-seq, spatial transcriptomics, behavioral tests, etc
- Generate vascularized human brain organoids with microglia incorporation
- Preclinical (using above models) and clinical development of lead phytochemical compounds and cocktails

Acknowledgements

SC ADRC Molecular Biology Group

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Personalized Approach to Brain Health & AD/ADRD

John R. Absher, MD, FAAN

October 10, 2025

Basic Thesis

- Basic sciences get at mechanisms
- Clinical sciences bring findings to people
- Epidemiology assesses populations
- Translational sciences bridge the gaps
- Optimizing brain health and addressing Alzheimer's Disease and Related Dementia Syndromes (AD/ADRD) requires a team

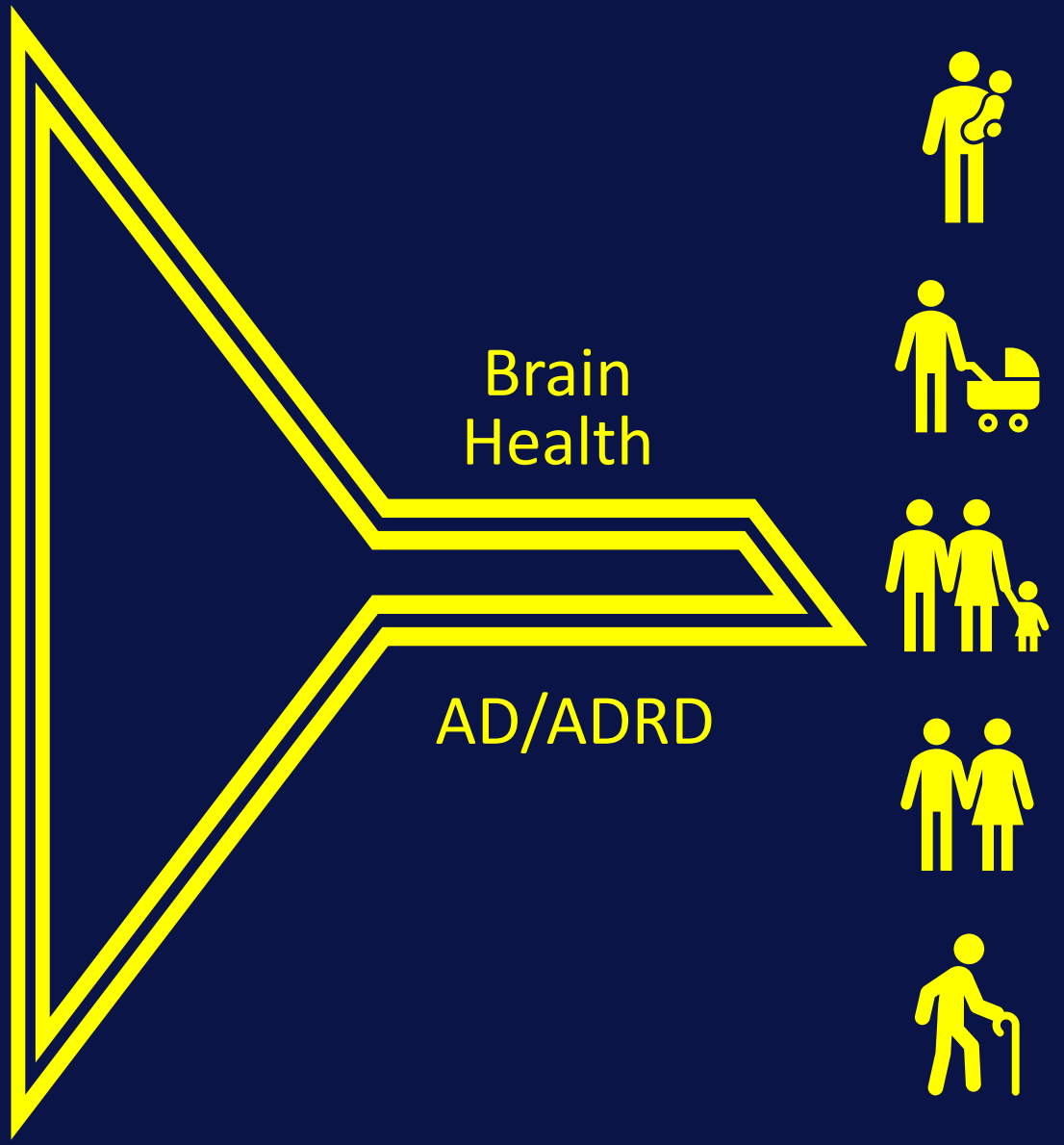
Neuroimaging is a cross-cutting tool

Background: The Goal is Brain Fingerprints

- Unique
- Clues to past actions
- Show effects of trauma
- Impacted by disease
- Influence “detectives”
- Often determine outcomes

Historical Factors Impacting Brain Health

- **Age, Sex, Race**
- Education: timing, quality
- **Diseases/disorders**
- **Geography**
- **Health care**: access, **quality**
- Immunizations/vaccinations
- Occupation/avocation
- Social/emotional support
- Self-care
  - Exercise/activity level
  - Oral health
  - ETOH/substance use
  - Sleep
  - Nutrition/diet
- Toxins/**environment**
- **Trauma** (all types)



Biomarkers Contribute to Fingerprints

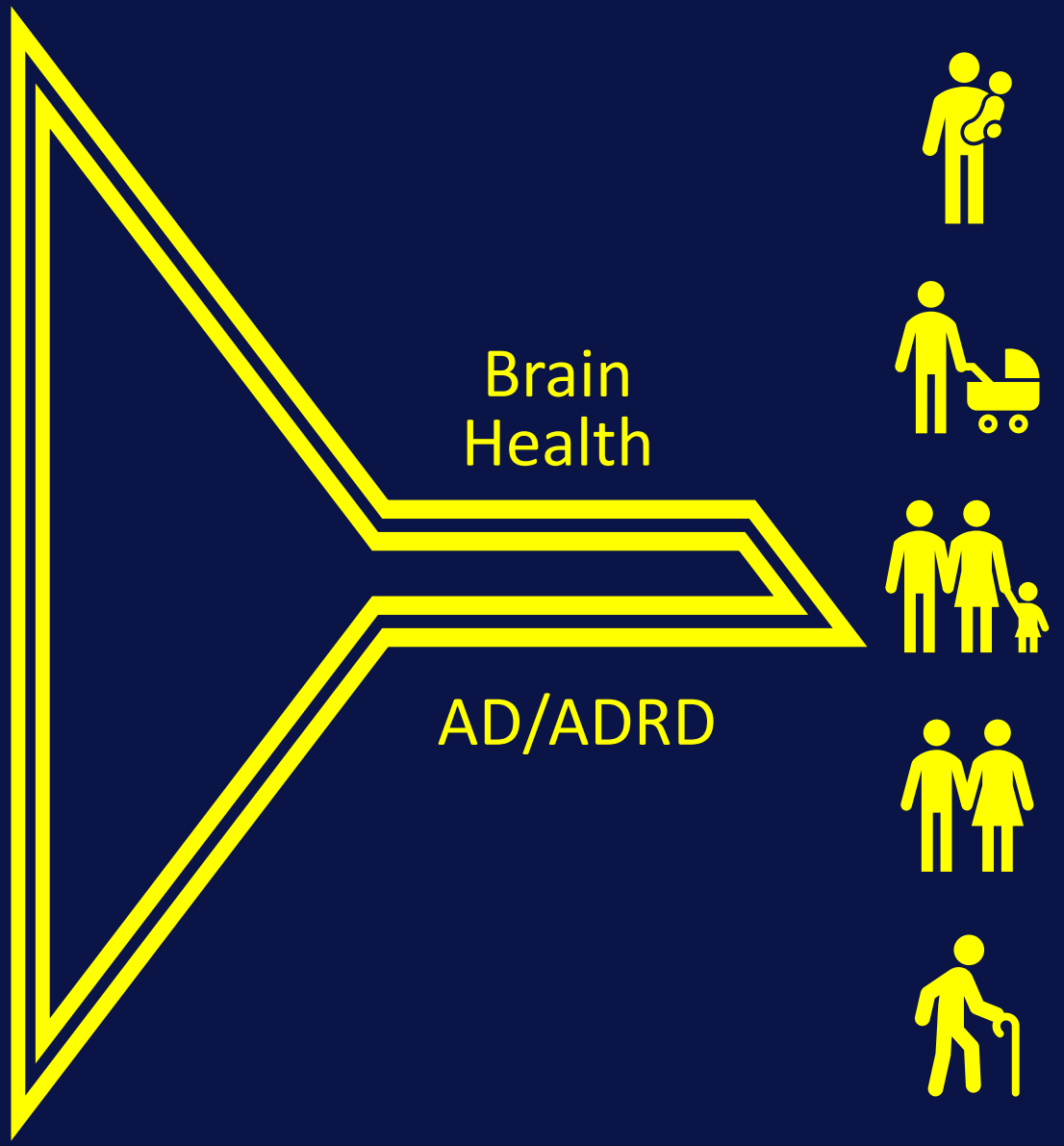
- **Blood:** cells, gases, **genes,** immune markers, infections, **lipids**, proteins, vitamins
- **CSF: amyloid**, **tau**, nfl, HIV, syphilis, pressure, ventricle size
- **Body: exam findings**
- **Brain:**

  <u>structure/connectivity</u>

  - shape, **thickness, volume, lesions,** cellularity, chemistry, synapses, genetics, architecture, network connections

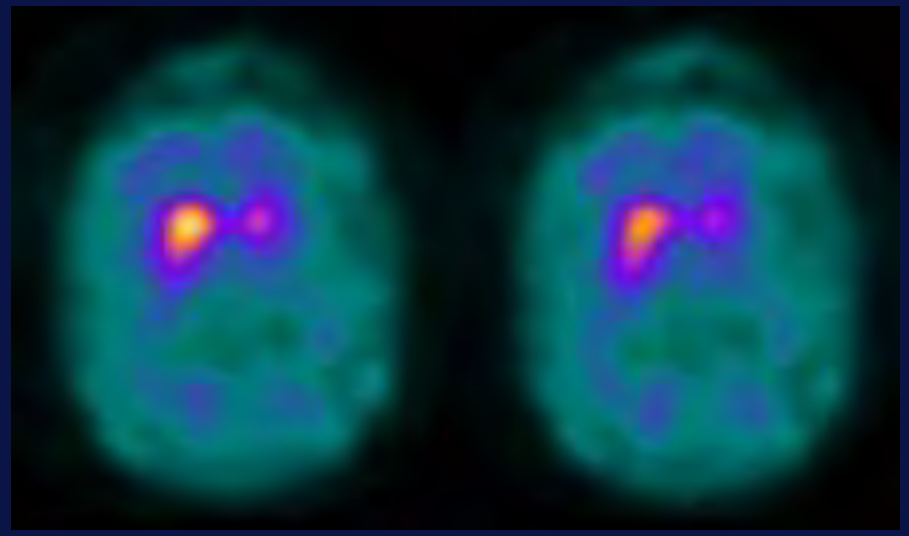
  <u>function</u>

  - blood flow, electrical activity, metabolism, network dynamics, interoception and exteroception



Problem: Heterogeneity and Overlap

- >70% mixed AD/ADRD
- Phenotype ≠ Genotype
- Incomplete penetrance
- Resilience
- Polygenic risks
- Epigenetics
- How to manage them when we detect them?



Hx: 63 yo F seen in 2020 with 2-year hx of progressive aphasia
PMH: T&A, bunionectomy, IBS
Exam: Normal except MoCA - 24
Labs: ANA, CRP, Folate, B12/MMA, ESR, Syphilis, and Thiamine – normal
MRI – normal.
CSF: T-Tau 786.25, P-Tau 103.9, ATI 0.38 suggesting AD diagnosis
Interpretation: Primary nonfluent aphasia due to Alzheimer's Disease
Plan: *Anti-amyloid therapy initiated*
FU: 2024 – rest tremor, rigidity and dystonic cramping on the right
2nd Dx: Corticobasal syndrome

Is it any wonder?

- Only 3 new AD/ADRD FDA-approved drugs after ~150 clinical trials over ~25+ years,
- Limited success in AD/ADRD prevention and brain health,
- Greater use of artificial intelligence (AI),
- Greater interdisciplinarity, and
- Greater use of **big data** to quantitate the effects of multiple pathogenic factors, biomarkers, and their interactions?

Primary Research

- ADNITBI Study (n = 724) and Brain Age Sub-study (n = 632)
- PPMI/RAAP Study (n = 600)
- SOOP, SOOPx and CAPS (n = 1734) and other sub-studies
- SC Alzheimer's Registry (n = 207,093 of approx. 400k)
- CDC WONDER (n = SC pop.)

NACC

ADNI Alzheimer's Disease Neuroimaging Initiative

Parkinson's Progression Markers Initiative

SC-ADRC
A statewide initiative of
MUSC Medical University of South Carolina
CLEMSON UNIVERSITY
University of South Carolina

Office for the Study of Aging
Arnold School of Public Health
UNIVERSITY OF SOUTH CAROLINA

Primary Research Results

Study Name

- ADNITBI Study and BrainAge Sub-study (TBI effects)
- PPMI/RAAP (Motor subtypes)
- SOOP, *SOOPx* and CAPS and BrainAge Sub-study (structure and function correlates)
- SC Alzheimer's Registry (comorbidity and mortality)
- *CDC WONDER (comorbidity and mortality)*

Outcome Snippets

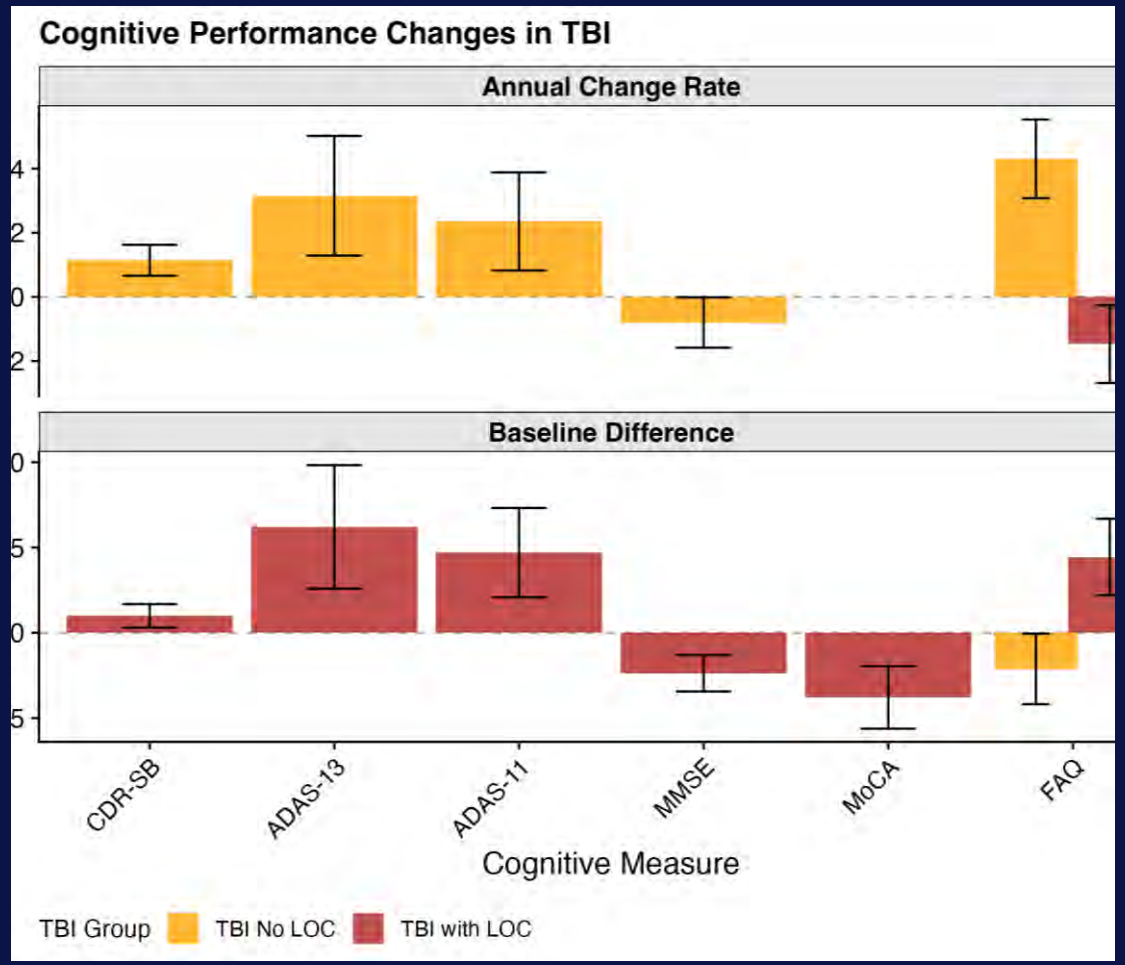
- TBI affects GMV, WMV and many areas of cognition/behavior
- Regional GMV reveals PD motor subtypes; *connectivity, too?*
- Stroke data sharing and collaboration for ML/AI
- Heart and lung diseases are leading causes of AD/ADRD death in SCADR
- *Why does a high-comorbidity group (Blacks) show lower mortality risk in SCADR study?*

Additional Results Snippets

- Not all contributors are credited
- Some work presented elsewhere
- Some work in preparation

Longitudinal neuroanatomical and cognitive effects of TBI within Alzheimer's Disease Neuroimaging Initiative Cohort

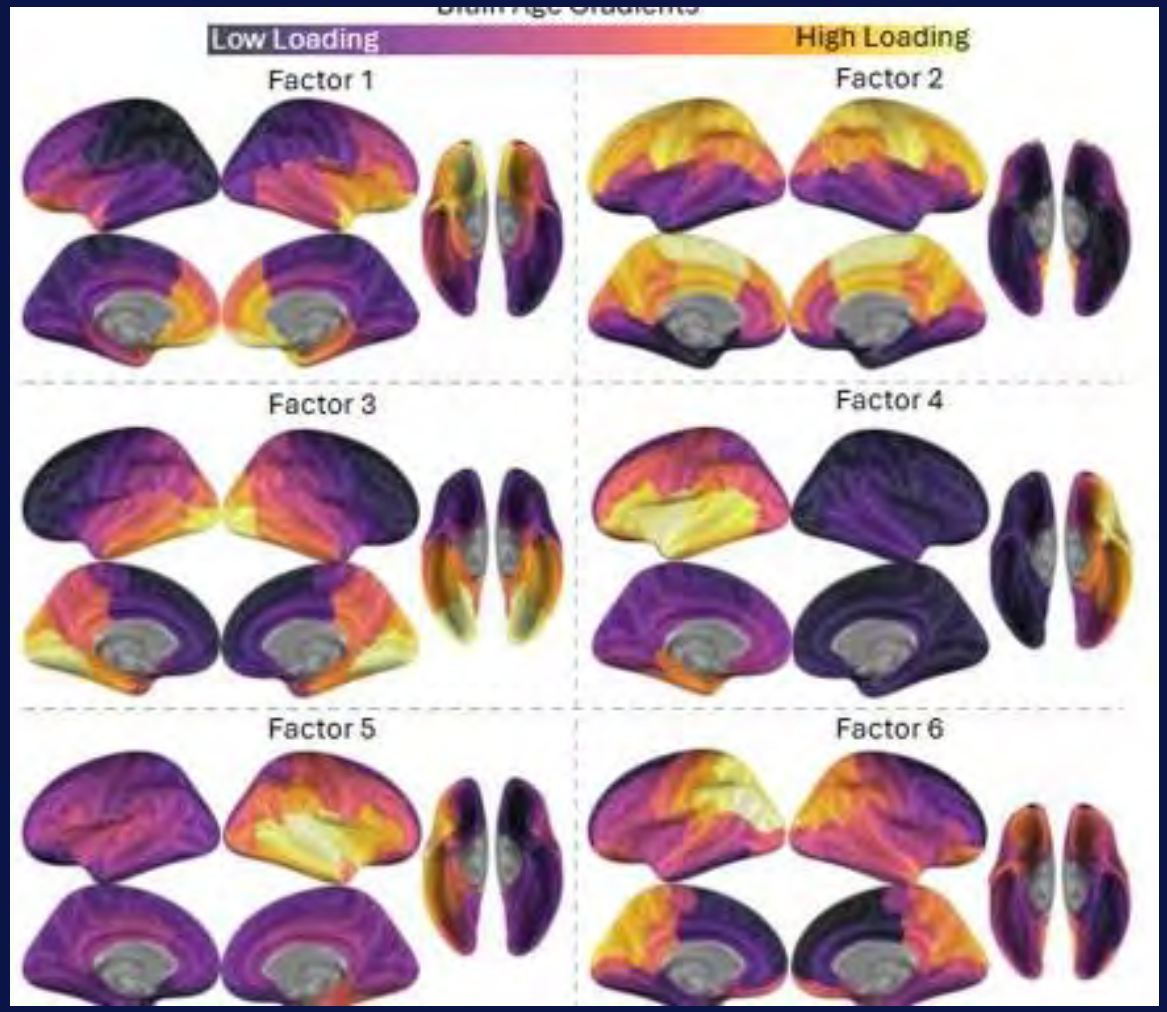
Wade J, Walton A, Riccardi N, the SNIRP investigators, the ADNI investigators, & Absher JR



ADNI subjects with TBI and LOC showed faster decline in cognition CDRSB ($\beta = 0.50$, $p = 0.004$), ADAS13 ($\beta = 3.10$, $p < 0.001$), and MMSE ($\beta = -1.19$, $p < 0.001$)] and greater brain (GM) atrophy in many brain areas, including the left posterior orbital gyrus ($\beta = -0.001$, $p = 0.022$) and anterior cingulate ($\beta = -0.002$, $p = 0.008$).

Cortical brain age gradients reveal structural signatures of traumatic brain injury

Walton AM, Riccardi N, Wade J, & Absher JR



- Validated 3D convolutional neural network (volBrain) estimated brain age in 191 ADNITBI subjects.
- Six patterns of cortical aging emerged from brain age gradient factors
- One gradient, centered in the right temporoparietal area, showed significantly lower expression in the TBI group ($p = .03$).
- Brain age gradient factors may represent a structural signature of TBI in the older adult population.

Lesion Mapping of Post-Stroke Acute Aphasia Severity: A Retrospective Analysis of NIHSS Best Language Scores and Clinical Neuroimaging

Sherzad N, Newman-Norlund R, Absher J, Bonilha L, Rorden C, Fridriksson J, & Kristinsson S

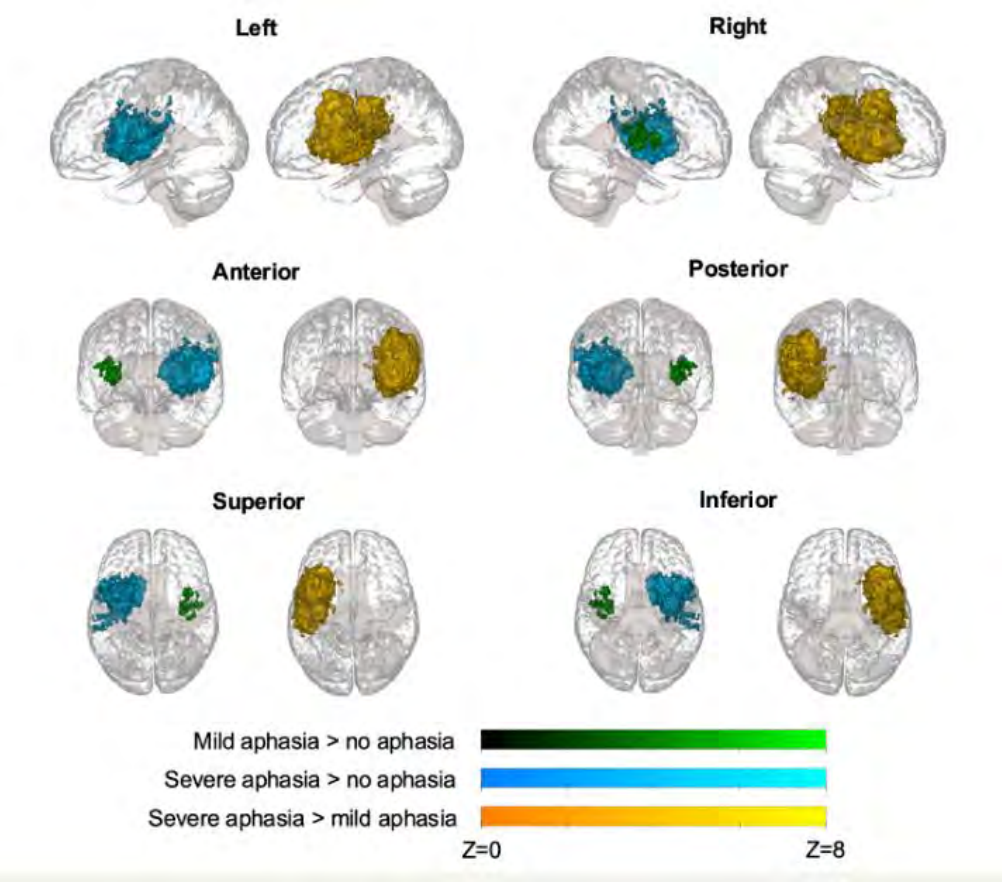


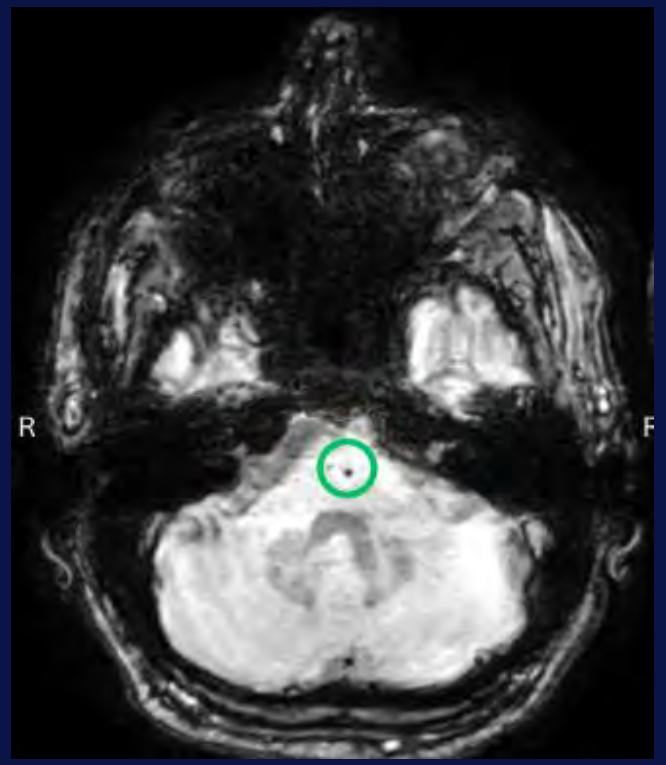
Figure 3. Voxelwise Lesion-Symptom Mapping of NIHSS Best Language Scores.

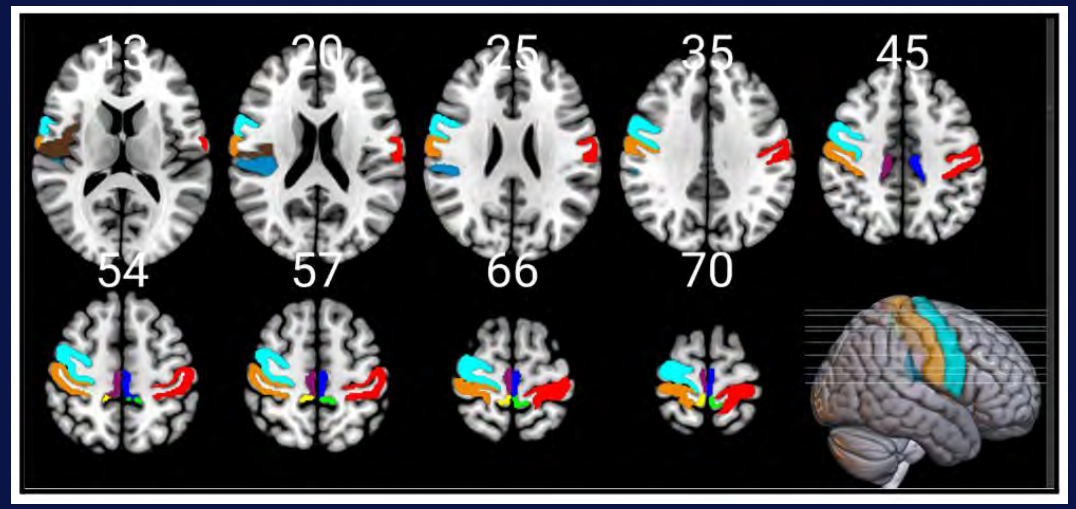
- Group contrasts: no aphasia (n = 227), mild aphasia (n = 149), and severe aphasia (n = 102)
- Clusters represent significant lesion-deficit associations following permutation-based correction ($p < 0.05$; 5,000 permutations), with lesion volume included as a covariate.
- Only voxels lesioned in ≥10 participants were included in analyses.
- Z-scores are mapped from 0 to 8, with warmer colors indicating stronger associations between lesion presence and aphasia severity.

Infratentorial CMB count was positively correlated with Brain Age Gap (BAG) in 9/14 sensorimotor regions

Palapothu R, Kudaravalli S, Absher J, Newman-Norlund R

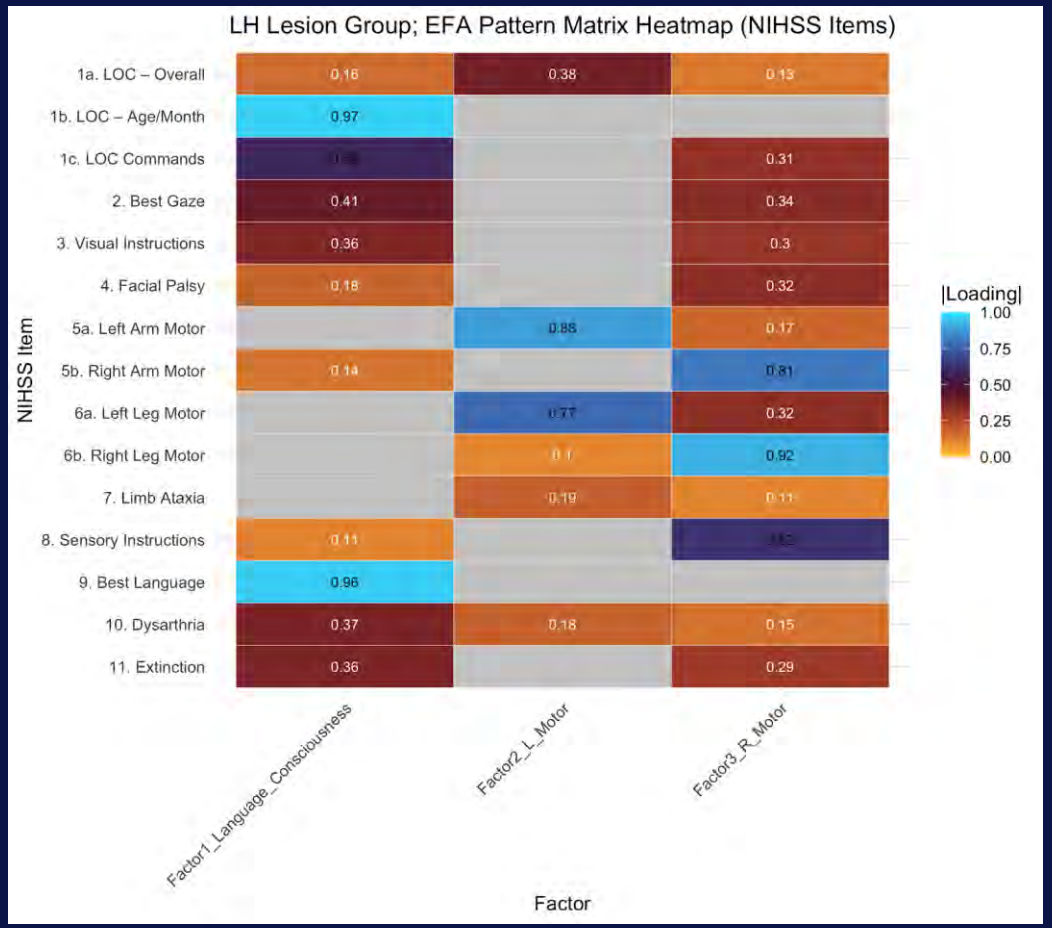
- 1725 subjects from SOOP study
- BAG may serve as a sensitive marker for cerebrovascular injury and guide targeted rehabilitation efforts.





Deconstructing the NIHSS: Cerebellar and Aging Biomarkers Improve Domain-Specific Stroke Prediction

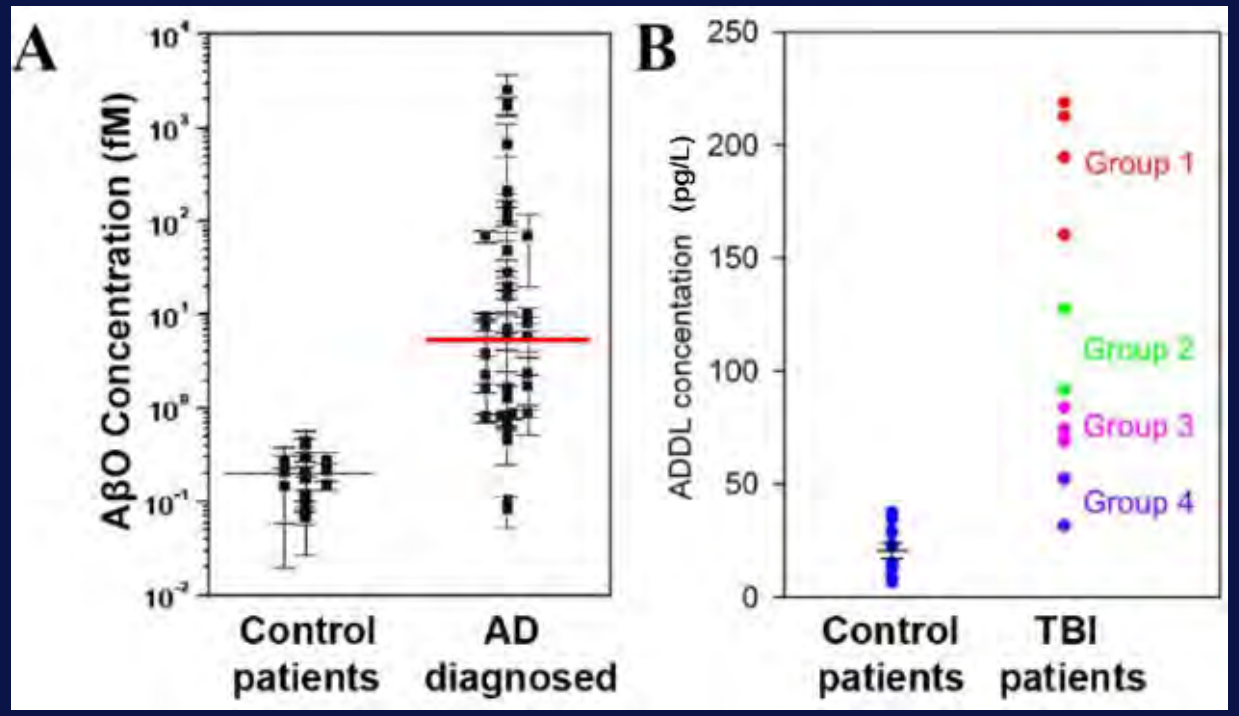
Gibson M, Maydeu-Olivares A, Riccardi N, Newman-Norlund R, Absher J, Rorden C



- Stroke outcomes extend beyond lesion characteristics alone.
- **Holding lesion size constant, patients with cerebellar atrophy and accelerated brain aging showed greater impairment.**
- This provides a framework for improved prognostic models, enabling domain-specific assessment that could guide personalized rehabilitation and improve outcome prediction

NIH Grant (under review): Developing affordable and ultrasensitive buoyant-analyte-magnetic (BAM) assays for Alzheimer's Disease biomarkers.

Jeff Anker, PhD (Clemson University PI) and colleagues at USC, MUSC and Prisma Health



AIM 3:
To develop a rapid (< 20 minutes) Buoyant and Magnetic (BAM) assay for amyloid beta oligomers in plasma, CSF, and mouse brain homogenate

Figure:

- BAM distinguished AD and TBI subjects from controls (A and B, respectively)
- Goal is a point-of-care, rapid, and inexpensive assay to detect AD biomarkers

DTI Tractography Characterizes Motor Symptoms in Parkinson's Disease

Fletcher G, Chaluvadi LS, Ilie D, Nassif J, Gitlitz S, Bergman M, Echekki Y, Absher JR

Aims

- Investigate white matter connectivity differences across PD motor subtypes using DTI.
- Identify associations between connectivity and motor symptoms.
- Explore sex-related differences in connectivity patterns.

Figure 2. Supplementary Motor Area (SMA)

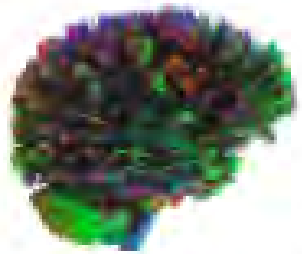
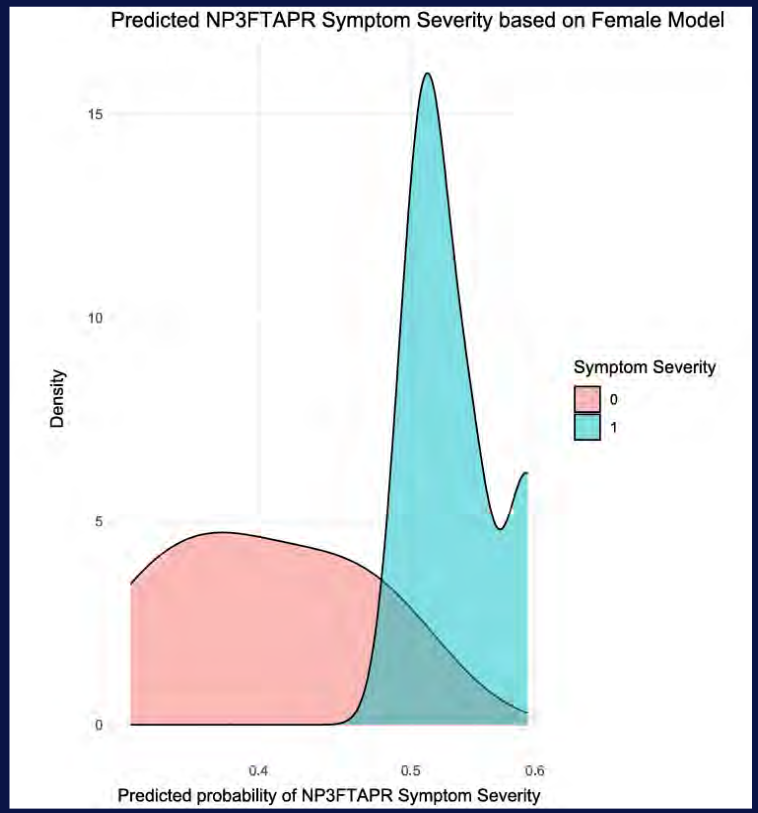


Figure 3. Sample image for whole brain DTI tractography



Adjacent Work

- USC Brain Health Network
- SC - ADRC
- In Our DNA SC
- Institute for Engaged Aging (PACT and Active Mind)
- Translational/Basic research
  - BAM beads for affordable POC Dx
  - NMDARs and AD treatment
- SNIRP/HPCNIRC for HPC and cloud-based training in AD/ADRD neuroimaging research

Tackling Multivariate Analysis

- ADNITBI Study – Longitudinal, mixed effects analysis with R:

$$y_i = \beta_0 + \beta_1 \cdot \text{Non-LOC TBI}_i + \beta_2 \cdot \text{LOC TBI}_i + \beta_3 \cdot \text{Dementia}_i + \beta_4 \cdot \text{MCI}_i + \beta_5 \cdot \text{GenderFemale}_i + \beta_6 \cdot \text{Age}_i + \beta_7 \cdot \text{Time since baseline} + \beta_8 \cdot \text{APOE4Alleles}_i + \beta_9 \cdot \text{TIV}_i + \beta_{10} \cdot \text{FieldStrength}_i + \beta_{11} \cdot (\text{Non-LOC TBI}_i \times \text{Time since baseline}_i) + \beta_{12} \cdot (\text{LOC TBI}_i \times \text{Time since baseline}_i) + u_{j[i]} + \epsilon_i \quad (1)$$

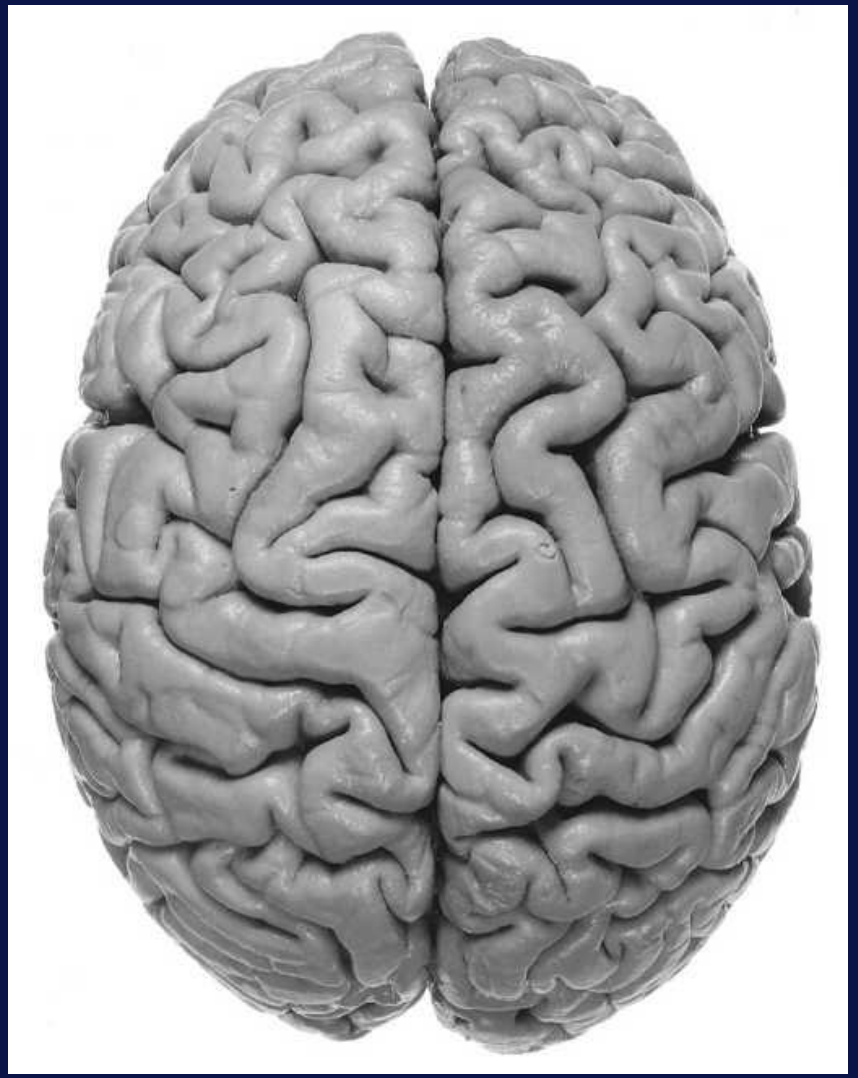
- BrainAge Substudies – AI/Deep Learning using VolBrain.net
- PPMI/RAAP Study – “multi-factor ANCOVA with covariates for age, sex, race, mean MDS-UPDRS I-III score, days since PD diagnosis, PD treatment status, and chosen ROIs was utilized”
- SC Alzheimer’s Registry – “We used $\chi 2$ test to compare participants' socio-demographic characteristics and mortality in the Registry …. Hazard ratios (HR) and 95% confidence intervals for the association between the LOCD, diagnostic category, and the risk of death in the Registry … were estimated using a fully adjusted multivariate extended Cox regression model.”

Research Toward Personalized AD/ADRD

- Basic, clinical, epidemiologic and translational research are all essential
- Neuroimaging is a valuable tool across these domains
- We have a great team with innovative ideas

Precision Brain Health & AD/ADRD

1. Expand array of brain health and AD/ADRD metrics (**care partners**)
2. Track **multiple** variables in large, mixed groups (SCADR, populations)
3. Validate Dx predictions (**autopsy**)
4. Model outcomes and relate to Dx and validated Dx (**component impacts**)
5. Refine Dx and outcome predictions **person-by-person**
6. Target key drivers of brain health and AD/ADRD outcomes (**prevention, treatment, and cure**)



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- Health Sciences Center Seed Grant program
- SC ADRC
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- Neurodesk, OHBM Brainhack, OCI/Oracle for Research
- NSF and ACCESS-CI
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MUSC
Medical University of South Carolina

Application of Advanced Diffusion MRI methods to Aging and Alzheimer's Disease

Jens Jensen
Department of Neuroscience
Medical University of South Carolina

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BRIDGE

BRAIN IMAGING DIFFUSION GROUP

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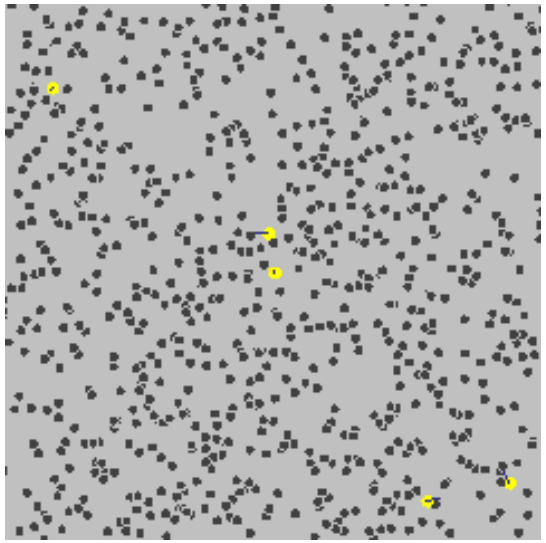
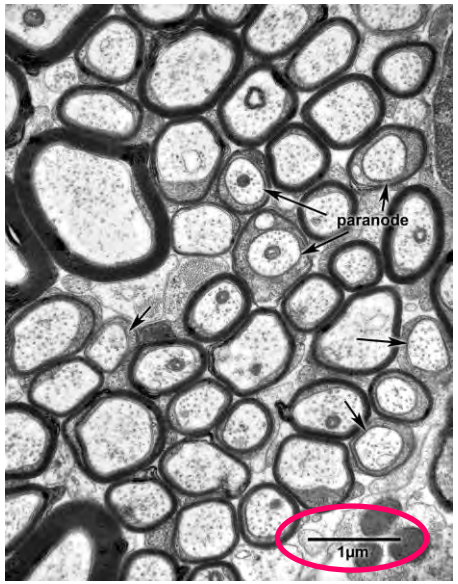
T32DC0014435

NIH
National Institutes of Health

What is Diffusion MRI (dMRI)?

- MRI method in which image contrast is sensitive to molecular diffusion of water.
- Quantifies basic diffusion properties of brain tissue including the **mean diffusivity (MD)**, **fractional anisotropy (FA)** and **mean kurtosis (MK)**.
- Detects changes in tissue microstructure on the scale of micrometers.
- When combined with a tissue model, quantifies microstructural features, such as **axonal water fraction (AWF).**



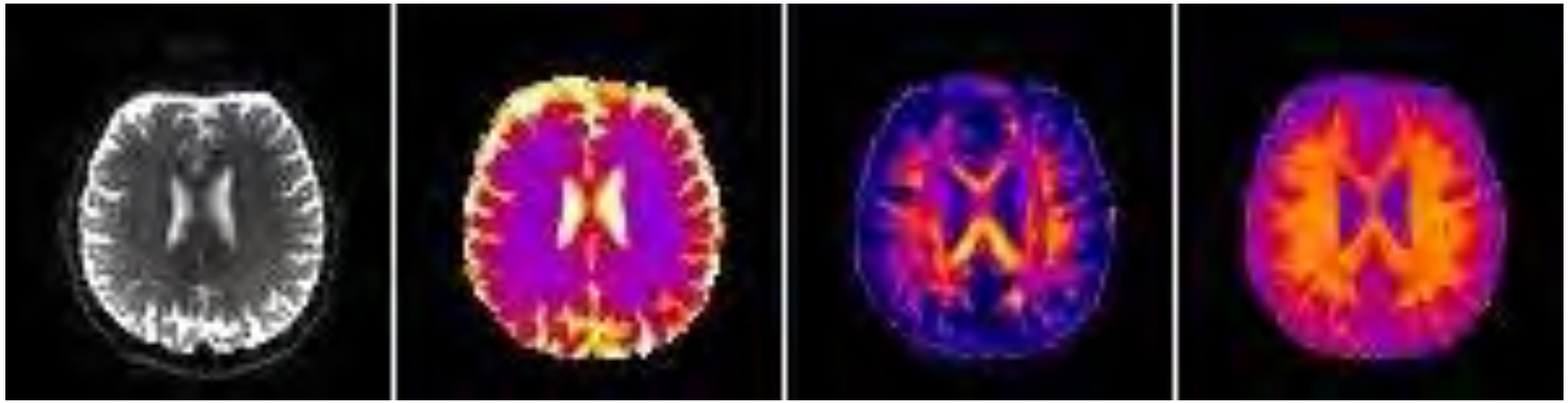


I will now reveal my methods, Watson, for assessing your brain microstructure.

The Big Three

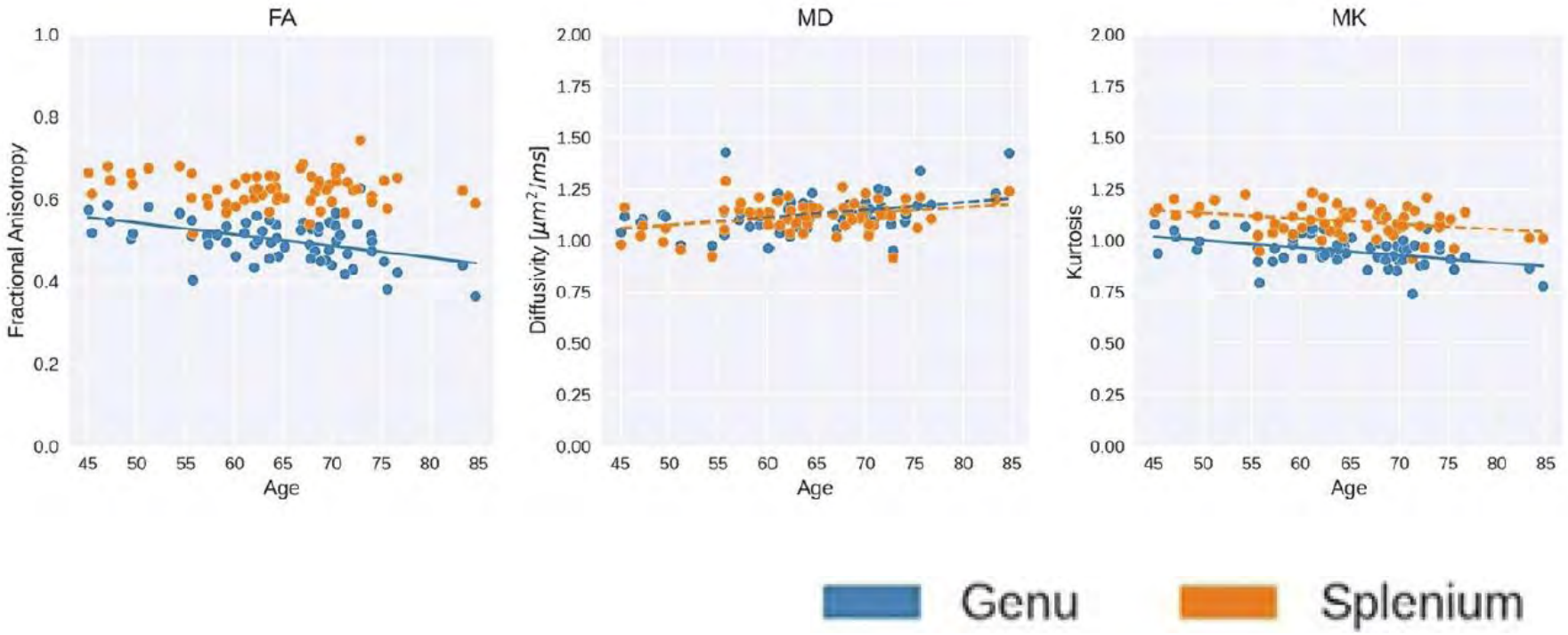
- **MD** measures the diffusion amplitude.
- **FA** measures the dependence of diffusion on direction.
- **MK** measures the heterogeneity of the diffusion environment.

The Big Three



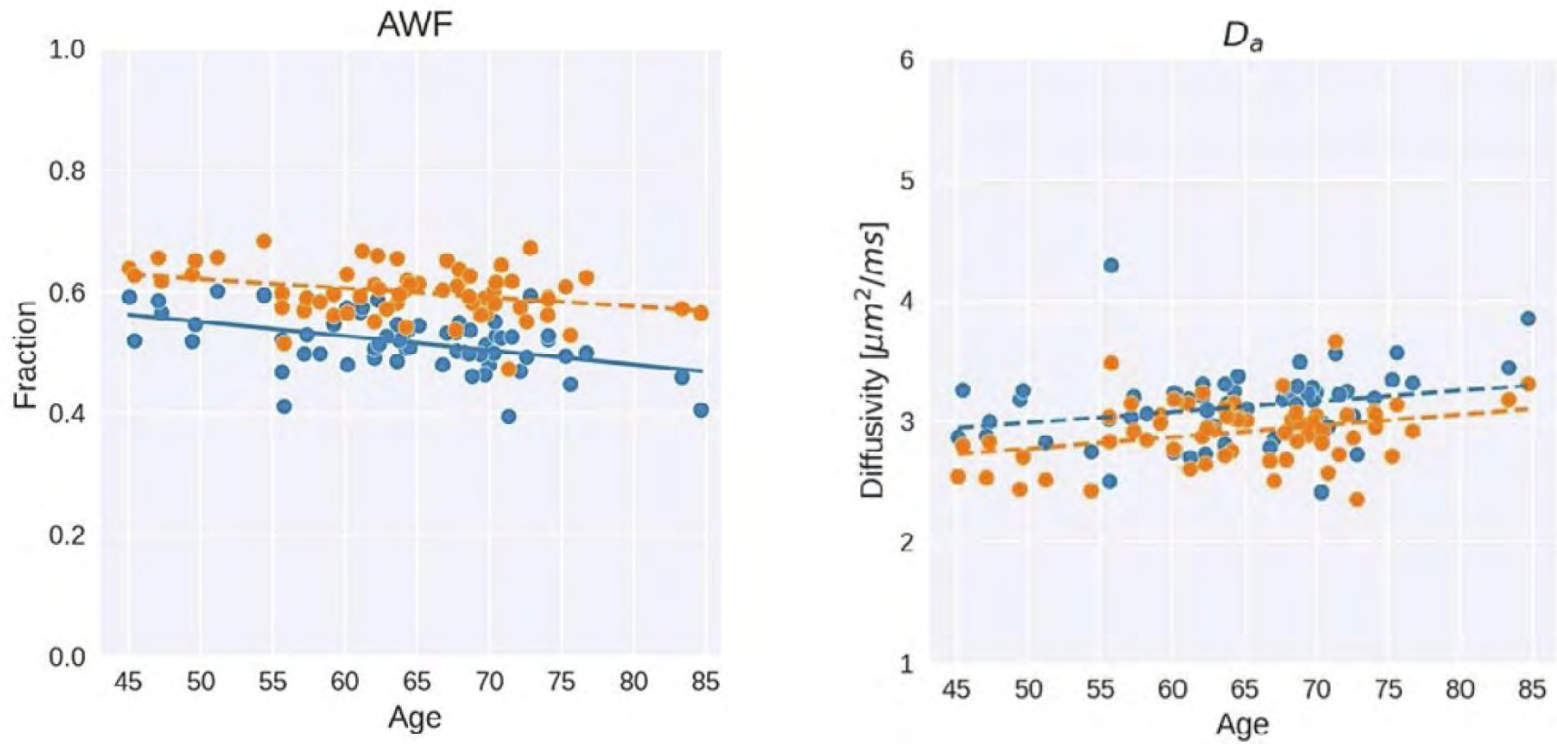
T2 MD FA MK

Healthy Aging



Dhiman et al., Aging Brain 2022

Healthy Aging



AWF = Axonal Water Fraction

D_a = Intra-axonal Diffusivity

Axon diameter increases with age

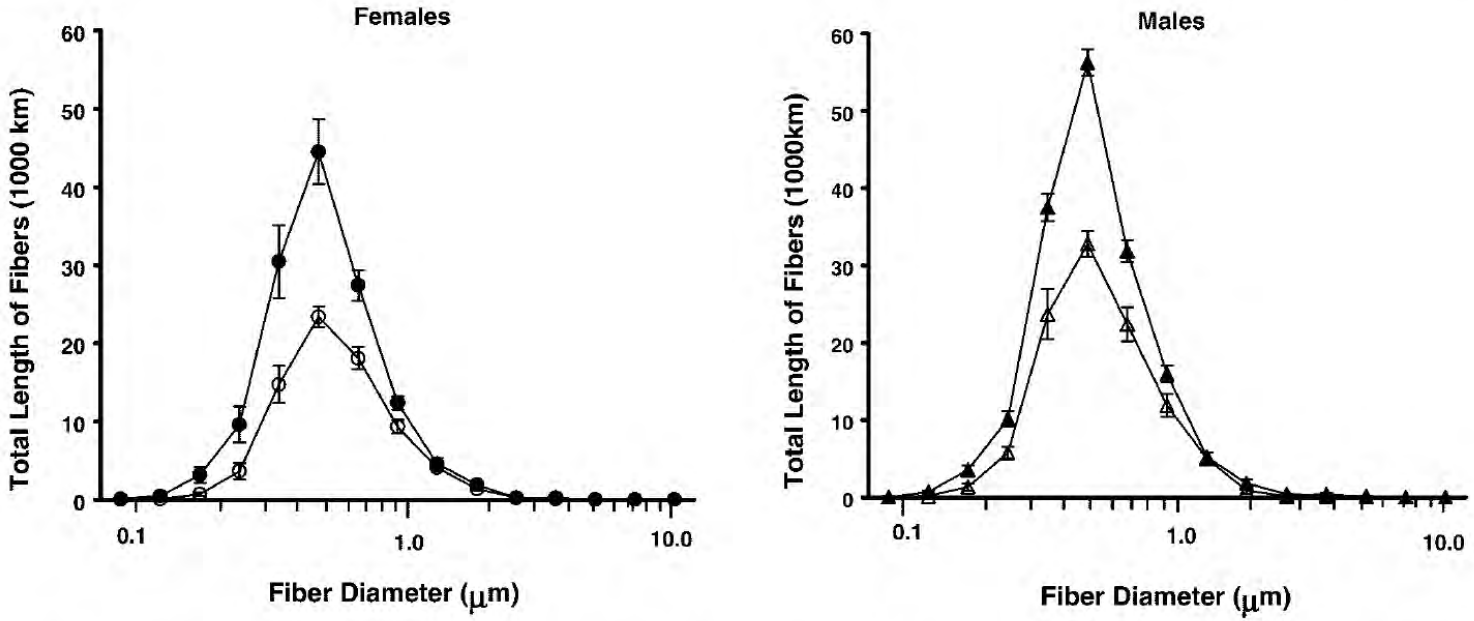
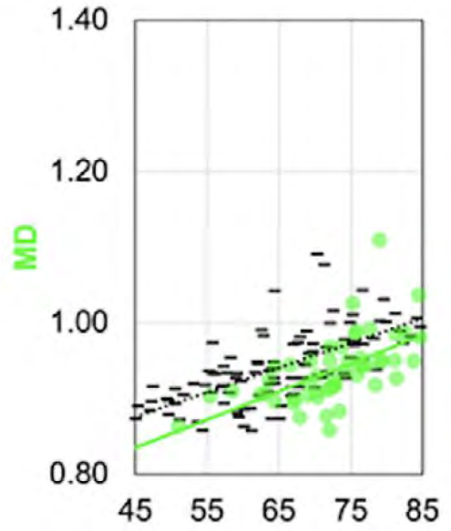


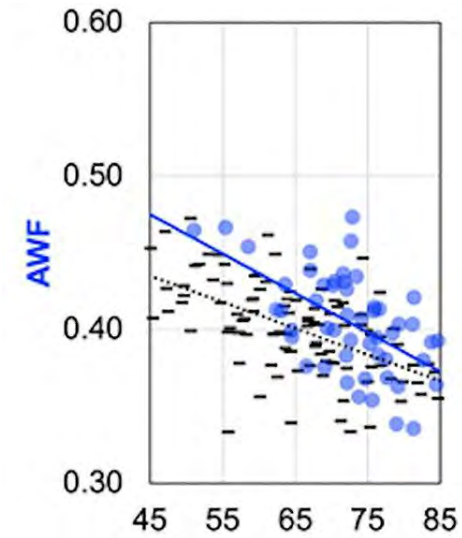
Fig. 5. The absolute diameter distribution of fibers separated for "young" (≤45 years of age; filled circles) and "old" (≥70 years of age; open circles) females and "young" (filled triangles) and "old" (open triangles) males. The total length of myelinated fibers is shown as a function of diameter on a logarithmic scale. Thirteen classes of fibers are shown with the width of each class being 38% of the local mean diameter. The standard errors are indicated.

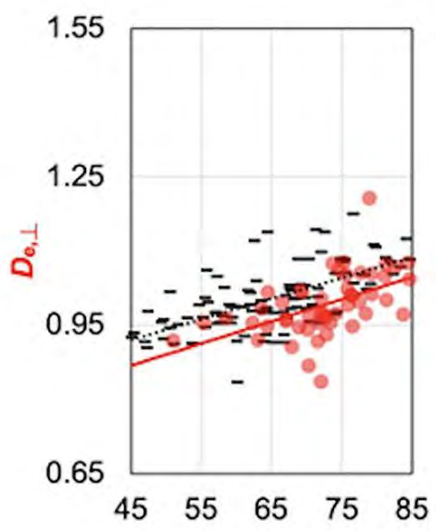
Marner et al., J Comp Neurol 2003

Greater diffusion restriction in white matter for preclinical AD

Benitez et al., Ann Neurol 2022

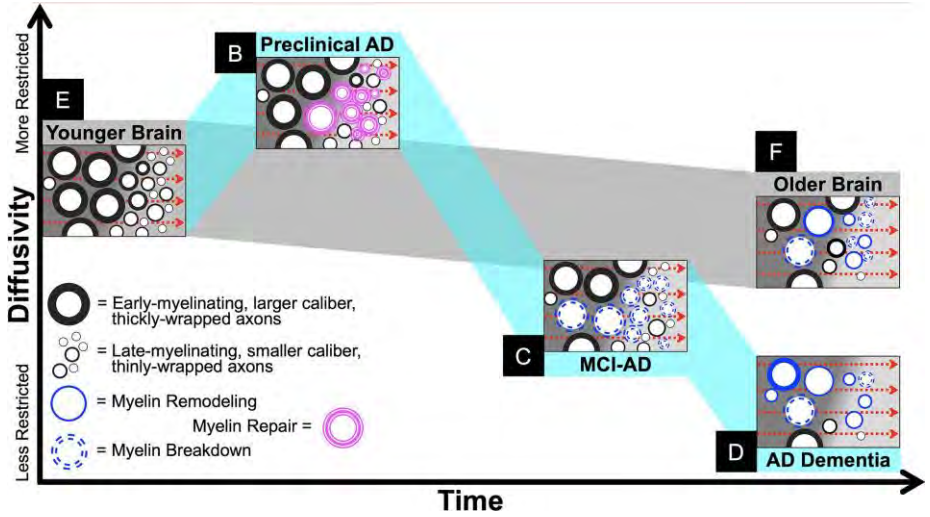






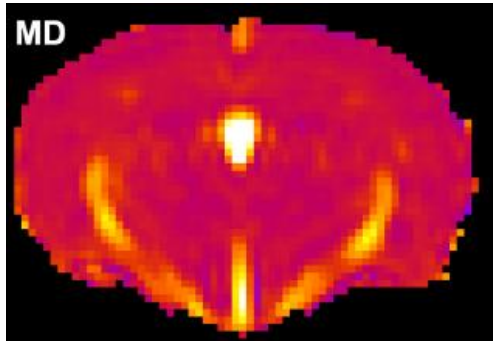
Black symbols = Aβ-

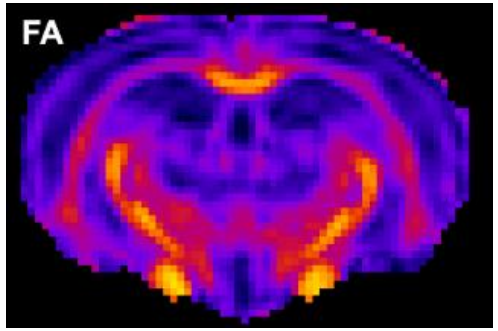
Colored symbols = Aβ+

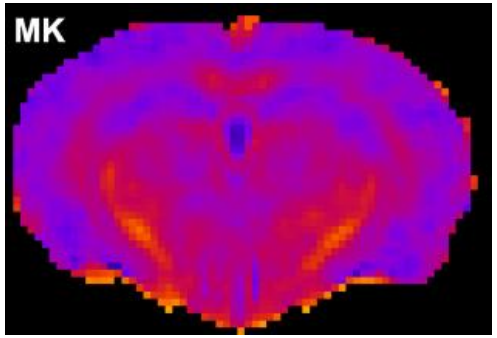


dMRI with machine learning can detect early brain abnormalities in AD mouse model

Falangola et al., NMR Biomed 2025







2 months old, 3xTG-AD mice (TG) + controls (NC)

Confusion Matrix

Predicted \ Actual	TG	NC
TG	23	0
NC	0	16

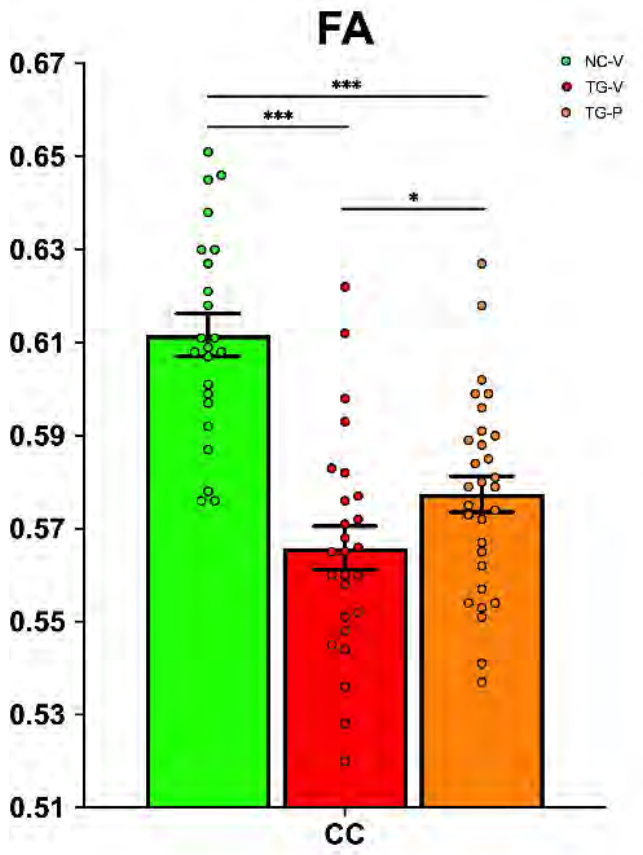
Accuracy = 1.00
Sensitivity = 1.00
Specificity = 1.00

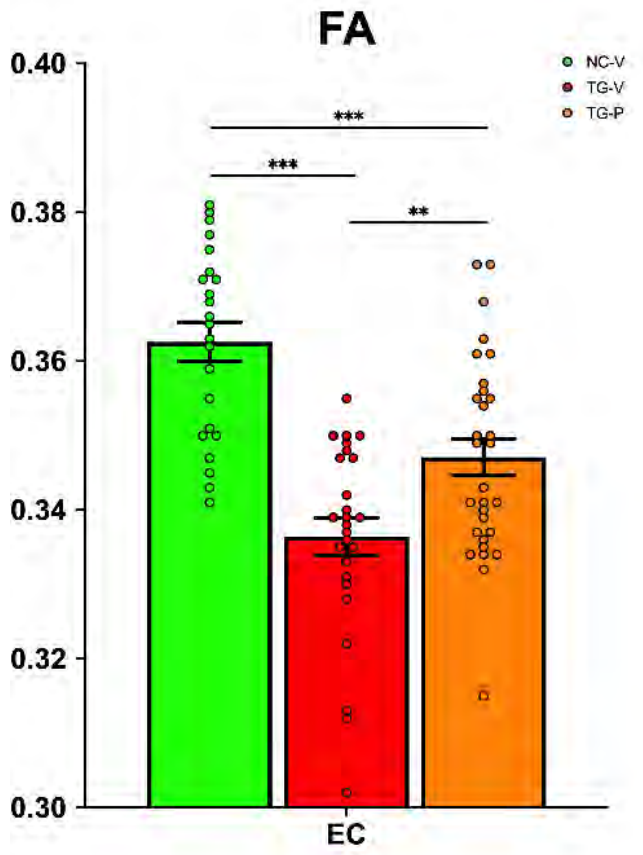
Predictor	Coefficient	Rank
FA-VH	66.65	1
FA-CC	38.58	2
FA-Ctx-Cg	34.89	3

dMRI can detect effect of drug therapy on microstructure in AD mouse model

8 months old, 3xTG-AD mice + controls

Neurotrophic peptide mimetic P021 → Increased BDNF expression





Takeaways

In the context of aging and AD, dMRI can:

- Detect subtle brain tissue changes
- Help elucidate how brain microstructure is affected
- Monitor biophysical changes associated with therapy

FROM RESEARCH TO REALITY: SUPPORTING CAREGIVERS THROUGH ACTIONABLE SCIENCE

Dr. Lesley Ross

Dr. Lorie Donelle

Dr. Shaun Owens

Panel Moderated by Dr. Maggi Miller

UNIVERSITY OF South Carolina

Caring For & About Caregivers: A Program of Research

Lorie Donelle RN (ON, Canada), PhD, FCAN, FAAN
College of Nursing, University of South Carolina
Director ACORN Research Center
Email: ldonelle@mailbox.sc.edu

UNIVERSITY OF South Carolina

Who are Unpaid Caregivers?

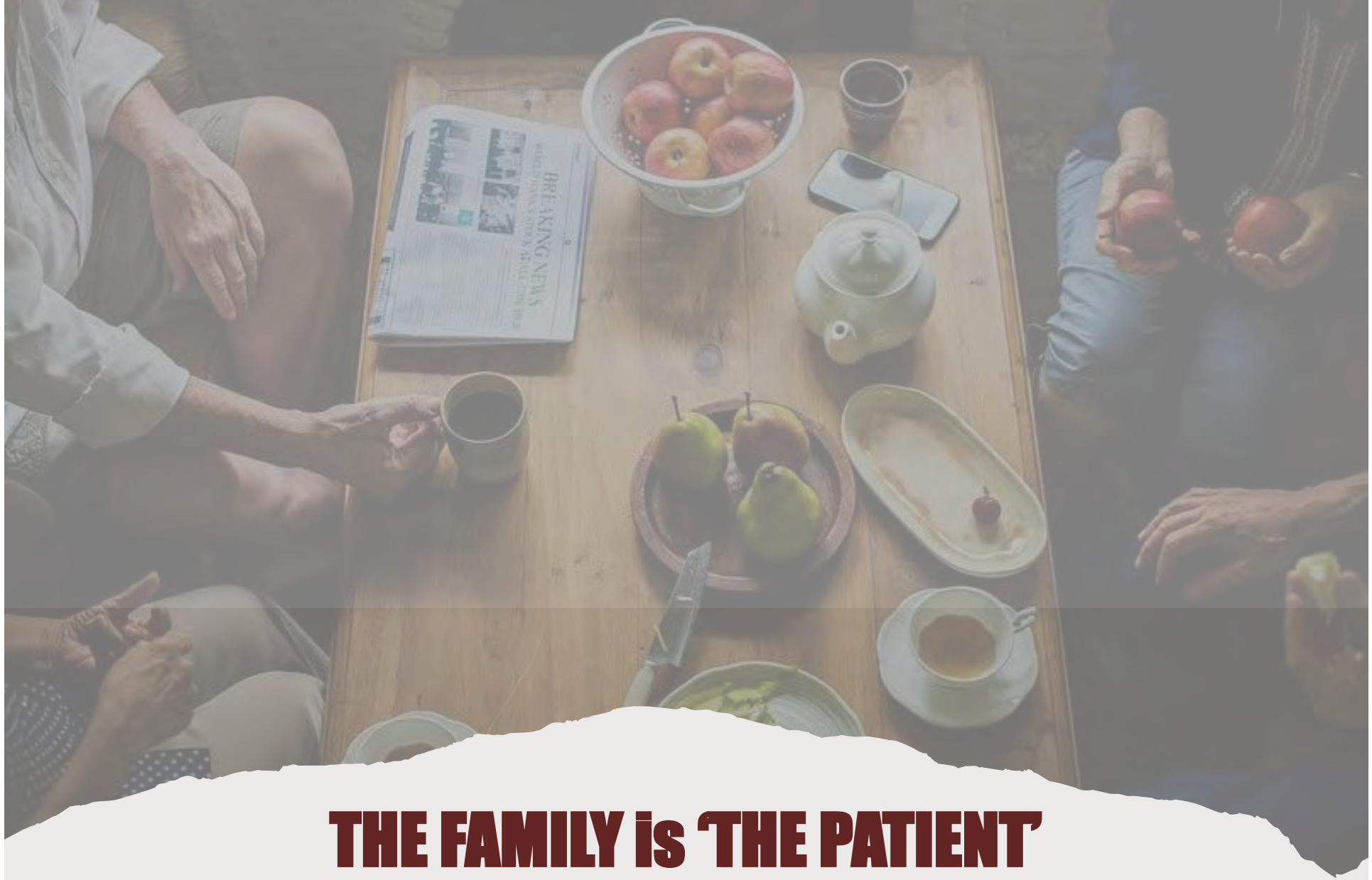
- Caregiving – helping with daily care & activities, medications, treatments, emotional support, advocacy, finances, and overall safety.
- Individuals providing support to a family member, friend, or neighbour of any age who is living with a chronic illness, injury, disability, or someone requiring end-of-life care.
  - ~ 53 million or 1 in 5 US adults are caregivers.
    - ‘Sandwich caregivers’
    - Invisible health care workforce

Unpaid Caregivers' Health & Wellbeing

- Uniquely impacted by:
  - Duration & intensity of their caregiving
  - Intersecting equity markers
    - gender, age, race, income, rural/urban.

Which can create:

- Financial strain
- Workplace challenges
- Increased loneliness
- Decline in emotional or mental health
- Reduced social activity
- Decline in physical health



THE FAMILY is 'THE PATIENT'

Generating Digital Markers of Care Needs Among **Unpaid Caregivers of Alzheimer's Disease and** Related Dementias (ADRD): a **Pilot Study**

(Donelle, Levkoff, Metts, Friedman, Yang, Rudisill, Yagateela)

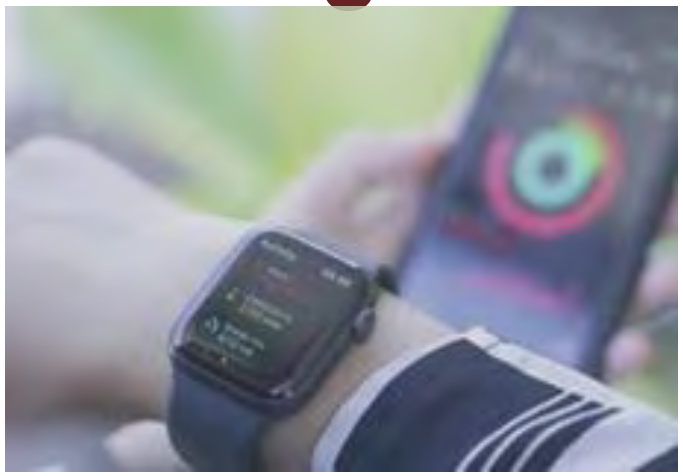
- Pilot project to:
  - monitor the health and wellbeing of unpaid caregivers of individuals with ADRC
  - assess feasibility

- Used mobile technology (iWatch, iPhone) + EMA to capture unpaid caregivers' **DAILY** health and wellbeing.

- The data collected will be analyzed to determine health related concerns /patterns by equity markers of the participating caregivers.

- Long-term = data used to explore associations of activities & outcomes to generate anticipatory models of care.

Pilot Study: Early Findings



Acceptability

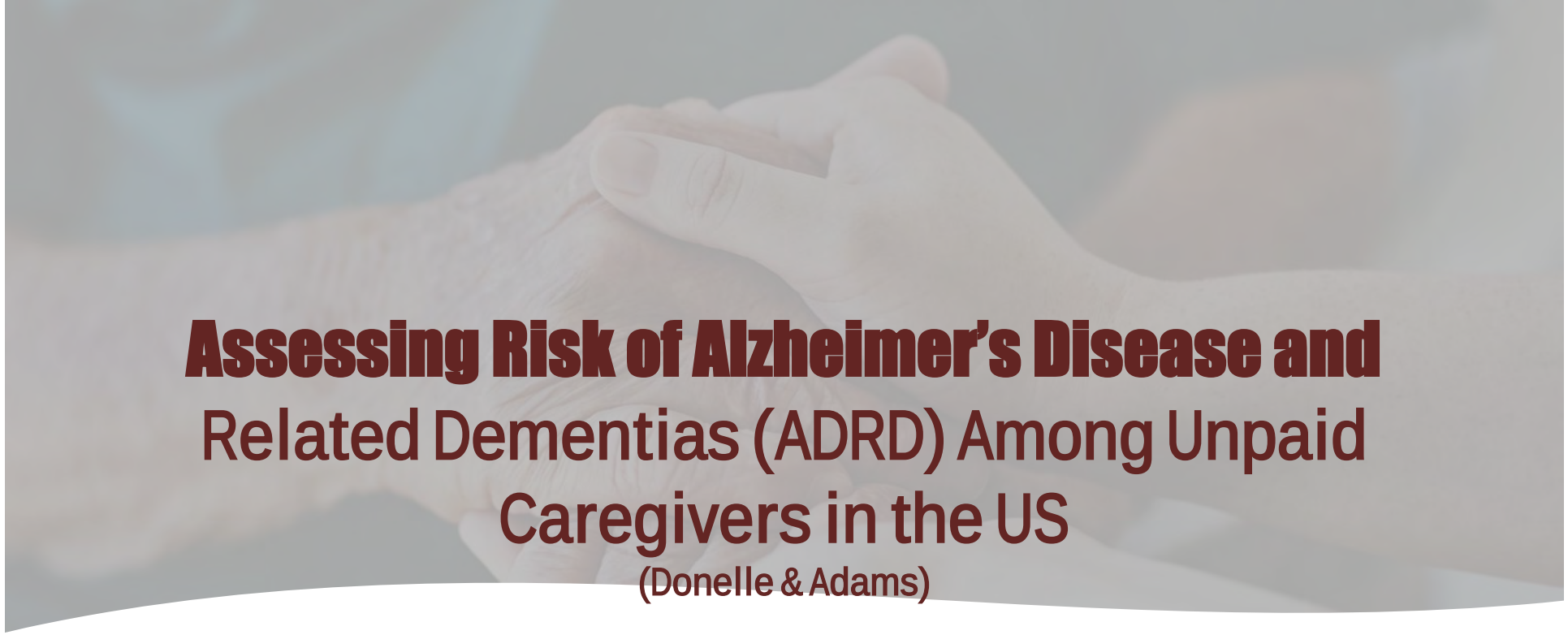
- Mobile surveys, iphone and iwatch generally easy to use and helpful for **accurate** recall, **in-the-moment reporting** and self-awareness

Research as the Intervention

- "I felt in a way the study helped me because it made me think through the day what I did or didn't do with her. And was I compassionate or not?" (CG participant)
- "I think for me it [participation in the study] made me check in with my own like my mental health." (CG participant)
- "I will say this, I did try to make sure that I was more intentional about doing the things that I like to do for myself." (CG participant)

Need for Research

- "So I, I think that there is definitely a lacking [of research] for the caregiver for what they go through and how they're being affected because it, it does affect you." (CG participant)



Assessing Risk of Alzheimer's Disease and Related Dementias (ADRD) Among Unpaid Caregivers in the US

(Donelle & Adams)

- We wondered about the **risk of ADRD among unpaid caregivers vs non-caregivers**
  - National data on health and lifestyle (BRFSS) 2023
    - health-related risk behaviors, chronic health conditions, and use of preventive services.

14 ADRD Risk Factors

ADRD Risk Factors among Unpaid Caregivers: Preliminary Findings

Mapped 12/14 risk factors for cognitive decline

- ***Education**
- ***Physical activity**
- Alcohol
- ***LDL (CHD, MI, STROKE)**
- ***Hypertension**
- ***Depression**
- ***Diabetes**
- ***Obesity**
- ***Smoking**
- ***Hearing**
- ***Vision**
- ***Social isolation / lonely**

Why Does This Matter?

The 2024 Lancet Commission identified 14 modifiable risk factors.

Those providing care may be at heightened risk for needing care themselves.

By making changes at any point of life, we may prevent or delay up to 45% of ADRD cases.

Caregiver Registry

Research

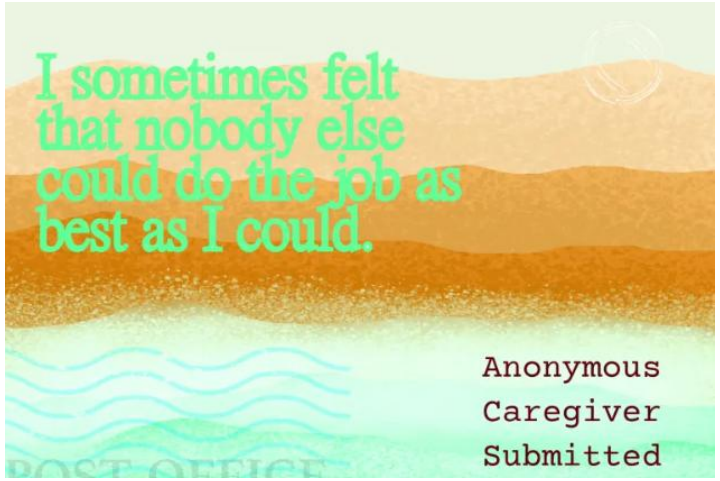
- Provide the infrastructure to monitor caregiver needs and contribute to ADRD prevention.
- An ‘early warning’ system able to identify caregivers at risk for developing ADRD
- Enhance ability to forecast and plan for caregiver prevention, respite, training programs
- Complement the existing SC state-wide Alzheimer’s Disease Registry

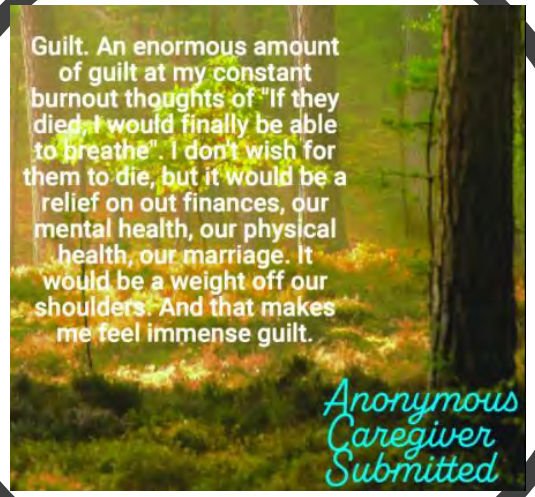
Shared Thoughts of Anonymous Caregivers (STACs)

caregiversanonymous.com/

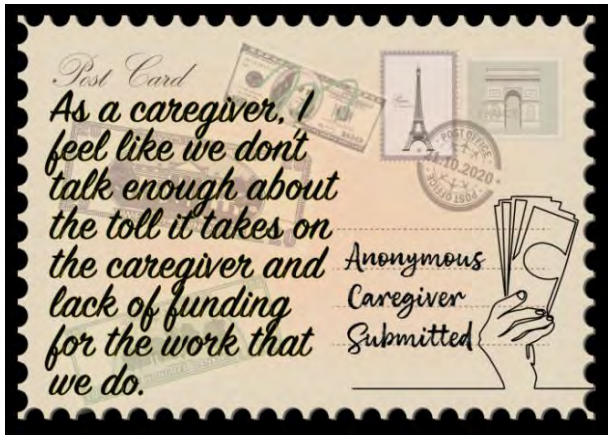
(Donelle, Hall, Patel)

STACs


I sometimes felt that nobody else could do the job as best as I could.
Anonymous Caregiver Submitted


Guilt. An enormous amount of guilt at my constant burnout thoughts of "If they died, I would finally be able to breathe". I don't wish for them to die, but it would be a relief on out finances, our mental health, our physical health, our marriage. It would be a weight off our shoulders. And that makes me feel immense guilt.
Anonymous Caregiver Submitted


AS A CAREGIVER SOMETIMES I FEEL ALONE AND USED AND ABUSED
Anonymous Caregiver Submitted


Post Card
As a caregiver, I feel like we don't talk enough about the toll it takes on the caregiver and lack of funding for the work that we do.
Anonymous Caregiver Submitted

SUMMARY

Research is intended to advance understanding of unpaid caregiving:

- Digital tools for monitoring and prediction
- Insights into caregiver health risks
- Support anonymous expressions of needs and emotion
- Long Term = Caregiver Registry
- Long Term = Proactive, data-driven models of care

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CONVERSATION
&
QUESTIONS

Contact Information
Dr. Lorie Donelle, Ph.D., FCAN, FAAN
ldonelle@mailbox.sc.edu

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EXAMINING THE FEASIBILITY AND USEFULNESS OF A REMOTE MONITORING SYSTEM (LAMP) AMONG RURAL-DWELLING AFRICAN AMERICANS IN SOUTH CAROLINA

Shaun Owens, MPH, PhD

Associate Professor, College of Social Work

UNIVERSITY OF
South Carolina

BACKGROUND

African Americans have higher mortality rates from the top six causes of death in the U.S. (cancer, heart disease, chronic lower respiratory disease, stroke, Alzheimer's disease) than other racial groups, but mortality rates are the highest among African Americans who live in rural areas.[1]

African American South Carolinians are 32% more likely to have ADRD as compared to non-Hispanic whites.[2]

Rural-dwelling, African-Americans may be reliant on care partner support due to their limited access to specialty and long-term care.[3,4]

Remote monitoring may be effective for supporting aging-in-place, but limited research exists on the usability, acceptability, and feasibility of deploying such technologies in the homes of rural dwelling African-Americans.[5,6,7]

RESEARCH AIM

To examine the usability, acceptability, and usefulness of deploying a remote monitoring system in the homes of rural African-Americans for supporting activities of daily living

LIFE ANALYTICS MONITORING PLATFORM

FUNCTIONAL MEASUREMENT & SENSOR EXAMPLES

Physical Activity
PIR MOTION SENSORS
Walking Speed, Time out of Home
WEARABLE
Daily Steps

Sleep
WEARABLE
Total Sleep
SLEEP MAT
Sleep Times, # of Awakenings

Physiological Health
SCALE
Weight, BMI
BP CUFF
Blood Pressure

Socialization
PIR MOTION SENSORS
Time out of Home

Health & Life Events
WEEKLY QUESTIONNAIRE
Self Reported Events

Medical Adherence
ELECTRONIC PILLBOX
Study Drug Adherence

Mobility
PIR MOTION SENSORS
Time out of Home

Cognitive Function
WEEKLY QUESTIONNAIRE
Time to Complete

CLINICAL & EXTERNAL DATA

External Environment

Electronic Medical Record

External Research

DATA

ANALYTICS/ DIGITAL BIOMARKERS

Technology

Pillbox
The pillbox measures when you take your medication.

Hub Computer
This small computer uses an Internet connection to communicate with the other devices. The devices send data to it and the computer sends that data to the research team. It must remain plugged in at all times.

Wall and Ceiling Sensors
Wall sensors measure how often you enter a room. Ceiling sensors measure your walking speed.

Computer and Cellphone Software
Software installed on your computer and a phone app measure the amount of time spent on devices and how often you login.

Door Sensor
Door Sensors measure how often you enter or exit your home.

Sleep Sensor
The strip part of the sensor sits under your side of the mattress.
It measures when you fall asleep, restlessness, and time spent in light, deep and REM cycles.

Watch
The waterproof watch measures how many steps you take and how many hours you sleep. It should be worn consistently.

Scale
The scale measures heart rate, body composition and weight. Remember to step on it daily.

METHODS

Recruitment (n=10)

- Identify as African-American
- Speak English
- Live in a rural area (U.S. Census)
- Have no self-reported memory impairment
- Consent to participation
- Consent to the installation of remote monitoring technology
- Have access to a home internet connection

METHODS

Study Protocol

1. Determine eligibility via telephone/schedule install appointment

2. Home visit (one)

- Explain technologies
- Administer baseline demographics and technology use survey (Qualtrics)

3. Telephone follow-up interviews (30 minutes, 8 questions)

4. Home visit (two)

- Uninstall equipment

MEASURES

Theoretical Constructs (Unified Theory of Technology Use and Acceptance) [8]	**Indicators/Outcomes of Interest**	**Data Source**
Performance Expectancy	Usefulness	In-Depth Interviews
Effort Expectancy	Ease of Use/Usability	In-Depth Interviews
Social Acceptance	Acceptability	In-Depth Interviews
Facilitating Conditions	Ease of Use	In-Depth Interviews
Technology Use Experience	Experience/Use Readiness	Technology Use Survey
	Individual Characteristics	Demographic Survey

DATA ANALYSIS

Quantitative Data Analysis

- Calculate descriptive statistics for demographics and technology use items

Qualitative Data Analysis

1. Read all transcripts for accuracy and become familiar with the data.
2. Independently open code transcripts to create a codebook
3. Recode (i.e., axial code) transcripts using Nvivo v17.17
4. Discuss emergent themes
5. Define a final set of themes.
6. Apply themes to data organization

RESULTS

Table 1

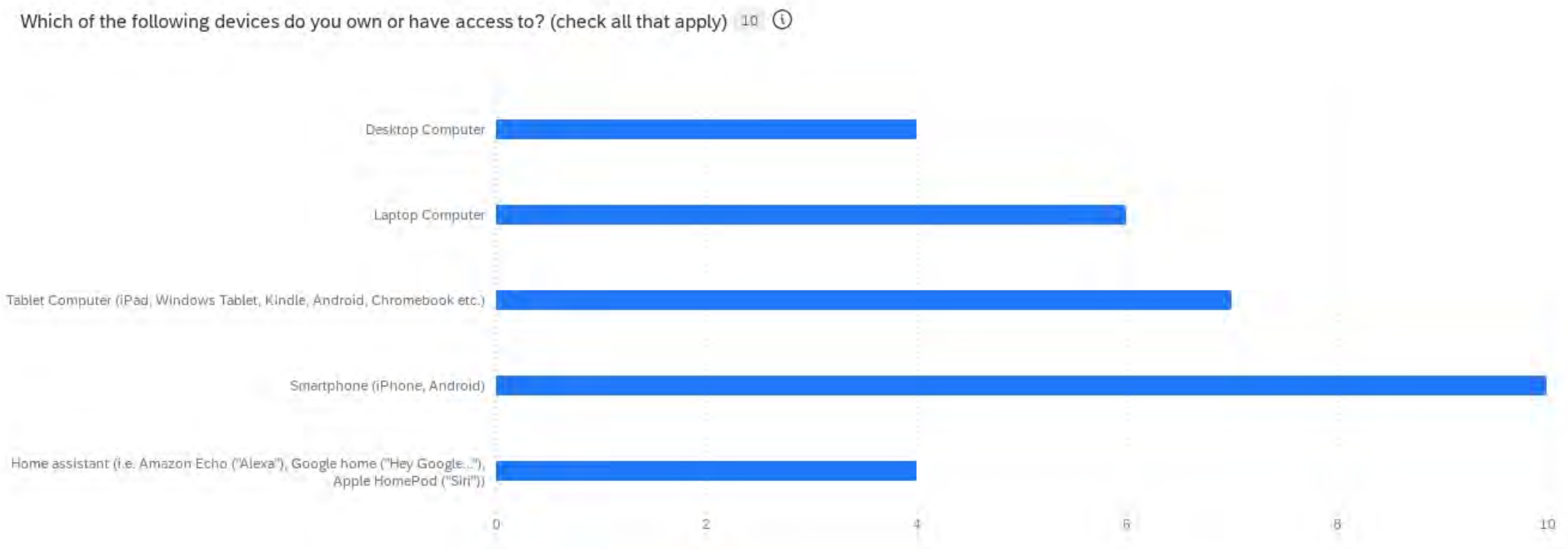
Demographics

Characteristics	N=10
Age in years, mean (SD)	72.1 (6.905794668)
Gender, n (%)	
Female	8 (80)
Male	2 (20)
What is your current marital status?	
Married	5 (50)
Divorced	2 (20)
Widowed	3 (30)
With whom do you live?	
Alone	4 (40)
With spouse or partner	5 (50)
With group	1 (10)
Other	1 (10)
What is your highest grade of education?	
Junior high school (9th Grade)	1 (10)
Bachelor's level degree (or other standard 4-year degree)	4 (40)
Master's level degree	5 (50)

RESULTS

Demographic Results

6 of 10 participants (60%) use smart phone as their main internet source



University of South Carolina

RESULTS

Health App Use

6 of 10 participants (60%) use health apps

Which of the following health apps do you currently use on your internet connected device(s)? (check all that apply) 6

intnt_ha_type - Which of the following health apps do you currently use on your internet connected device(s)? (check all that apply) - Selected Choice	Percentage	Count
Weight tracking	50%	3
Blood pressure	33%	2
Medication management (tracking, alerts, etc)	33%	2
Mood	17%	1
Sleep	33%	2
Exercise, fitness, pedometer, or heart rate monitoring (includes specific types of exercise like running, yoga, etc.)	67%	4
Other (specify)	17%	1

RESULTS

Health Device Use

6 of 10 participants (60%) use electronic devices

Which of the following electronic health-related devices have you used? (check all that apply) 6

medtech_edev_type - Which of the following electronic health-related devices have you used? (check all that apply) - Selected Choice	Percentage	Count
Blood glucose testing	33%	2
Digital blood pressure machine	100%	6
Digital home pulse oximeters	17%	1
Digital thermometer	50%	3
Electronic pillbox	33%	2
Wireless bathroom scale	83%	5
Other (specify)	17%	1

RESULTS

Technology Use Satisfaction

Non-Invasive

“They really do not bother you. It's nonexistent. They're not aggravating or going off or doing anything to annoy anyone. Like I said, you don't even know it's there unless you look up at the wall.

“[I like] that it's silent and you really don't know it's there. And you can just go on about your daily routines and not wonder if someone is watching over you or listening to you.”

Creates Self-Awareness

“It made me more aware of what I should be doing rather than just sitting down or going and watering the flowers. Like I said, it gave you purpose. And I guess, as older people, we are intended to do what we need to do.”

I actually thought it was beneficial….I was like, "Okay." In the morning, I'm conscious about my [medicine], "Okay, I got to go there and get it," and then at night to do my night meds. I think it [pillbox] kind of kept me on track because there may have been times where I was like, "Oh, gosh, I didn't take my night meds." But that was very helpful to me**.**

RESULTS

Technology Ease of Use and Usefulness

Passive Nature of LAMP

“It was almost to the point that I had forgotten I was in the study. It just became natural. It basically has become like a part of my life. I mean, I wear a watch, so I wear this. I take medicine, but I got a better pill box. I weigh, but I got a better scale. I'm moving around, but now I know someone is noticing me moving around.”

“I didn't have to do anything except charge the watch. The only thing I needed to do was make sure that the watch was on charge. Other than that, I had nothing. There was nothing I needed to do except go about my daily chores.”

Openness to Remote Monitoring/Acceptability

“I would certainly do it, and I would recommend it highly….particularly in rural areas, this is a great health asset to provide for those who and it's not just for, I don't think, lower income, but for anybody who's working to age a little more successfully at home”

“I guess I'm kind of I don't know. I guess I'm kind of 50/50. I could use it. I mean, it doesn't bother me because I'm not really in a decline, bad decline in my health, I don't see the benefit in me saying, "Oh, yeah, 85%. I'm all in. Bring it back. Monitor me”

RESULTS

Comfort with LAMP

“The first day, I was a little apprehensive about it, just because I feel like Big Brother's always watching, and now you've got these monitors in my house where you're watching when I go in and out. And so, I think just being apprehensive about knowing that they were there before they were. But honestly, once they were there, they didn't bother me.

“I got pretty much more comfortable over time. When I first got it, I didn't know what to expect. I didn't know whether the alarm was going to be going off or whatever. But after that [installation], I mean, everything just kind of settled down.”

“I was comfortable with everything that you actually, with all the sensors and stuff, I never saw or felt that it was an issue at all.”

RESULTS

Suggestions for Improving LAMP (Usability/Usefulness)

Share remote monitoring data with participants

“If I have the system in my home and it's long-term…and this [LAMP] is what we're going to use to determine if something is going on, who's doing the monitoring”

“I was thinking about that in terms of for me, it would be maybe more frequent feedback or report to show whether I'm progressing in my stated goals of monitoring, getting the feedback in terms of the status that the system is picking up”.

Provide more watch band options

“The only issue I had was you know the watch, which I was allergic to. It caused me to break out, and I certainly didn't like that, but the one thing you told me immediately, you did try to resolve it and just wasn't able to do it at that time.”

“Not complaining about the little strap on the watch because we were supposed to wear it all the time except for when it would be charging up. And that was the only little discomfort, this little rubber strap on your wrist”

RESULTS

Suggestions for Improving LAMP (Usability/Usefulness)

Offer Multiple Pillbox Sizes

“Oh, the pillbox, I think, was the only thing about the pillbox for me is that it does not have enough space for me to sort my medicines a little bit more precisely. It just has one…category for each day.” I need at least three or four compartments.”

" Unfortunately, I never used the pillbox. I go out and do things during the day… I didn't want to risk not having what I needed on me at all times. So, I kept my little pill container [with me]. I never used that [pillbox].”

CONCLUSIONS

- Remote monitoring may be culturally-appropriate for empowering rural-dwelling African Americans to age-in-place, but these systems should be easy-to-use and designed with community input.
- LAMP was usable, acceptable, and useful.
- Detailed explanations about the potential long-term benefits of LAMP related to their current health could increase acceptance of LAMP for long-term use.
- Data sharing and more diverse technology options may also enhance LAMP uptake.

NEXT STEPS (CURRENT STUDY)

Revolutionizing Empowerment of African Americans' Cognitive Health through Innovative Technology (REAACH-IT) Study

Aim: To identify barriers to aging-in-place, current technology use behaviors, and attitudes toward remote monitoring technologies among African Americans living with ADRD and their care partners

Eligibility- African-American adults who:

(1) Live in rural SC

(2) Have mild cognitive impairment or early-stage dementia

(3) Have a care partner who is willing to participate

Call Shaun Owens at 803-777-0384

Help Us Design An In-Home Health Monitoring for African Americans with Dementia

PURPOSE:

To help faculty at the University of South Carolina learn more about the feasibility, acceptability, and usability of a technology system that monitors a person's activity and health in their home environment using simple devices such as smartwatches, electronic pill boxes, and bed mats.

WHO IS INVITED TO PARTICIPATE:

African-American adults who:

(1) Live in rural areas of South Carolina
(2) Have memory issues or have an early-stage diagnosis of Alzheimer's Disease or other related dementia
(3) Have a care partner who is also willing to participate

CONTACT:

Interested in participating? Please contact Dr. Shaun Owens at (803) 777-0384, owenso@mailbox.sc.edu, or scan QR code

COMPLETE 1 QUESTIONNAIRE ABOUT YOUR HEALTH AND YOUR EXPERIENCE USING TECHNOLOGY

PARTICIPATE IN ONE 45-MINUTE INTERVIEW ABOUT YOUR CHALLENGES WITH AGING AT HOME AND THOUGHTS ABOUT REMOTE HEALTH MONITORING TECHNOLOGY

RECEIVE a $100 "THANK YOU" Gift card

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1512 Pendelton Street
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This research is funded by the National Institutes for Health

South Carolina

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FROM INSIGHTS TO ACTION: COMMUNITY ENGAGEMENT AND POPULATION **RESEARCH IN ALZHEIMER'S DISEASE**

Dr. Matthew Lohman

Dr. Monique Brown

Dr. Maggi Miller

Dr. Daniel Kilpatrick

Dr. Dwayne Porter

Panel Moderated by Dr. Swann Adams

UNIVERSITY OF South Carolina

THE SUPPLEMENTAL NUTRITION ASSISTANCE PROGRAM (SNAP) AND COGNITIVE HEALTH: A CAUSAL INFERENCE ANALYSIS

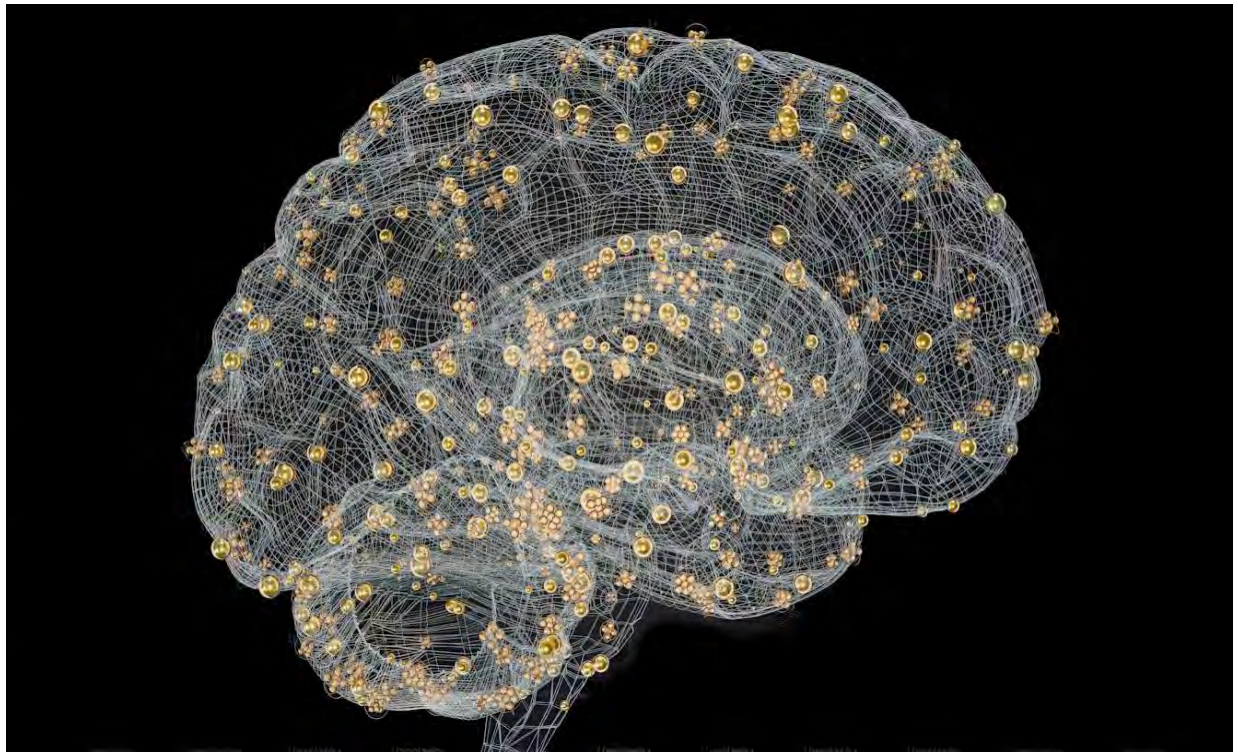
Matthew Lohman

Associate Professor, University of South Carolina,

Department of Epidemiology and Biostatistics

COGNITIVE DECLINE AND DEMENTIA

- Dementia affects over 6M Americans
- No cure → prevention relies on lifestyle factors
- Nutrition = key modifiable risk factor
- Mediterranean & DASH diets → lower risk of dementia.



FOOD INSECURITY AND COGNITIVE AGING

- 1 in 7 older adults are food insecure
- Food insecurity → diabetes, obesity, medication non-adherence, depression.
- Effect of food access (food insecurity, SNAP) less studied longitudinally.

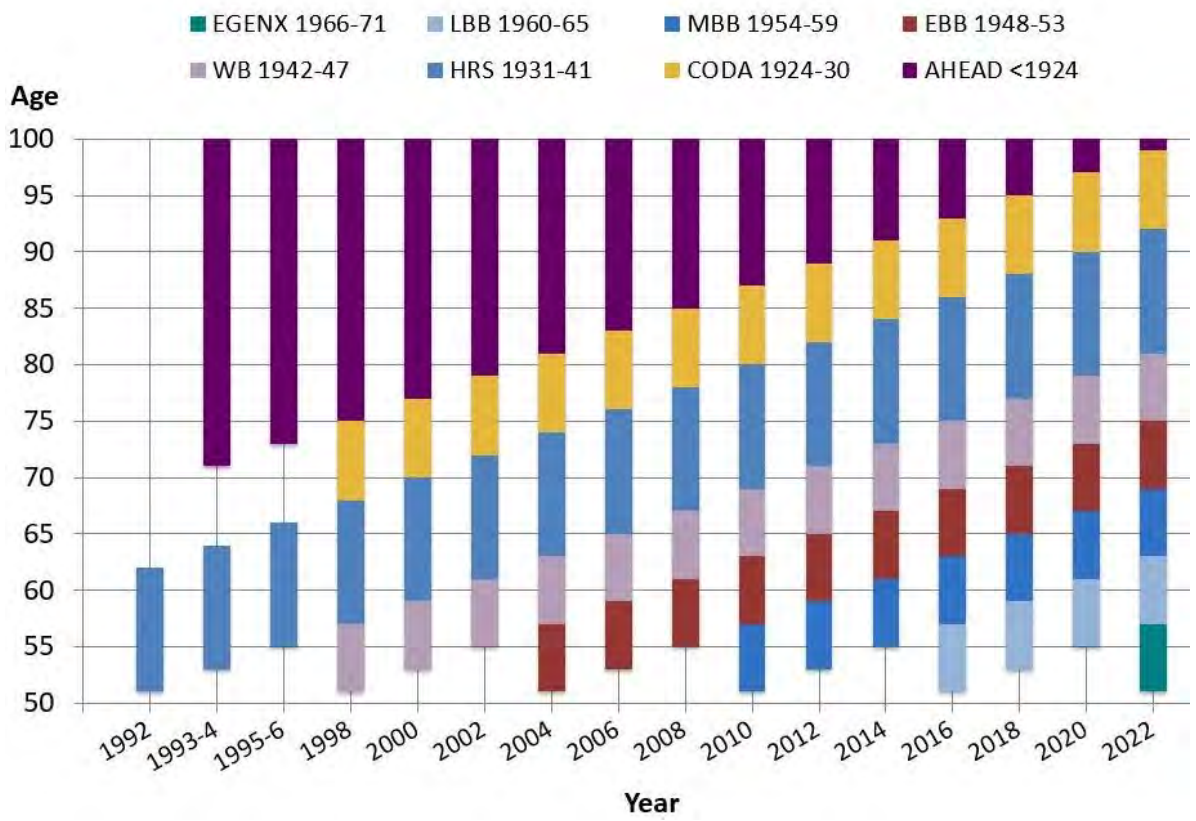
SUPPLEMENTAL NUTRITION AND HEALTH

- SNAP benefits improve food security and diet quality
- Federal program available in all 50 states
- Fewer than half of eligible older adults use SNAP benefits
- Longitudinal effects on cognition unclear

Supplemental
Nutrition
Assistance
Program

METHODS - DATA

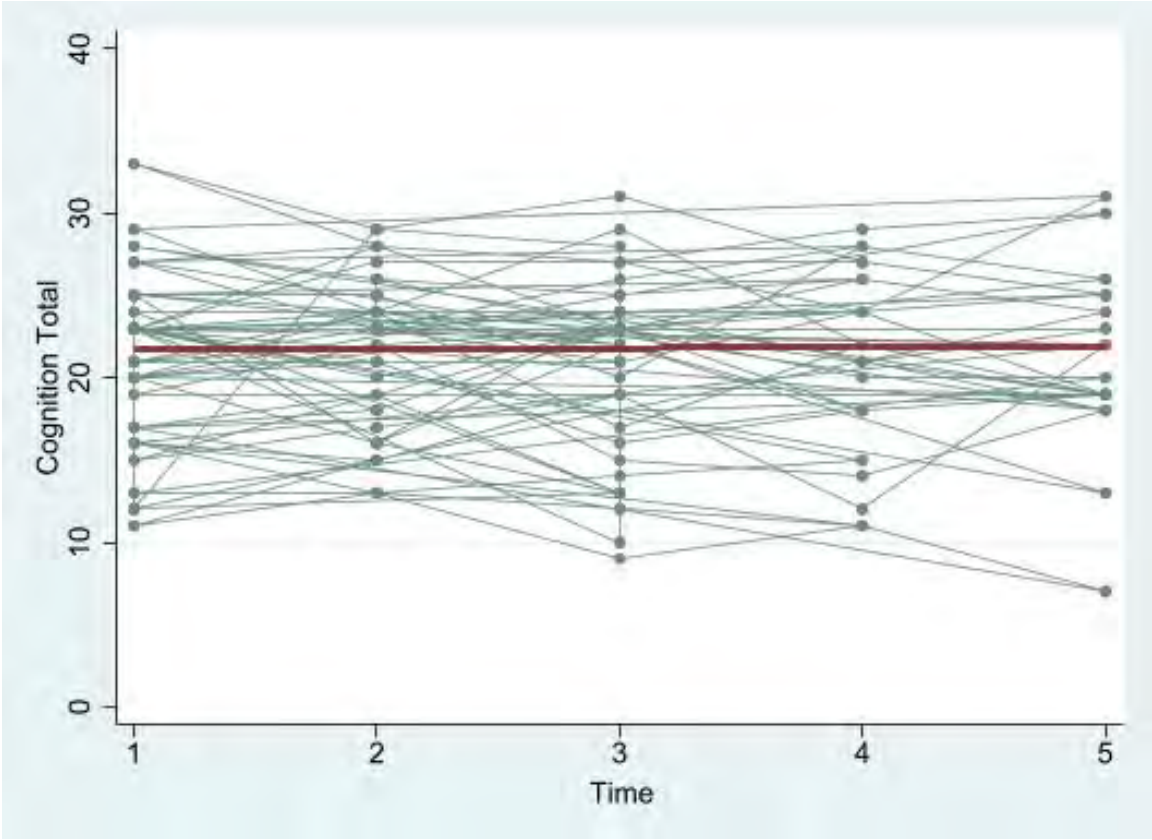
HRS | HEALTH AND RETIREMENT STUDY



- 6,968 participants age > 50
  - 3,735 age > 64
- Followed from 2010 – 2020
- Comprehensive dietary assessments
  - Harvard FFQ
  - Healthy eating index (HEI)
- Cognitive scores (0-35)
  - Based on mini-mental state exam (MMSE)

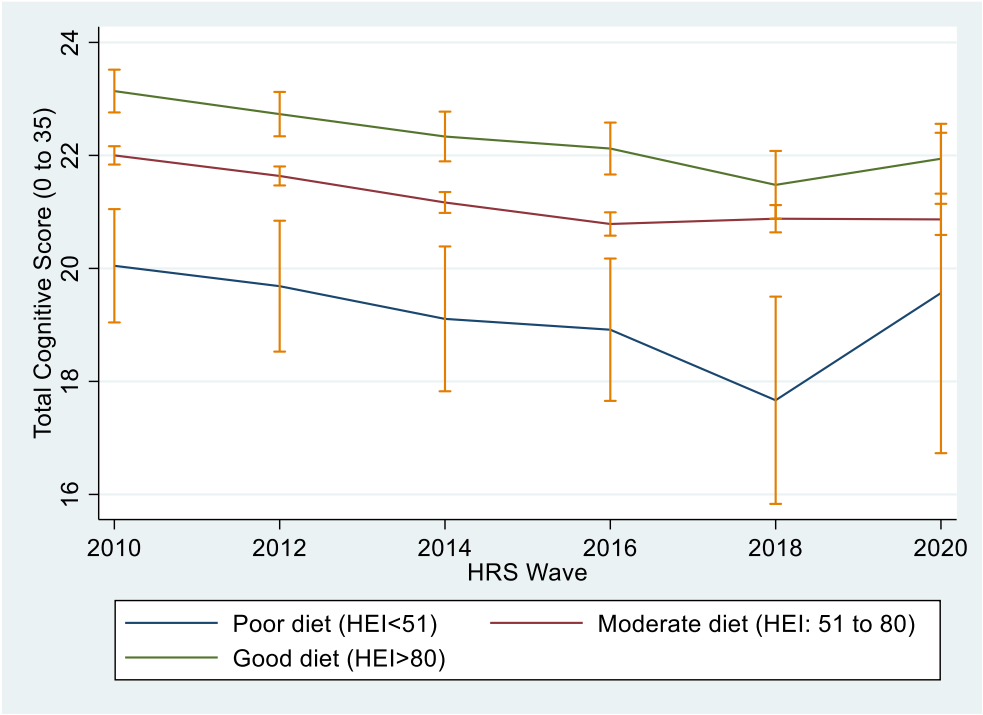
METHODS - ANALYSIS

- Mixed effects models
  - Estimates change over time
  - Accounts for within-person correlations
  - Control for demographic and health factors:
    - Age, race, gender, education, chronic conditions, alcohol use, smoking status, HH income
- Negative controls – more later

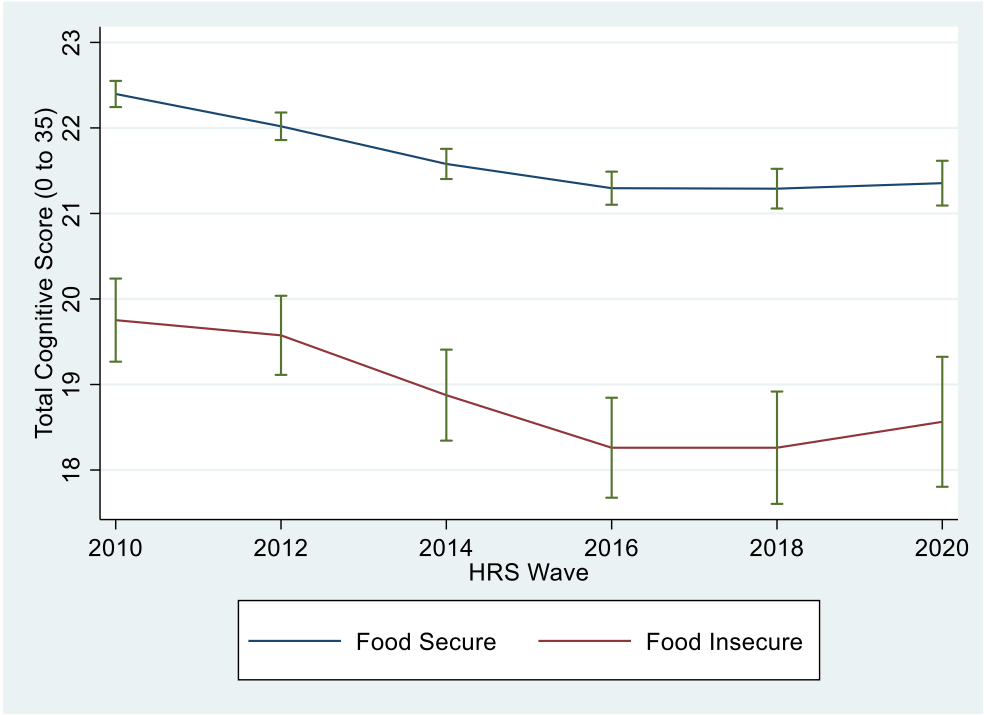


RESULTS

Diet quality

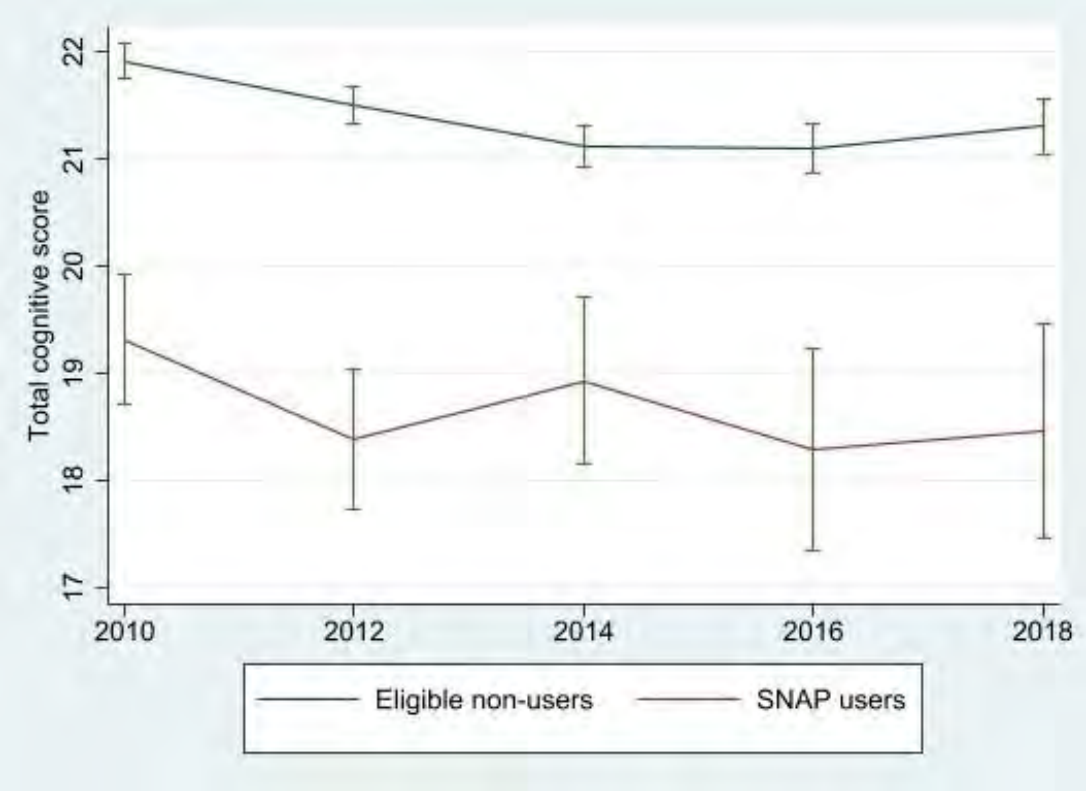


Food security



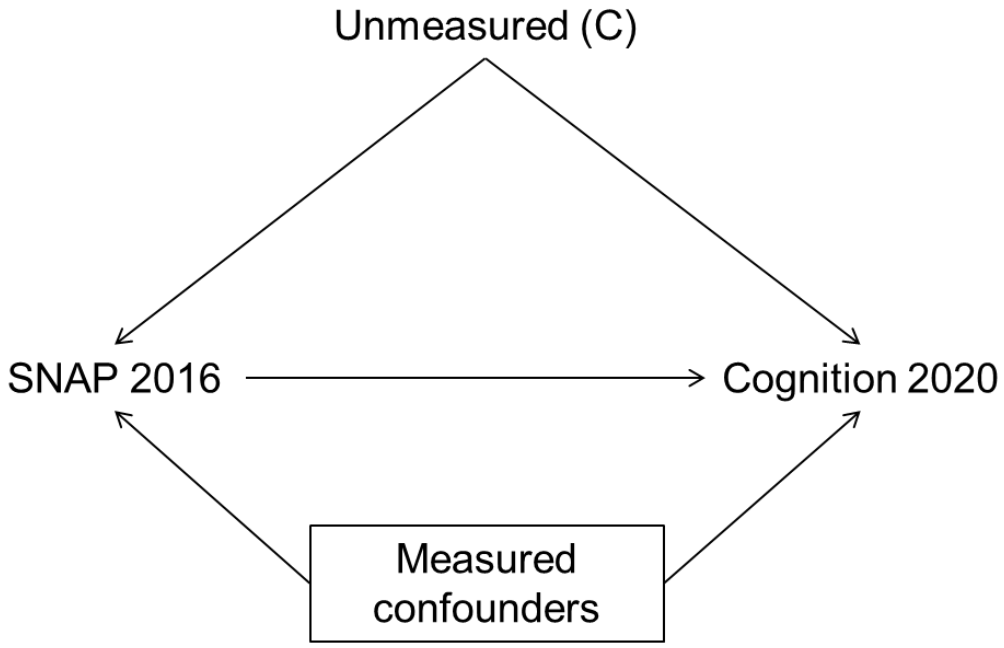
South Carolina

RESULTS

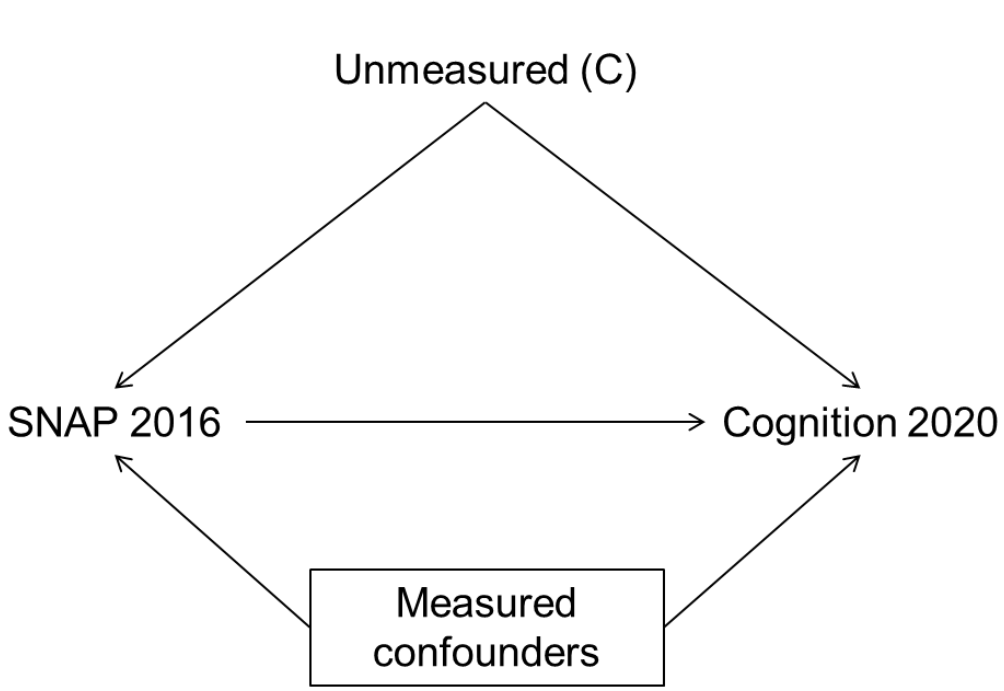


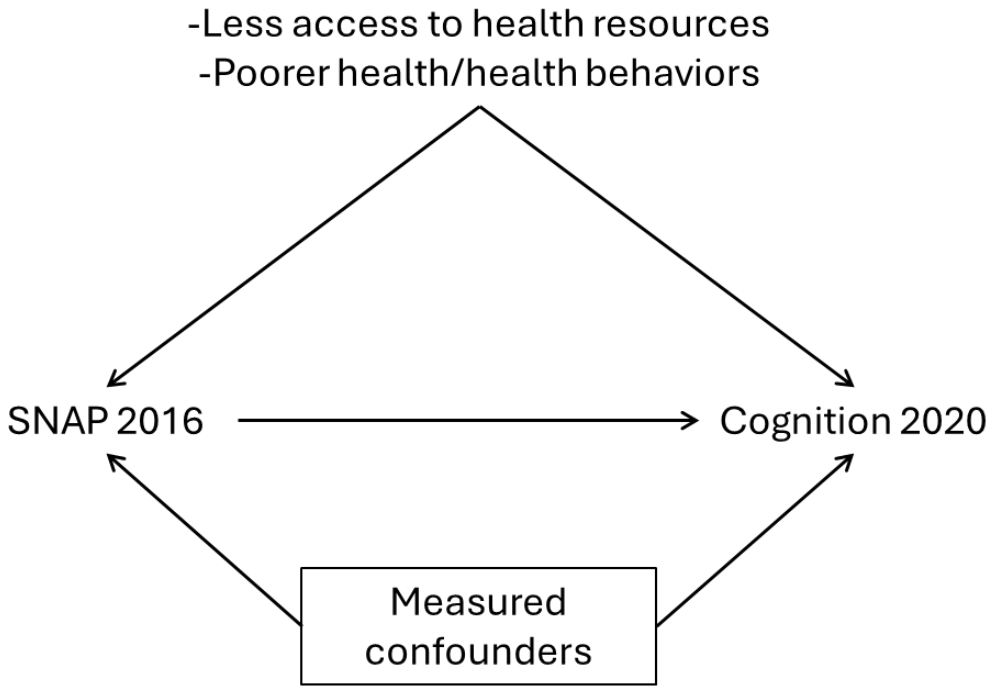
- Contrary to expectations – SNAP users had poorer cognitive performance than eligible non-users
- Paradoxical results suggest potential analysis problem
- Unmeasured confounding from self-selection*

CONFOUNDING

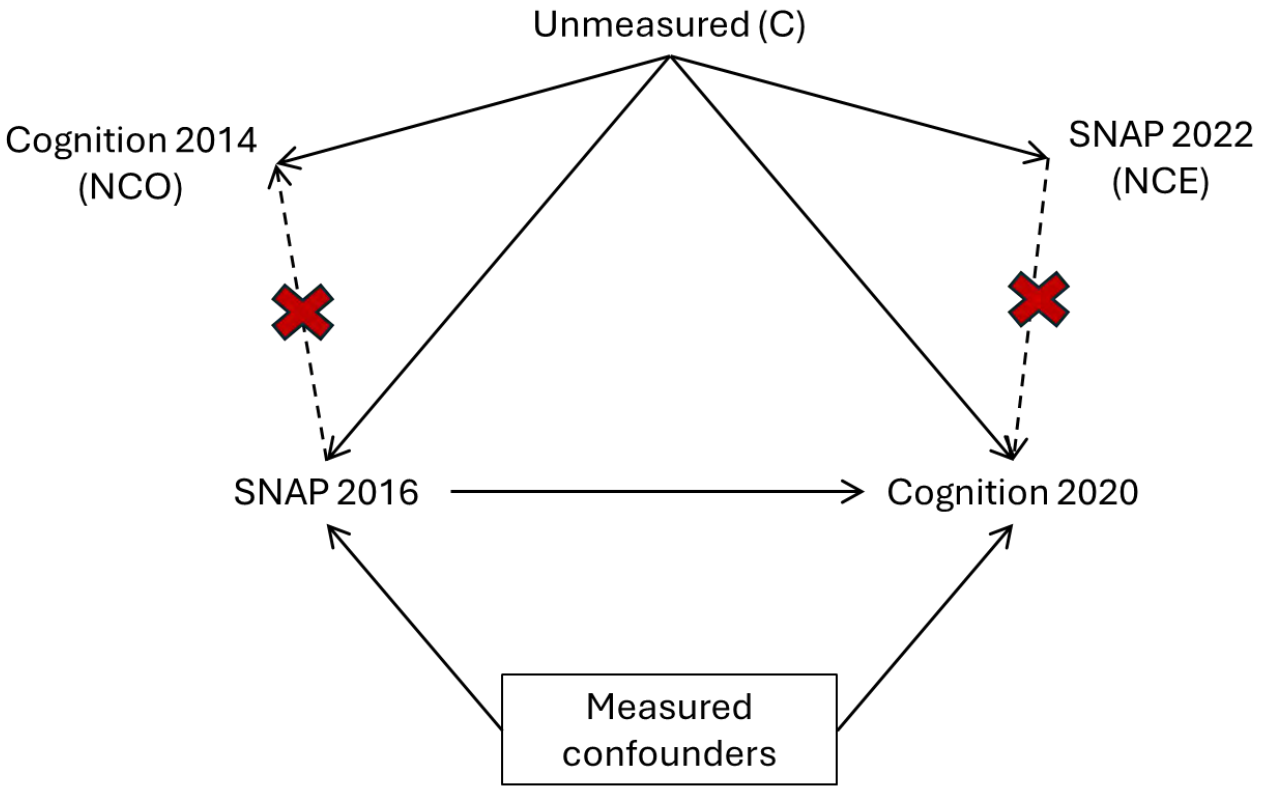


CONFOUNDING





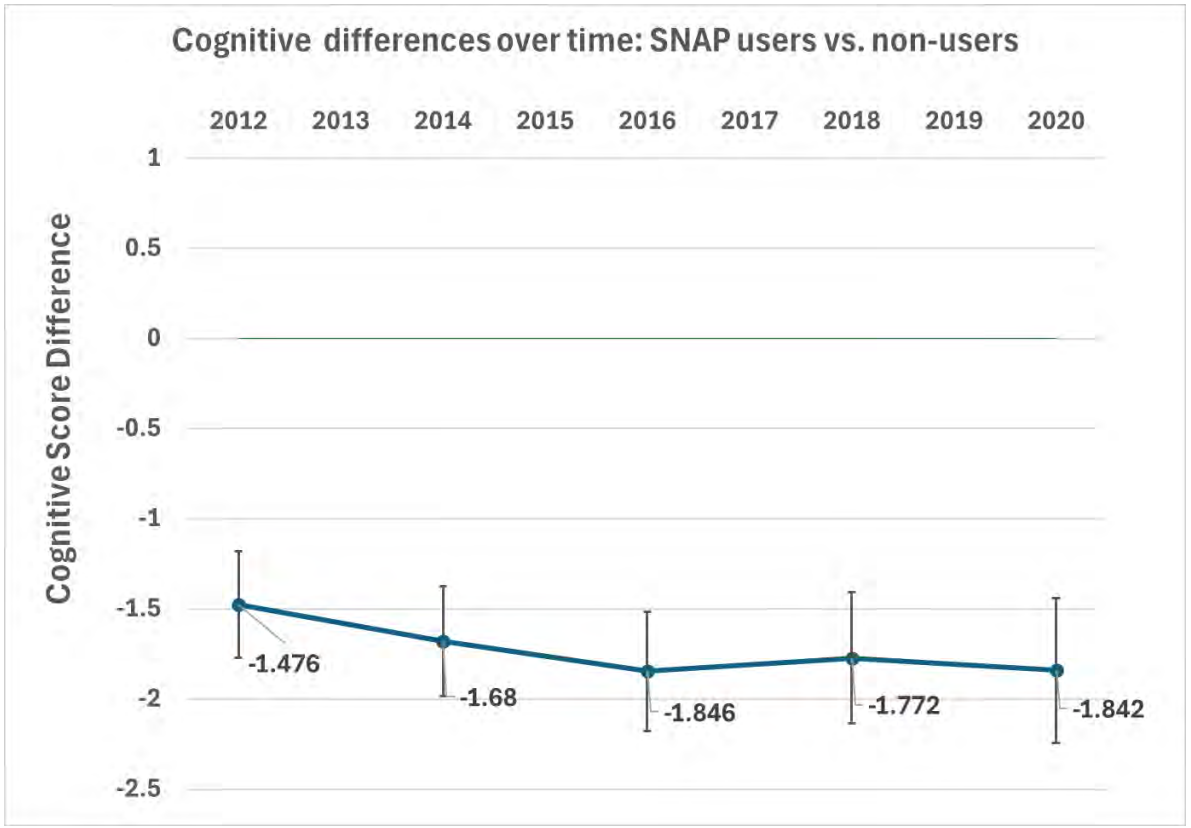
NEGATIVE CONTROL ANALYSIS



- Negative controls are proxies for confounding
- Negative control outcome (NCO) – a variable that can't be causally by SNAP use
- Negative control exposure (NCE) – a variable that can't causally effect cognition

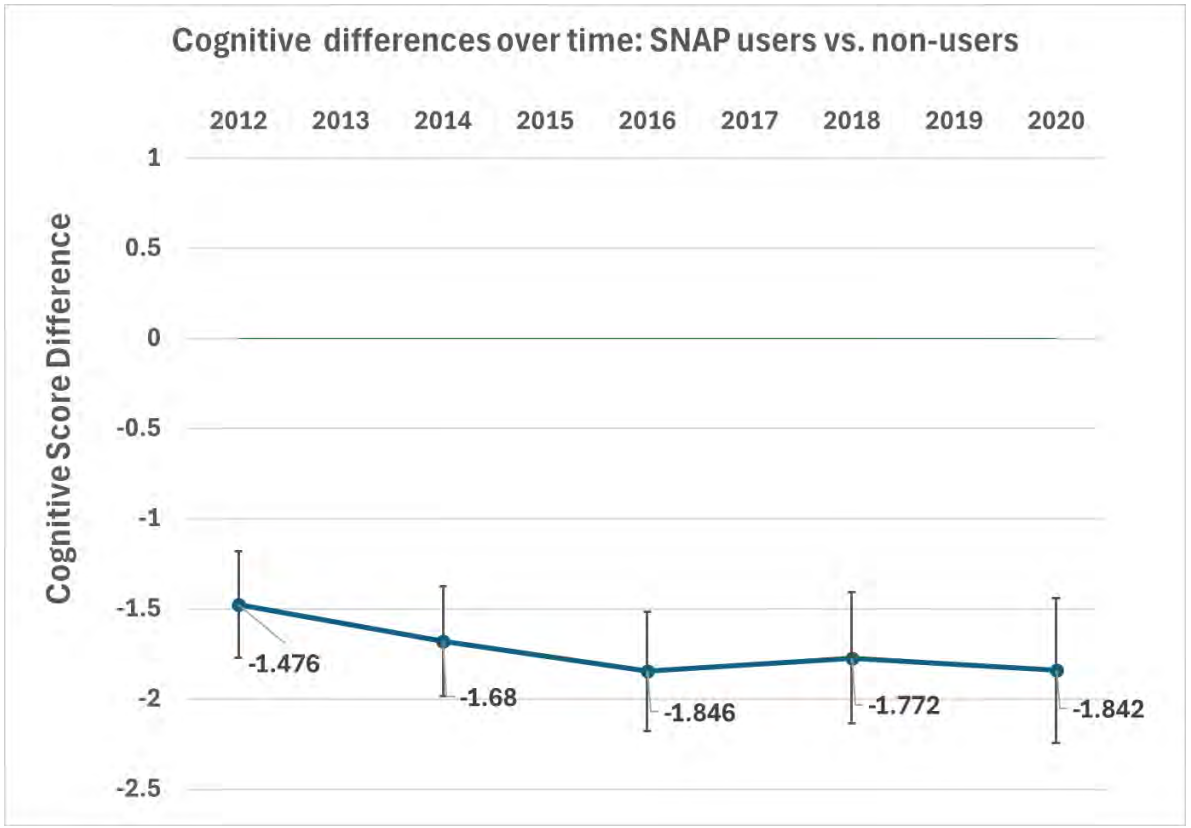
NEGATIVE CONTROL ANALYSIS RESULTS

Multivariable regression

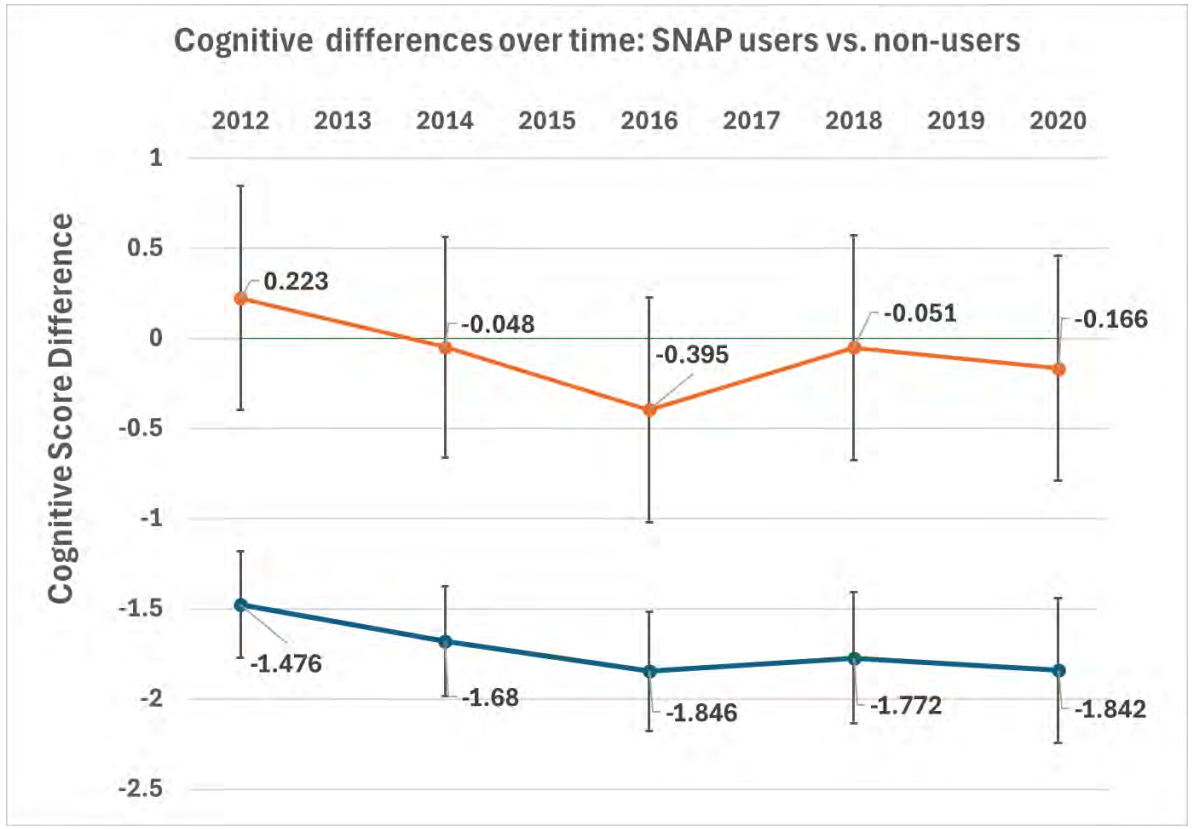


NEGATIVE CONTROL ANALYSIS RESULTS

Multivariable regression



Negative control adjustment



DISCUSSION

- Better diet quality → higher baseline cognition & slower decline
- Food insecurity → lower baseline cognition & faster decline
- SNAP use → lower baseline cognition & faster decline

but…

- This appears to be due to bias/confounding
- Measuring cumulative SNAP exposure may show cognitive benefit

POLICY AND PREVENTION IMPLICATIONS

- Address food insecurity and poor diets as dementia risk factors.
- Improve SNAP enrollment among older adults (~42% uptake).
    - Simplify applications, extend recertifications, expand outreach.
    - Qualitative research to determine reasons for underuse.
- Improve accuracy of policy-related analyses

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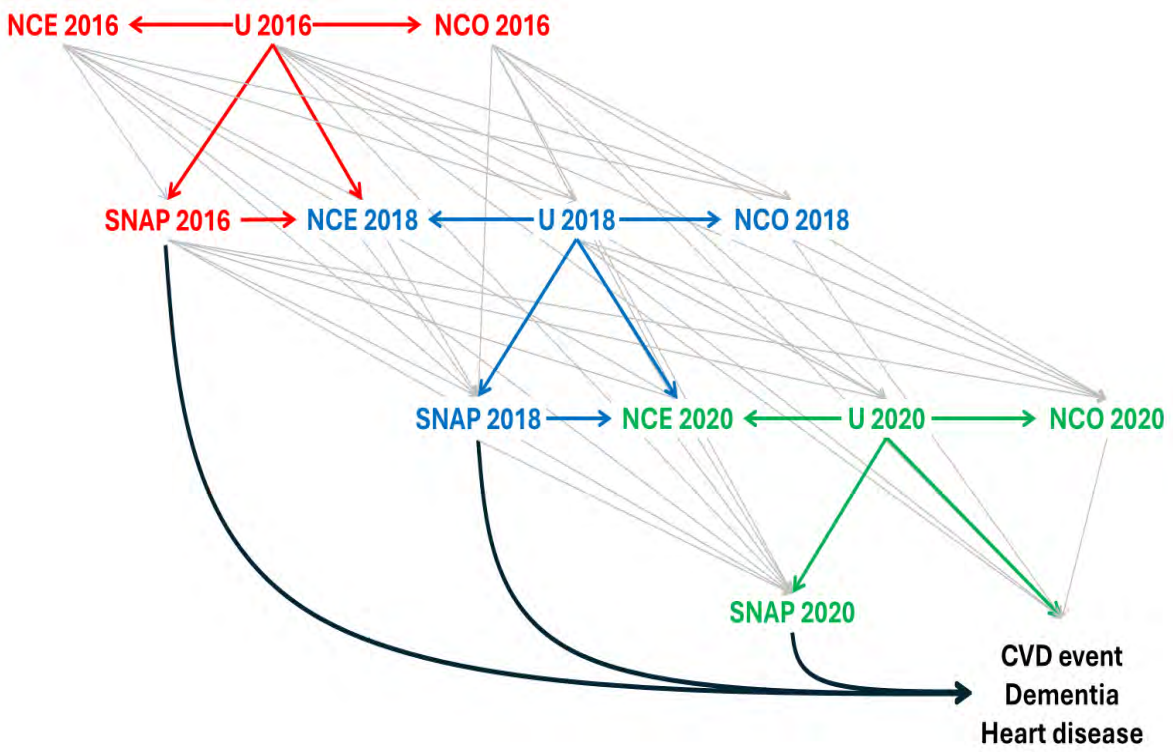
NEXT STEPS



- Longitudinal NC analyses to account for cumulative SNAP use
- Study SNAP effects on leading causes of morbidity and mortality – e.g., heart disease and stroke
- Broaden policy and program research
- Qualitative work on SNAP uptake reasons

THANKS!

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PATTERNS OF HIV-ASSOCIATED DEMENTIA IN SOUTH CAROLINA: CURRENT RESEARCH AND FUTURE DIRECTIONS

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Associate Professor, Department of Epidemiology and Biostatistics

Research Fellow, University of the Free State, South Africa

October 10, 2025

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OUTLINE

- Background
- **Research Study 1:** Sociodemographic Characteristics of HIV-Associated Dementia in South Carolina
- **Research Study 2:** Health Disparities in Mortality among Individuals with HIV-Associated Dementia in South Carolina
- Discussion and Future Directions

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BACKGROUND

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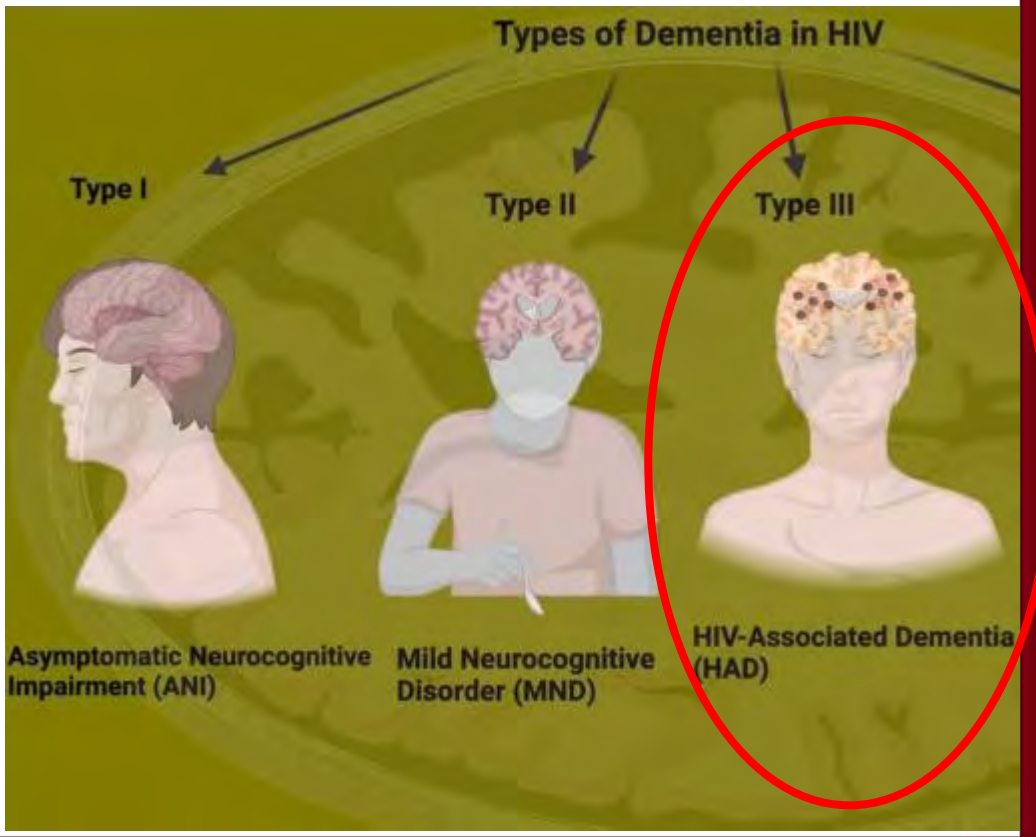
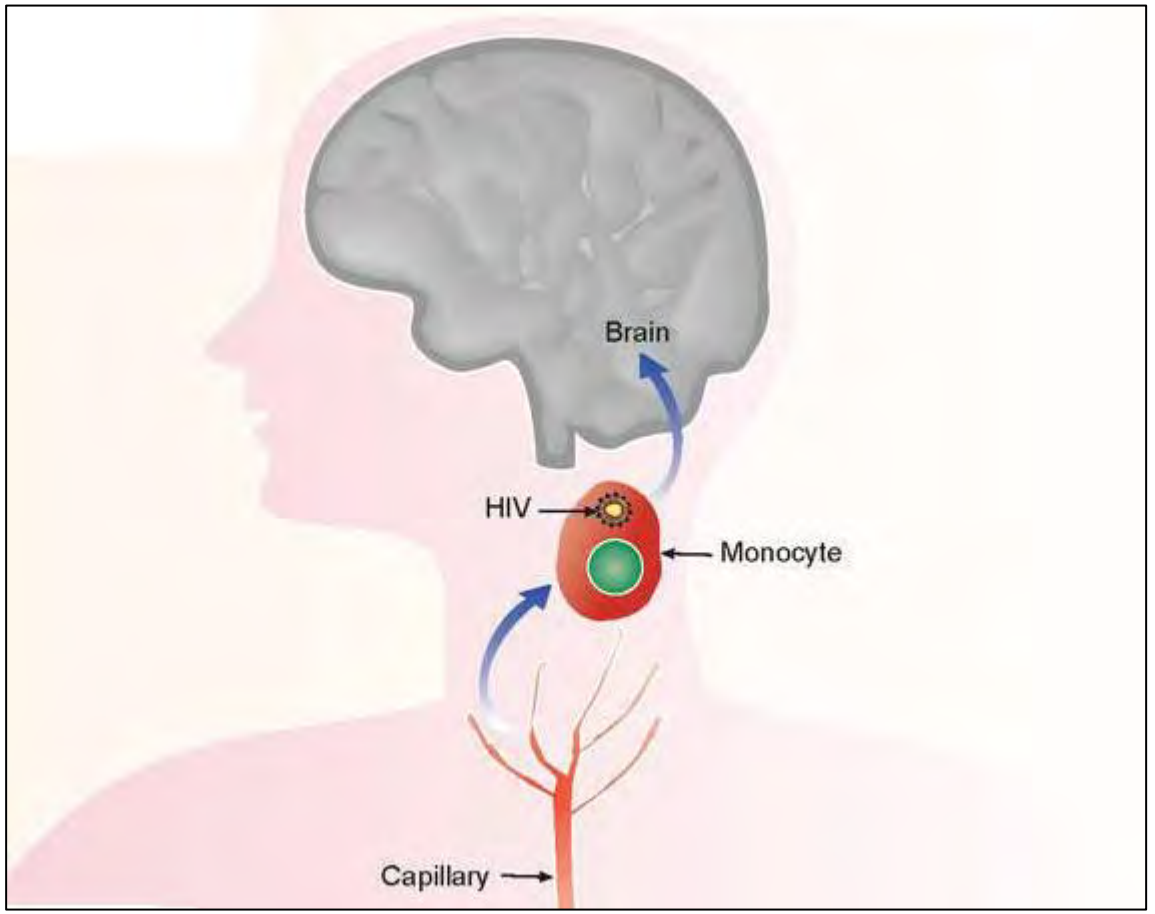
HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS

- Before antiretroviral therapy (ART), acquired immunodeficiency syndrome (AIDS) dementia complex was a common adverse health outcome of living with HIV
- AIDS dementia complex is now called HIV-associated neurocognitive disorders (HAND)
- HAND includes:
  - Asymptomatic neurocognitive impairment (ANI)
  - Minor neurocognitive disorder (MND)
  - HIV-associated dementia (HAD)



HIV-ASSOCIATED DEMENTIA (HAD)

- Most severe form of HAND
- Independent risk factor for mortality among people living with HIV (PLWH)
- Occurs when HIV crosses the blood brain barrier
- Can develop into a debilitating disease



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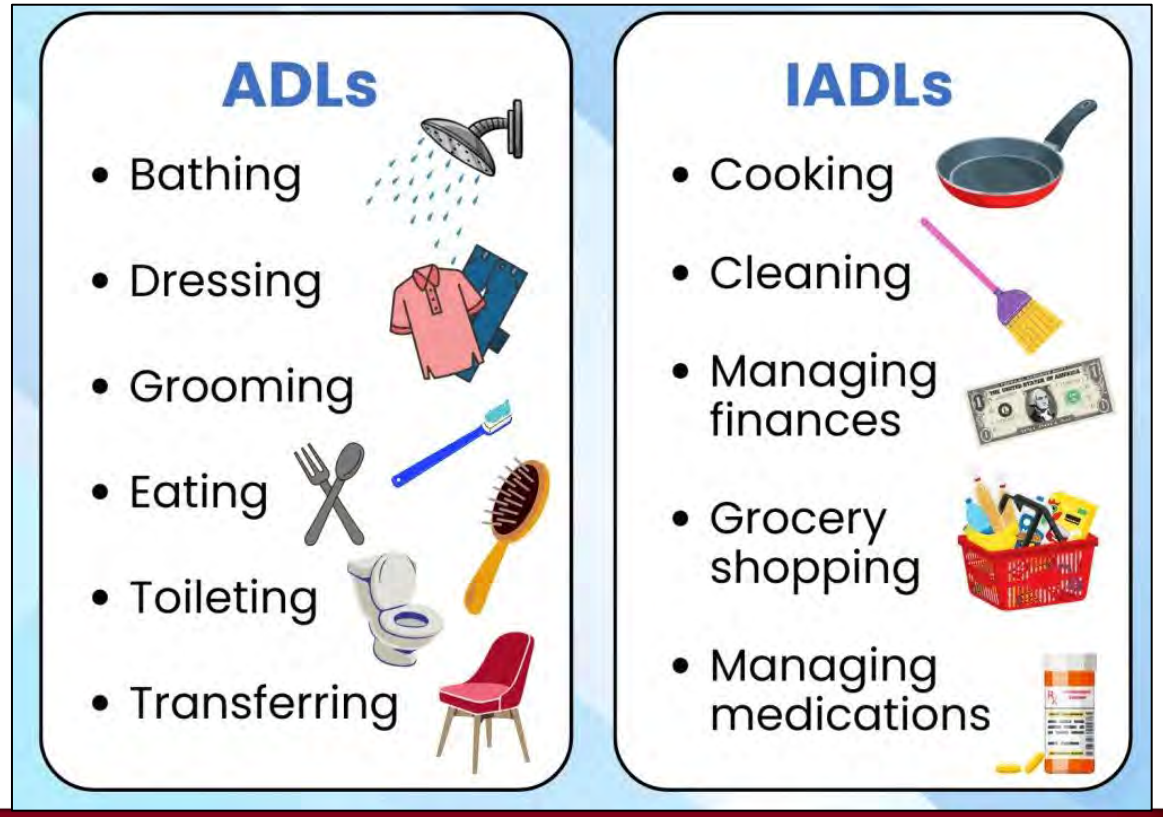
HIV-ASSOCIATED DEMENTIA (HAD) (CONT.)

- HAD is characterized by memory loss, difficulties with thinking and/or concentrating, speaking clearly and loss of motor skills

- HAD can also affect:
  - Activities of daily living (ADLs)
  - Instrumental activities of daily living (IADLs)
  - Adherence to ART
  - Viral suppression



GAPS IN THE SCIENTIFIC LITERATURE

- Lack of studies examining the sociodemographic characteristics of HAD, especially in the southern United States
- Studies examining disparities associated with mortality among individuals living with HAD are scarce
- More studies are needed to determine potential ways to reduce or prevent HAD among people living with HIV

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AIMS

- **Research Study 1**

Published in final edited form as:
South Med J. 2023 October ; 116(10): 833–838. doi:10.14423/SMJ.0000000000001607.

Sociodemographic Characteristics of HIV-Associated Dementia in the South Carolina Alzheimer's Disease Registry

Monique J. Brown, PhD, MPH[1,2,3,4], Maggi C. Miller, PhD[1,4], Omar Bagasra, MD, PhD[5], Lucy A. Ingram, PhD[4,6]

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AIMS (CONT.)

- **Research Study 2:**

AIDS CARE
2024, VOL. 36, NO. 3, 291–295
https://doi.org/10.1080/09540121.2023.2221424

Health disparities in mortality among individuals with HIV-associated dementia in South Carolina

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METHODS

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DATA SOURCE

- Data were obtained from the South Carolina Alzheimer's Disease Registry (SC ADR)
- The SC ADR is a comprehensive dataset of South Carolina residents who have been diagnosed as having Alzheimer's disease and related dementias (ADRD)
- The SC ADR has maintained a record of ADRD diagnoses since 1988 and identifies individuals with ADRD when they (or their family members) seek provider services

RESEARCH STUDY 1 METHODS

- Descriptive statistics were used to describe the study population and by HAD status and determined HAD prevalence estimates
- Crude and multivariable logistic regression models were used to determine sociodemographic characteristics associated with HAD by time period (2000-2006 and 2010-2016)
- Multivariable models adjusted for age, race, sex, rurality, and place of diagnosis

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RESEARCH STUDY 2 METHODS

- Descriptive statistics were used to describe the overall sample of those with HAD (N = 503), and statistically significant differences by mortality status.

- Multivariable logistic regression and Cox proportional hazards models were used to determine risk factors for mortality

- Multivariable models controlled for age, race, sex, rurality, and place of diagnosis

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RESULTS: RESEARCH STUDY 1

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PREVALENCE OF HAD, SC AD REGISTRY

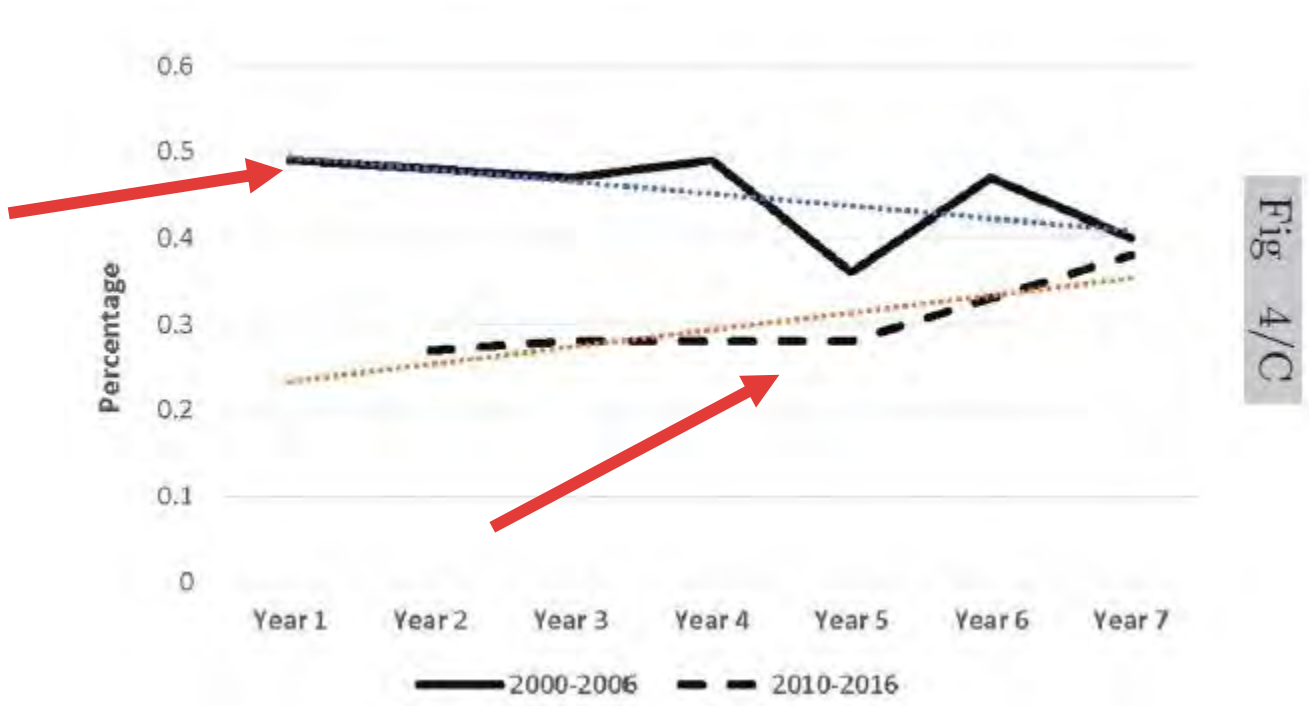

Fig 4/C

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SOCIODEMOGRAPHIC CHARACTERISTICS BY HAD

	N (%) N = 165,487	HAD n = 505	No HAD n = 164,982	*P*
Age group, y				<0.001
18–34	149 (0.10)	5 (1.08)	144 (0.09)	
35–44	560 (0.37)	74 (16.0)	486 (0.32)	
45–54	3136 (2.06)	138 (29.7)	2998 (1.98)	
55–64	16,607 (10.9)	146 (31.5)	16,461 (10.9)	
65–74	31,955 (21.0)	68 (14.7)	31,887 (21.0)	
75–84	54,073 (35.5)	24 (5.17)	54,049 (35.6)	
≥85	45,658 (30.0)	9 (1.94)	45,649 (30.1)	
Race				<0.001
Black	42,626 (27.0)	368 (74.7)	42,258 (26.9)	
White	109,578 (69.5)	109 (22.1)	109,469 (69.6)	
Other	4851 (3.1)	15 (3.0)	4836 (3.1)	
Hispanic	660 (0.4)	1 (0.2)	659 (0.4)	
Sex				<0.001
Female	103,330 (62.6)	165 (32.7)	103,165 (62.6)	
Male	61,873 (37.5)	339 (67.3)	61,534 (37.4)	
Location				0.313
Urban	110,773 (72.9)	356 (75.0)	110,417 (72.9)	
Rural	41,197 (27.1)	119 (25.1)	41,078 (27.1)	
Place of diagnosis				0.010
Nursing facility	52,870 (34.0)	134 (28.4)	52,736 (34.0)	
Living in the community	102,730 (66.0)	338 (71.6)	102,392 (66.0)	

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SOCIODEMOGRAPHIC CHARACTERISTICS OF HAD

Table 2. Association between sociodemographic characteristics and HIV-associated dementia in South Carolina

	2000–2006				2010–2016			
Characteristic	**Crude OR**	**95% CI**	**aOR**	**95% CI**	**Crude OR**	**95% CI**	**aOR**	**95% CI**
18–34 y vs ≥85 y	**405.2**	**190.8–860.5**	**196.7**	**91.0–425.3**	**175.9**	**58.2–531.1**	**97.0**	**31.6–297.8**
35–44 y vs ≥85 y	**913.3**	**544.1–>1000.0**	**426.3**	**250.0–726.9**	**771.2**	**384–>1000.0**	**371.0**	**181.5–758.4**
45–54 y vs ≥85 y	**274.9**	**167.7–450.7**	**135.2**	**81.5–224.1**	**233.1**	**188.7–457.8**	**128.0**	**64.5–254.3**
55–64 y vs ≥85 y	**59.1**	**36.2–96.6**	**32.7**	**19.8–53.8**	**44.9**	**22.9–88.1**	**27.7**	**14.0–54.8**
65–74 y vs ≥85 y	**12.6**	**7.56–20.9**	**8.08**	**4.84–13.5**	**10.8**	**5.39–21.6**	**7.24**	**3.58–14.7**
75–84 y vs ≥85 y	**2.68**	**1.55–4.65**	**1.90**	**1.08–3.36**	**2.25**	**1.05–4.84**	1.69	0.77–3.72
Black vs White	**10.1**	**8.49–12.1**	**5.98**	**4.87–7.34**	**8.75**	**7.06–10.8**	**4.91**	**3.84–6.28**
Other vs White	**5.24**	**3.35–8.19**	**6.64**	**4.12–10.7**	**3.12**	**1.81–5.35**	**5.17**	**2.95–9.07**
Hispanic vs White	1.22	0.17–8.74	1.03	0.14–7.41	1.52	0.21–10.9	1.23	0.17–8.97
Men vs Women	**3.16**	**2.72–3.66**	**1.66**	**1.40–1.96**	**3.45**	**2.86–4.15**	**1.69**	**1.37–2.08**
Urban vs rural	0.97	0.82–1.13	**1.20**	**1.01–1.43**	1.11	0.90–1.37	**1.39**	**1.10–1.74**
Nursing facility vs living in the community	**0.48**	**0.41–0.57**	0.94	0.79–1.12	**0.77**	**0.63–0.94**	**1.31**	**1.05–1.63**

Boldface type indicates statistical significance. aOR, adjusted odds ratio; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio.

RESULTS: RESEARCH STUDY 2

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HAD MORTALITY IN SOUTH CAROLINA

Table 1. Distribution of sociodemographic characteristics and HAD mortality in SC.

Characteristics	Overall (N = 503)	Alive (N = 377)	Dead (N = 126)	*P*-value
Current age (Mean, SD)	62.9 (9.8)	62.7 (9.7)	63.6 (10.2)	0.3699
<55	116 (23.06)	92 (24.4)	24 (19.05)	0.6093
55–64	220 (43.74)	163 (43.24)	57 (45.24)	
65–74	113 (22.47)	84 (22.28)	29 (23.02)	
75–84	35 (6.96)	26 (6.9)	9 (7.14)	
>85	19 (3.78)	12 (3.18)	7 (5.56)	
Race				0.7023
White	108 (21.47)	84 (22.28)	24 (19.05)	
African American	367 (72.96)	273 (72.41)	94 (74.6)	
Other/Unknown	28 (5.57)	20 (5.31)	8 (6.35)	
Sex				0.3063
Male	338 (67.2)	258 (68.44)	80 (63.49)	
Female	165 (32.8)	119 (31.56)	46 (36.51)	
Rurality				**0.033**
Rural	119 (23.66)	81 (21.49)	38 (30.16)	
Urban	354 (70.38)	269 (71.35)	85 (67.46)	
Unknown	30 (5.96)	27 (7.16)	3 (2.38)	
Nursing home/ community				**<.0001**
Community	336 (66.8)	275 (72.94)	61 (48.41)	
Nursing Facility	134 (26.64)	78 (20.69)	56 (44.44)	
Unknown	33 (6.56)	24 (6.37)	9 (7.14)	

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SOCIODEMOGRAPHIC CHARACTERISTICS OF HAD MORTALITY

Table 3. Sociodemographic Characteristic differences in HAD mortality.

Characteristics	OR	95% C.I.	*P*-value
Current age	1.00	0.98–1.02	0.8426
Female vs. male	1.30	0.83–2.02	0.2555
African American vs. White	1.11	0.65–1.90	0.7022
Other/Unknown vs. White	1.70	0.62–4.68	0.3070
Urban vs. Rural	0.66	0.41–1.07	0.0905
Nursing Facility vs. Community	**3.27**	**2.08–5.15**	**<0.0001**

Bolded odds ratios, 95% confidence intervals and *p*-values are statistically significant at $p < 0.05$

SOCIODEMOGRAPHIC CHARACTERISTICS OF HAD MORTALITY (CONT.)

Table 4. Sociodemographic Characteristics and HAD mortality using a Cox Proportional Hazard model.

Characteristics	HR	95% C.I.	*P*-value
Female vs. male	0.858	(0.589-1.25)	0.4255
African American vs. White	1.518	(0.953-2.42)	0.0791
Other/Unknown vs. White	0.921	(0.404-2.099)	0.845
Urban vs. Rural	0.787	(0.533-1.161)	0.2265
Nursing Facility vs. Community	1.738	**(1.204-2.508)**	**0.0032**

Bolded hazard ratios, 95% confidence intervals and *p*-values are statistically significant at $p < 0.05$

DISCUSSION AND FUTURE DIRECTIONS

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DISCUSSION

- Younger populations (younger than 74 years), communities of color, men, urban populations, and nursing facility populations were more likely to have HAD
- HIV is the most prevalent cause of dementia among younger adults
- Black men and urban populations have higher HIV rates
- Disparities in mortality among patients with HAD were found in place of diagnosis (nursing facility vs. community)

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LIMITATIONS

- Place of diagnosis of ADRD – individuals could have changed their living situations
- Small sample sizes for other racial/ethnic groups
- Alzheimer's disease and vascular dementia given priority in the data
  - Individuals could have also been diagnosed with HAD but may not have been indicated
- Other common HAND diagnoses (ANI, MND) not being available in the data

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FUTURE DIRECTIONS

- Focus on the association between HAD and risk for Alzheimer's disease
  - Determine the mediators and moderators that may play a role in the link between HAD and Alzheimer's disease
  - Examine sociodemographic disparities in HAD and Alzheimer's disease
- Determine if mortality among individuals with HAD was due to HAD or non-HIV related decline
- Assess health outcomes among people who provide (unpaid) care (caregivers) for individuals with HAD

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NIH National Institute on Aging

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THANK YOU!!

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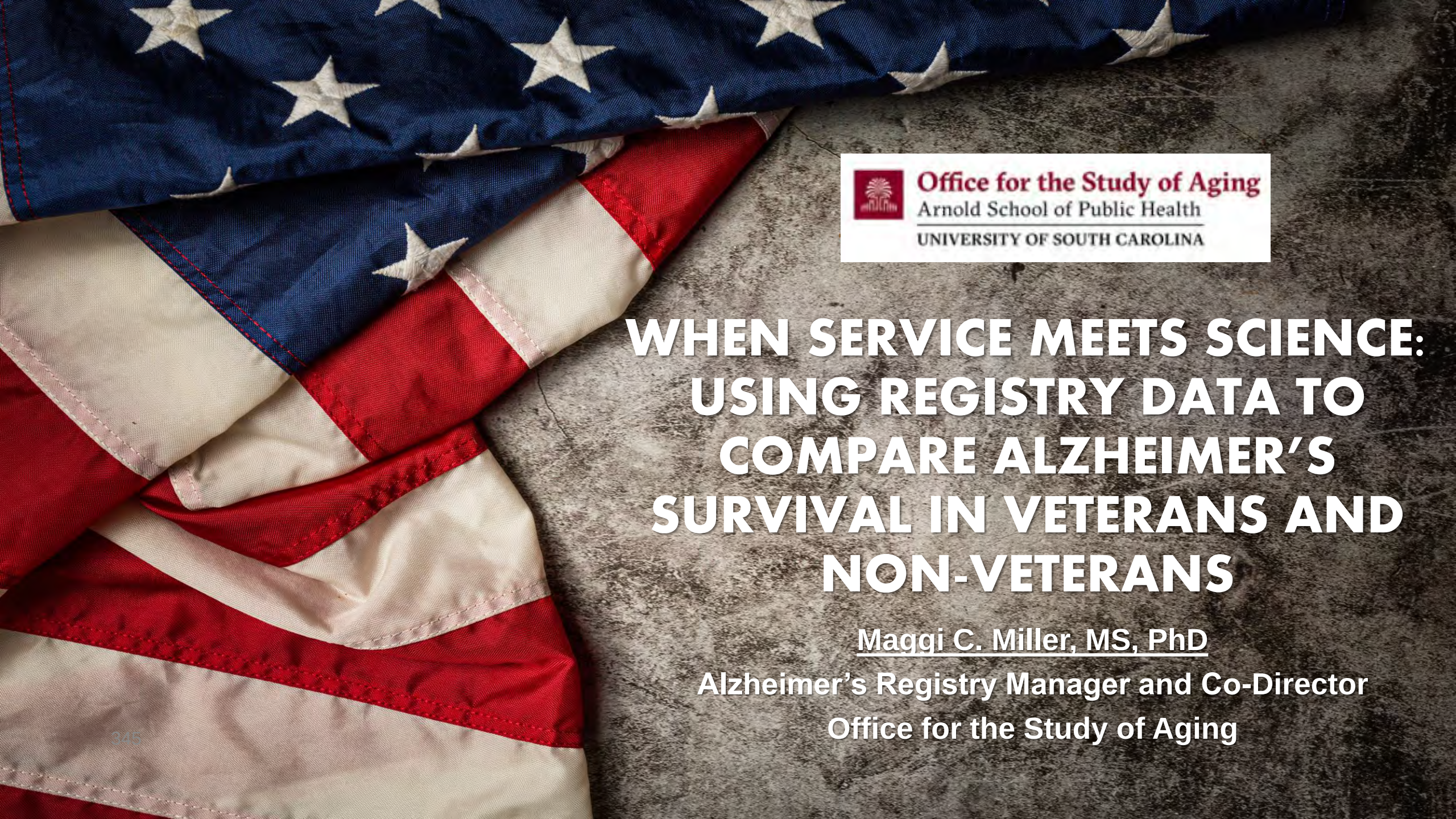

Office for the Study of Aging
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WHEN SERVICE MEETS SCIENCE: USING REGISTRY DATA TO COMPARE ALZHEIMER'S SURVIVAL IN VETERANS AND NON-VETERANS

Maggi C. Miller, MS, PhD
Alzheimer's Registry Manager and Co-Director
Office for the Study of Aging

INTRODUCTION

- Individuals diagnosed with ADRDs have lower survival and a higher risk of mortality
  - Among those aged 70, 61% of those with AD are expected to die before 80 years compared to 30% of those without AD. (Better, 2023)

- Global deaths from ADRDs have increased from 0.56 million in 1990 to 1.62 million in 2019, essentially tripling over the last 3 decades (Li, et al, 2022).

- The median longevity in the South Carolina Alzheimer's Disease Registry ranges from 24 to 36 months. (Miller, et al., 2024)

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VETERAN POPULATION

- As of 2023, nationally there are 8.1 million veterans ages 65+.

- In 2022, South Carolina had 344,664 veterans
  - Representing 8.4% of the state's adult civilian population
  - An estimated 168,800 veterans were aged 65 and over
- The state ranks 8th nationally in its military retiree population compared to other states.
- The largest proportion of veterans in SC served during the Vietnam era (≈ 32.6 %)

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ELEVATED RISK IN VETERANS

- Predictors of poor survival in ADRD include increasing age, comorbidities, male sex, white race, and lower socioeconomic status (Alzheimer's Association, 2024)

- Veterans share many of these risk factors:
  - 91% male and 76% white (2019 VA data)
  - Higher prevalence of comorbidities and lower SES (Betancourt et al., 2021)

- Mortality risk is further compounded by:
  - PTSD
  - Combat exposure
  - Combat-related injuries (Kang & Bullman, 2008)

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STUDY AIM

- While previous studies have examined survival among veterans, there is a paucity of data on survival among veterans with ADRDs in relation to non-veterans.

- This study aims to compare post-diagnosis survival between Veterans and non-Veterans with AD/ADRD using data from the South Carolina Alzheimer's Disease Registry.

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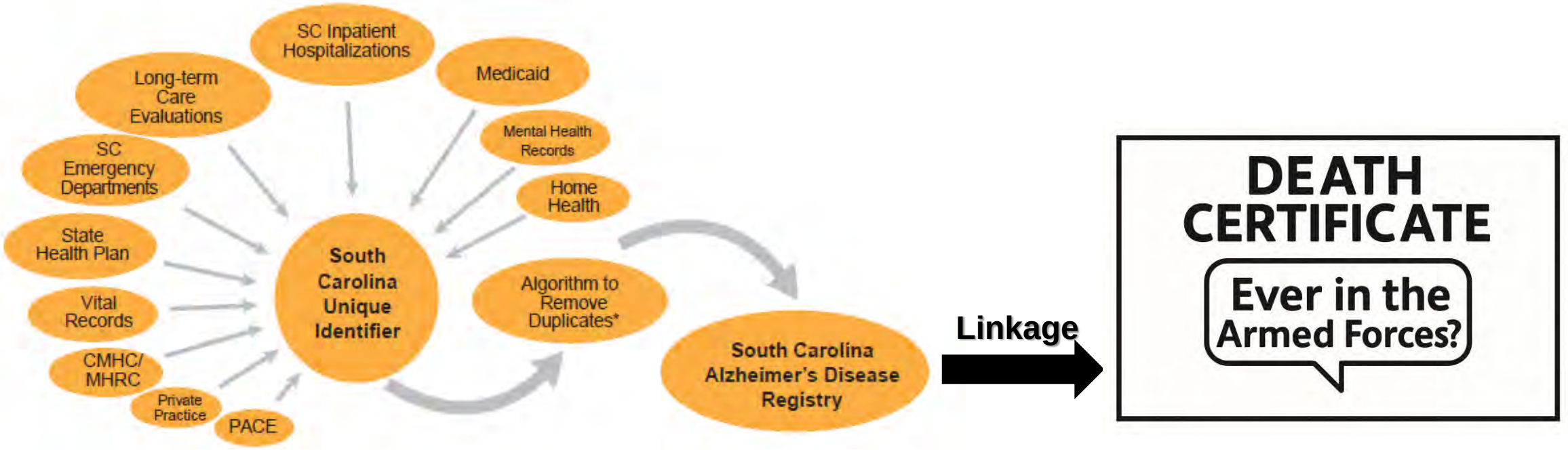
METHODS

- South Carolina Alzheimer's Disease Registry (SCADR) data was used. SCADR is population-based and incorporates records from multiple sources.
  - Additional linkages are available to obtain more in-depth information.



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METHODS

- **Participants**
- Included all participants in registry (n=377,143)
- Excluded for missing veteran status and/or unknown veteran status (n=175,073)
- Grouped into veterans (n=43,302) and non-veterans (n=154,768)
- Propensity Score Matching (PSM) was used to match veterans and non-veterans on age, sex, and race
  - PSM sample: veterans (n=26,032), civilians (n=26,032)

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METHODS

- **Variables and Measures**
- Outcome: time to death, estimated as the time between year of diagnosis and year of death
- Main exposure: Veteran status classified as veteran or non-veteran
- Other covariates : Age, sex, race, location, education, dementia type, and tobacco use contributing to death

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METHODS

Statistical Analysis

- Pearson Chi-square test used to compare differences in baseline characteristics
- Log-log survival plots were used to assess the proportional hazards assumption
- COX model stratified on age, sex, race, education, dementia type, and location was fit to evaluate the relationship between veteran status and time to death
- Analysis conducted in SAS version 9.4

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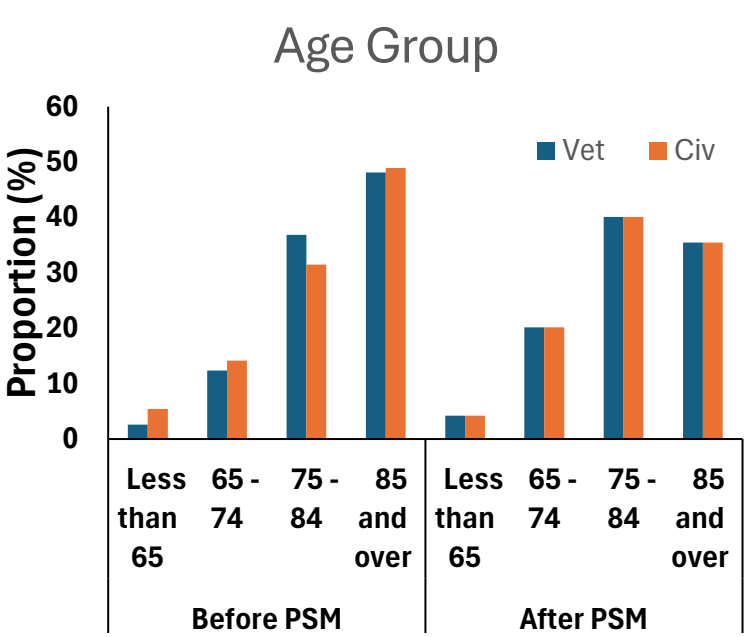
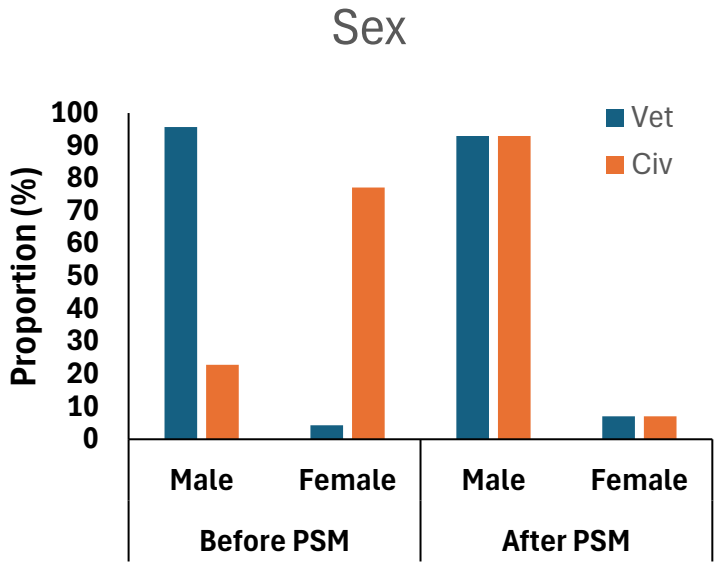
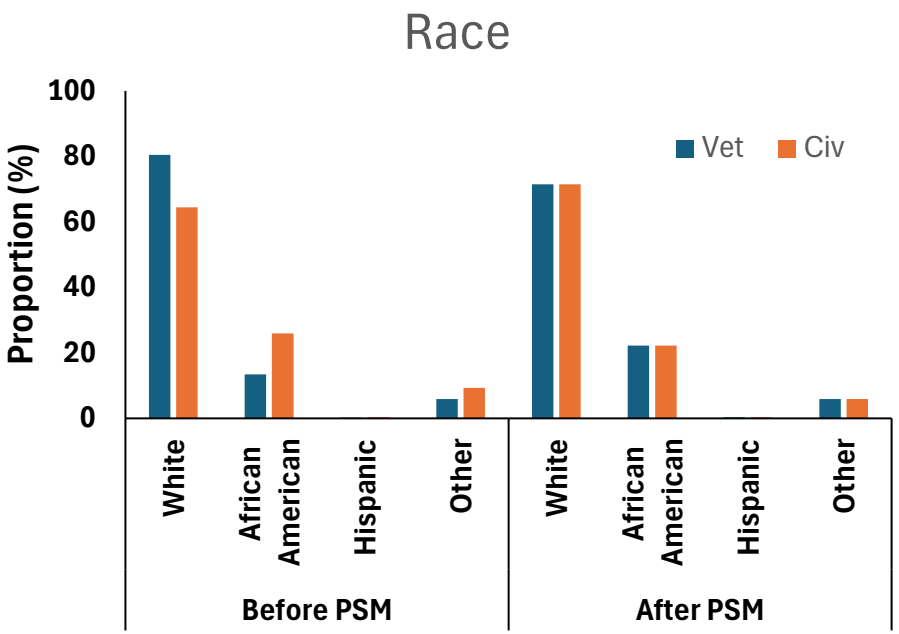
KEY FINDINGS



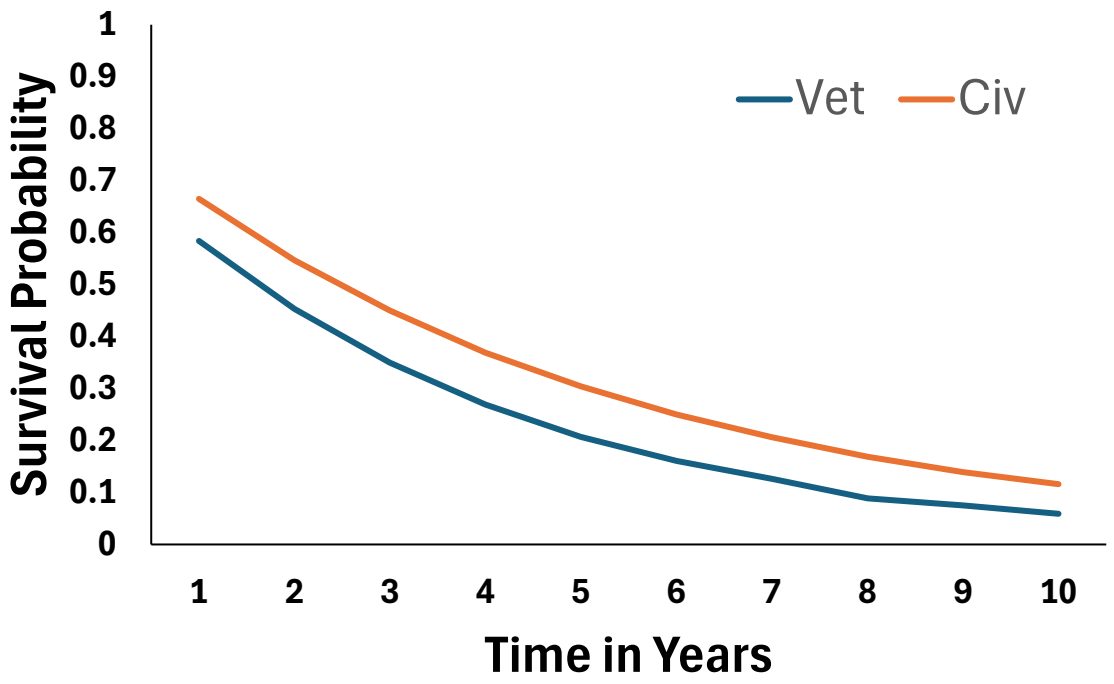




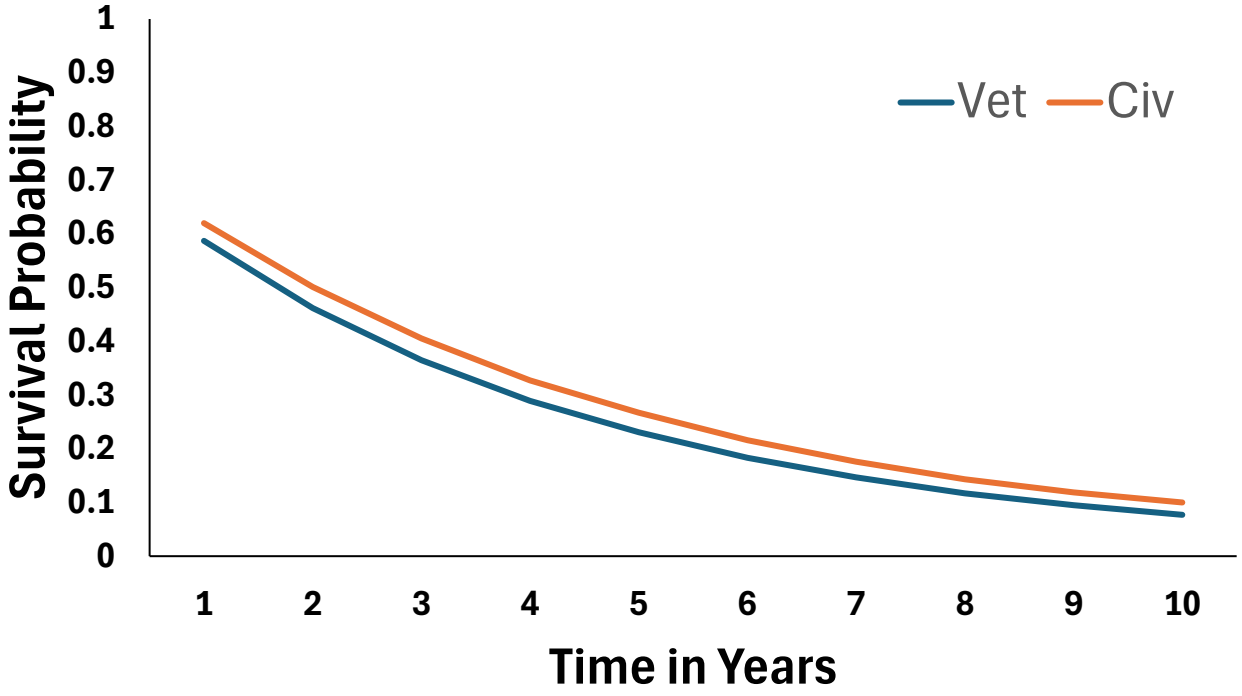
- Before PSM, the distribution of all covariates among veterans was different ($p<0.0001$) from that of non-veterans. However, after PSM, there was no difference ($P=1.000$) in the distribution of age, sex, and race.

KEY FINDINGS

Survival Probability before PSM

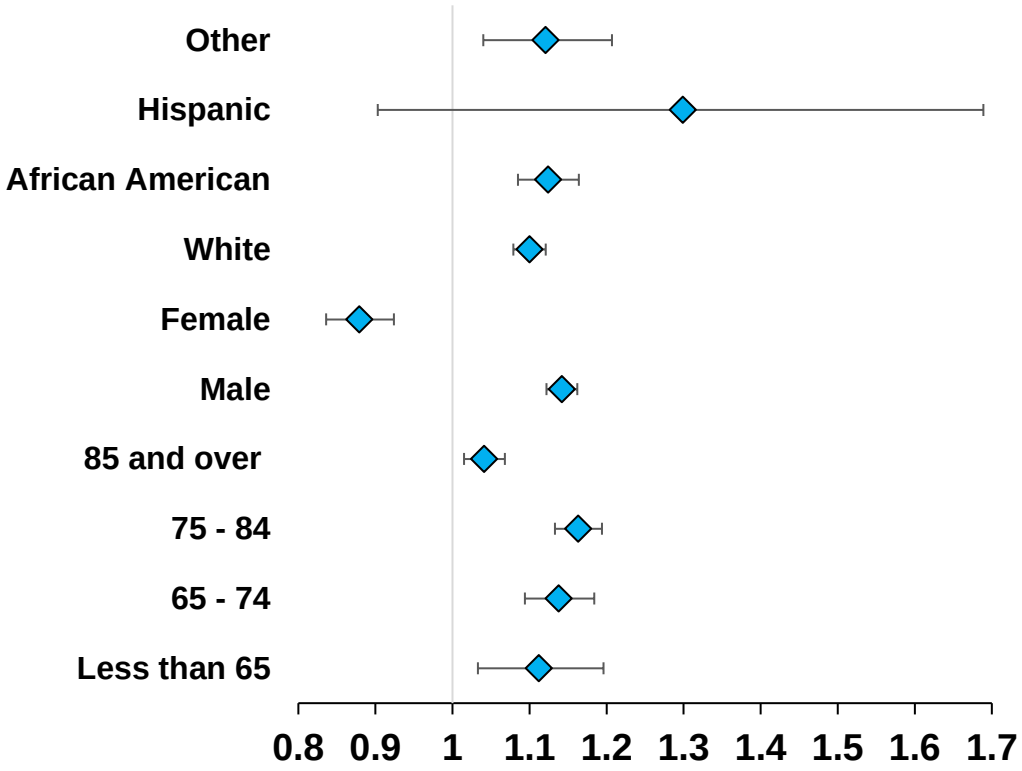


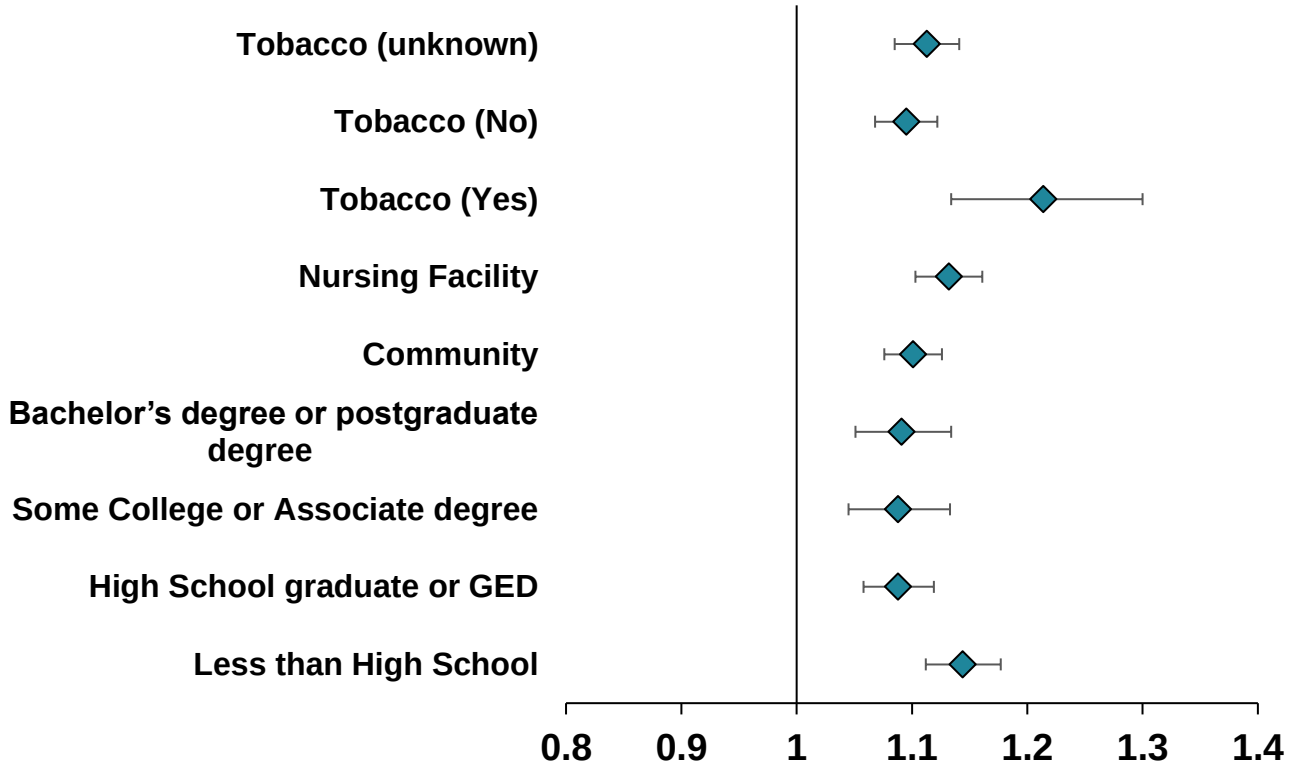
Survival Probability after PSM



KEY FINDINGS

Stratum Specific Hazard Ratios before PSM (Ref = Non-Veteran)





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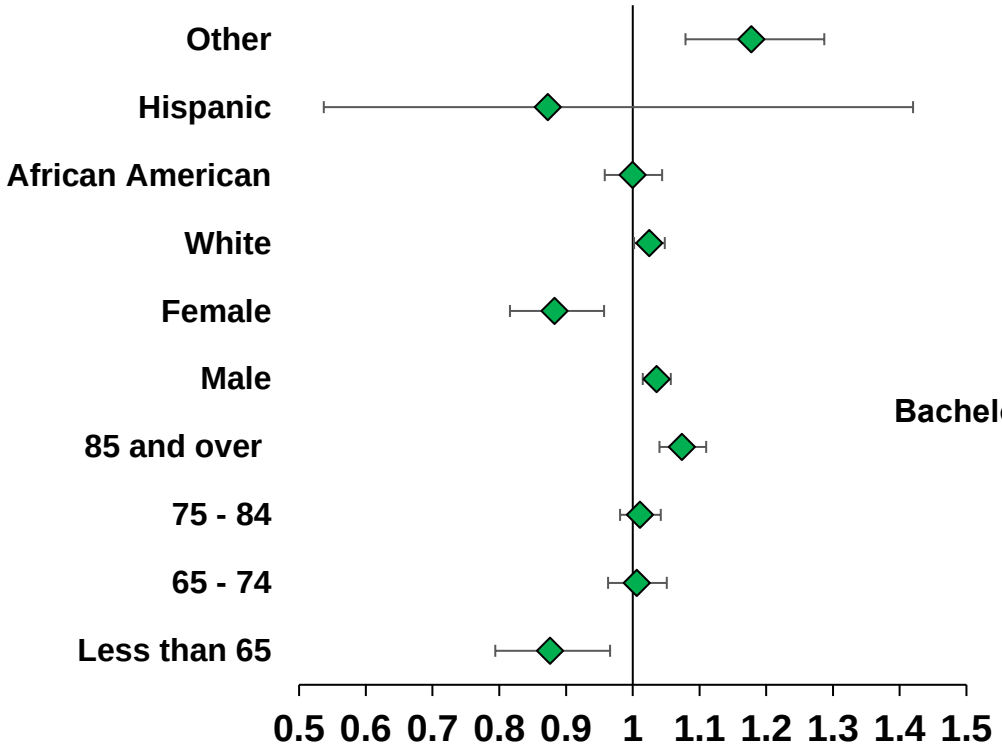
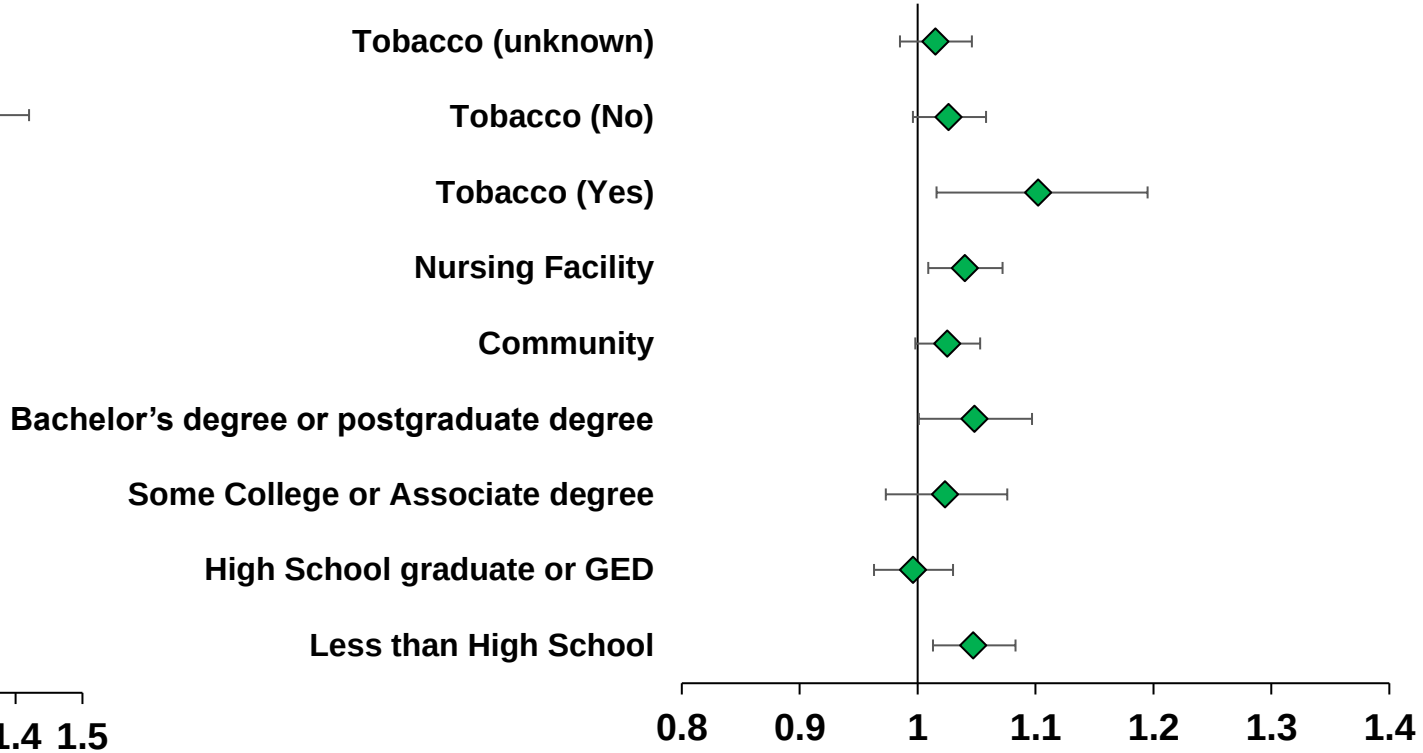
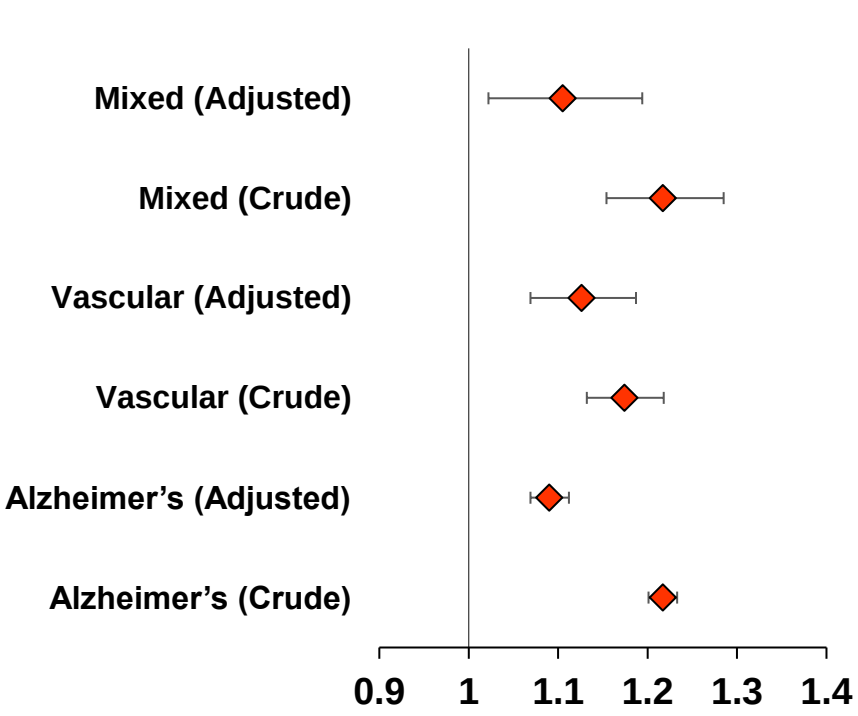
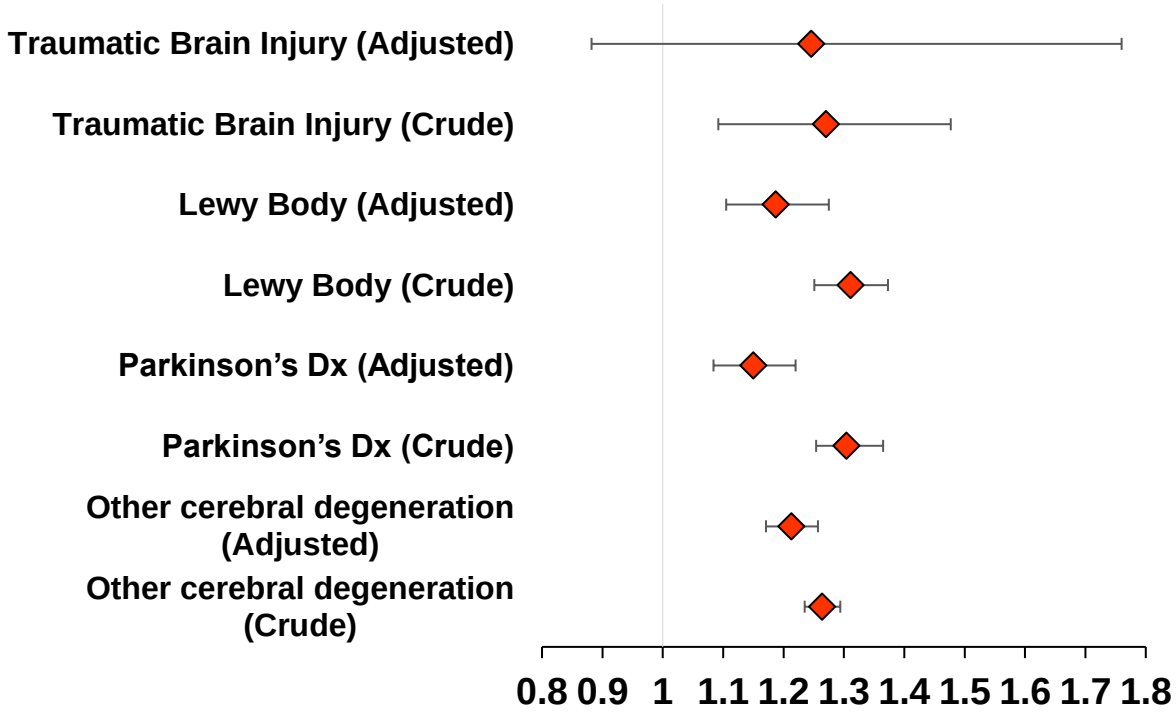




KEY FINDINGS

Hazard ratios by Dementia type before PSM





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KEY FINDINGS

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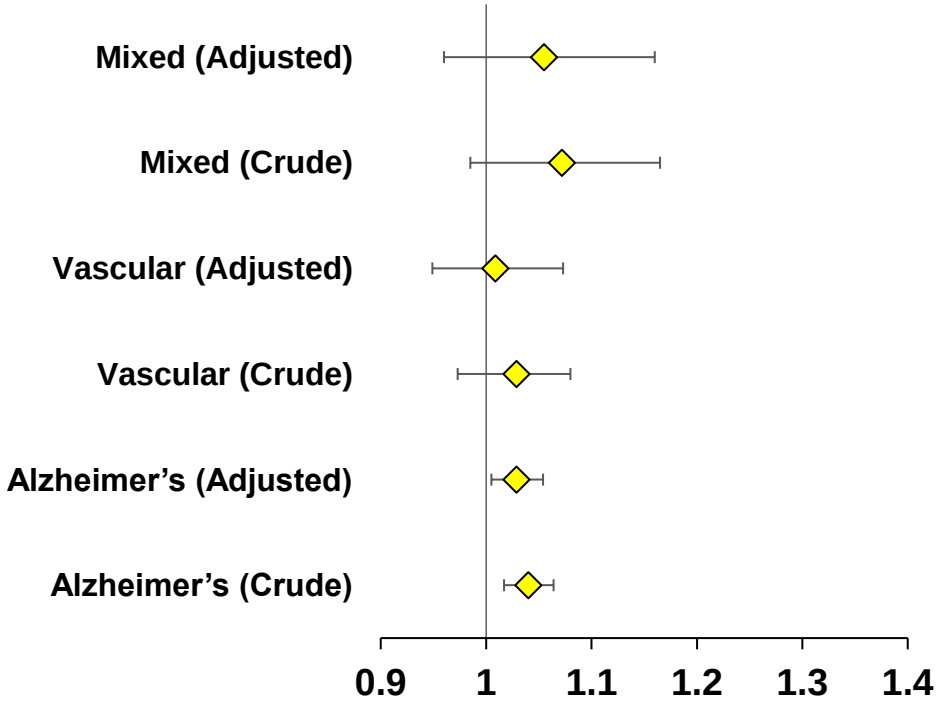

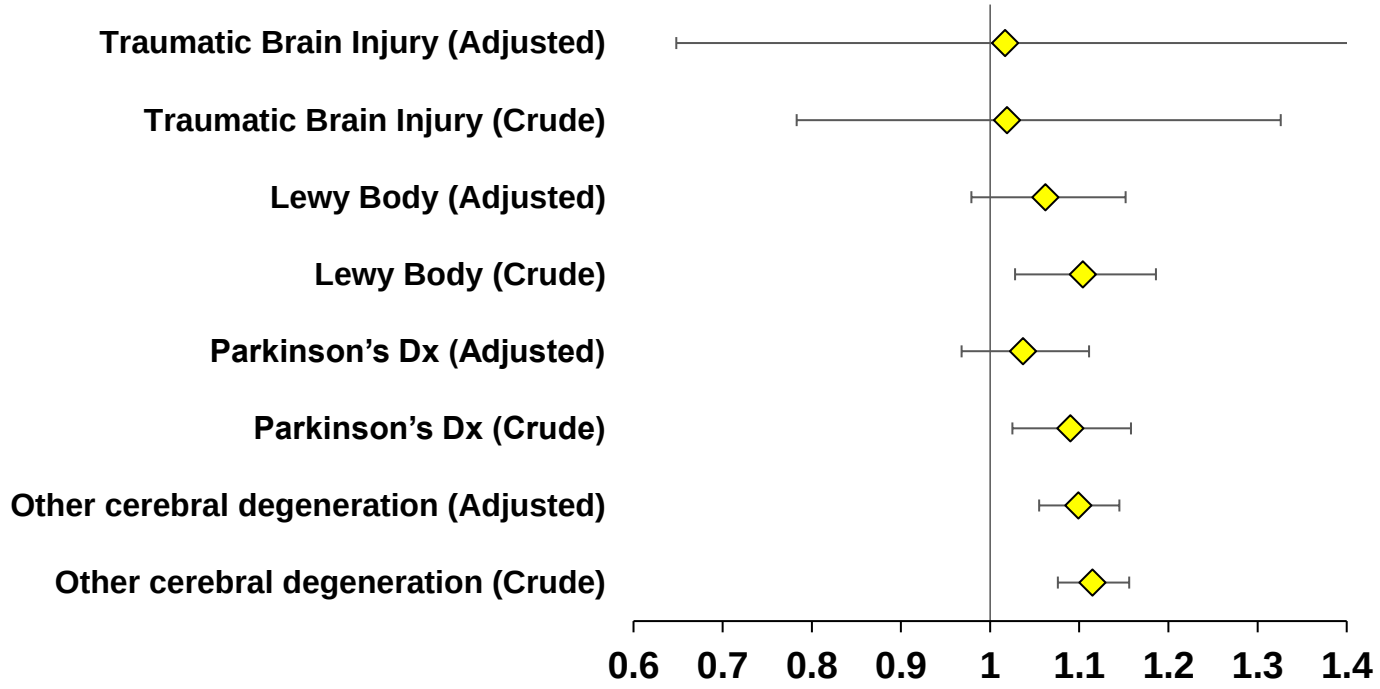

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STRENGTHS AND WEAKNESSES

- **Strengths**
  - A large sample from a population-based registry
  - Findings generalizable to the southeastern U.S.
  - Propensity score matching reduced demographic bias

- **Weaknesses**
  - Veteran population limited to only those identified in the registry
  - Does not capture service area, branch, or VHA enrollment
  - Potential survivor bias due to elevated suicide risk among veterans

CONCLUSION

- Veterans had lower survival probabilities and higher hazards of death than non-veterans, both before and after matching.
- Alzheimer’s disease and other cerebral degeneration dementias showed significantly higher mortality among veterans after matching.
- Female veterans had a lower risk of death compared to female non-veterans.
- Tobacco-related deaths were more common among veterans, reflecting higher tobacco use prevalence.

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IMPLICATIONS

- Targeted interventions are needed to address mortality risks among veterans with ADRDs.
- Integrated care models should link VA and non-VA healthcare systems for comprehensive support.
- Tobacco cessation and mental health programs should be prioritized during and after service.
- Enhanced social support and community-based care may improve survival outcomes

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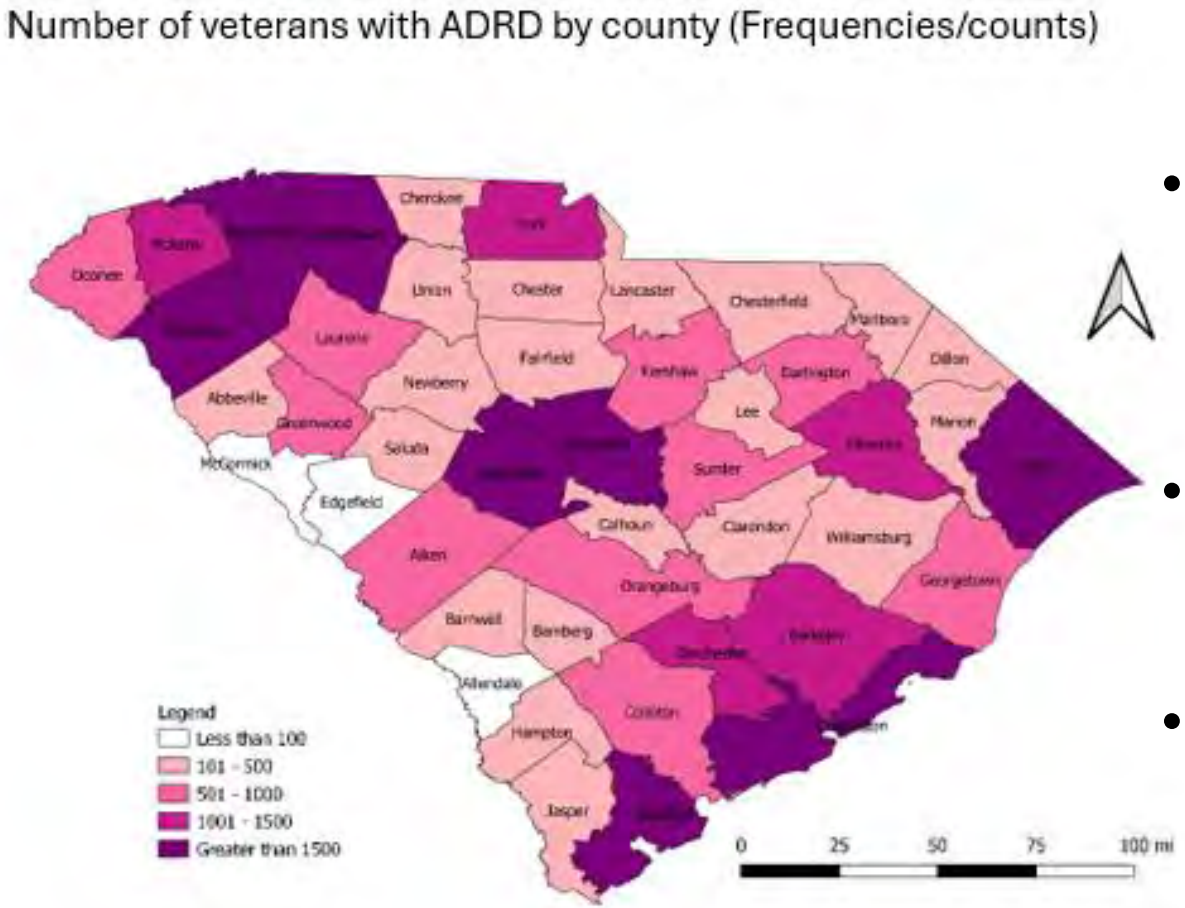
FUTURE RESEARCH



- Regional analysis of ADRD cases and mortality across South Carolina.
- Geospatial mapping of veteran and non-veteran ADRD cases across South Carolina counties.
- Investigation of rural–urban disparities in ADRD outcomes among veterans.
- Examination of healthcare access and service utilization among veterans outside the VA system.

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THANK YOU

Collaboration team:

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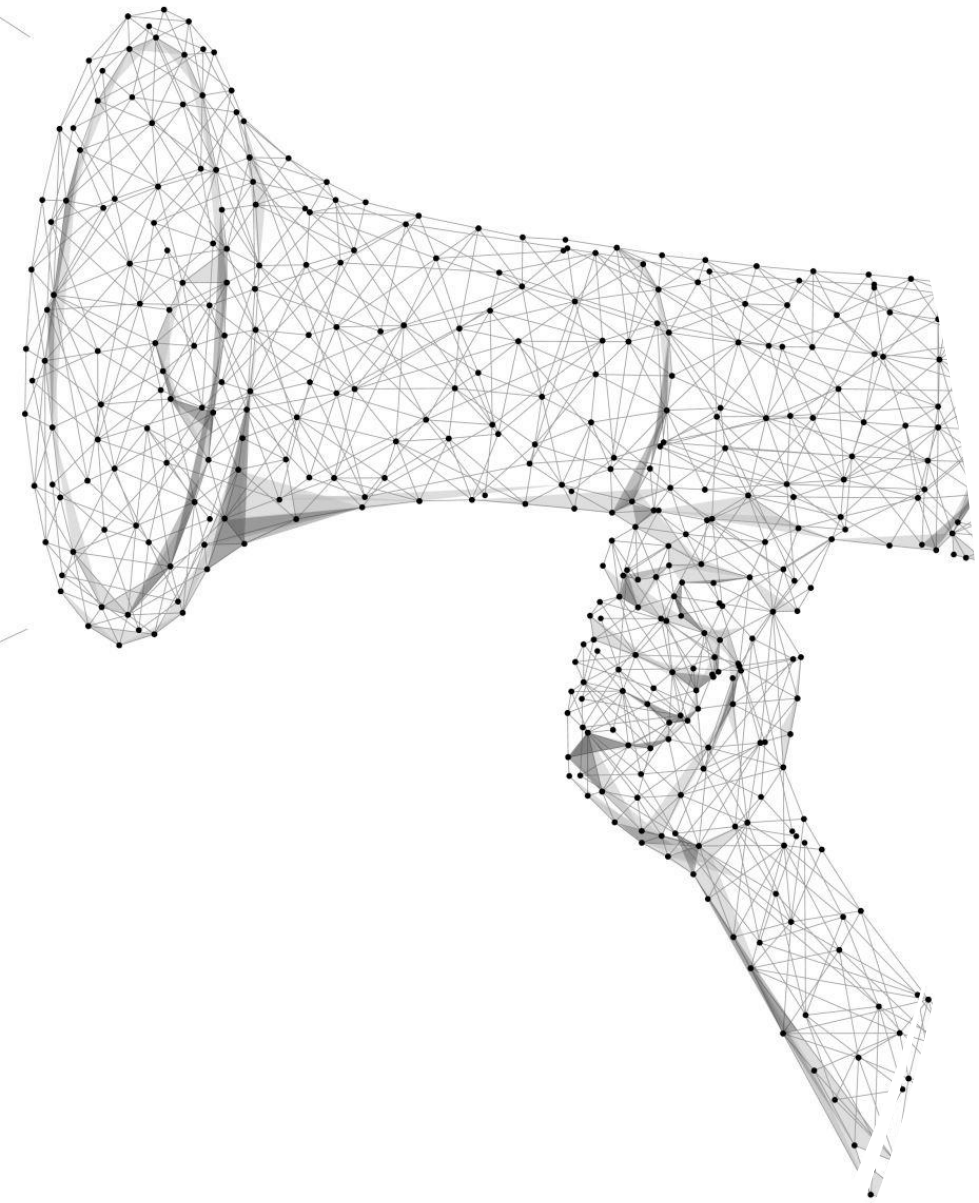


Using data and sound science to make noise*:

Working with vulnerable and low-capacity communities to address Alzheimer's risk from air pollution.

*A favorite statement used by Mr. Herbert Maybank, local resident & member of both the Lowcountry Alliance for Model Communities and the Charleston Research to Action Board.

2024 Lancet Commission Report

- Air pollution (AP) identified as a risk factor for ADRD, among others
- Exact mechanisms unclear, proposed theories include:
  - Decreased brain volume
  - Increased plaque
- Link

Technical Brief & Recent Publication on AP

- ADRD, air pollution, and climate change are major health issues worldwide.
- Burden of AP in the U.S.
- Lack air pollution surveillance in granular spaces
- Article
- Technical Brief

NACDD Work in Rosemont, SC

- Disseminating scientifically sound and culturally relevant information about these concerns is a significant issue.
  - Literature review
  - Community engagement survey
  - Draft outreach materials

Community Partnerships to Address Quality of Life Issues

Community Partnerships to Address Quality of Life Issues

COMMUNITY SPOTLIGHT:

- Identified community needs: water level and air quality monitoring and notification
- Cross project collaboration (WebCOOS, PurpleAir, OHHC^{2}I, EJ STRONG, Southeast Water Level Network)
- Extensive community bi-directional engagement
- Multi-organization collaboration
- Community transition plan

USER ENGAGEMENT:

- Primary focus to engage with community members
- Recognition that using sound science is more effective than emotions
- Establish community engagement and trust to identify community defined needs; cannot be perceived as a 'parachuting scientist'
- Collaborate with communities to design situational monitoring and reporting tools
- Develop outreach material for engagement and educational purposes

Community Partnerships to Address Quality of Life Issues

ROSEMONT COMMUNITY
ENVIRONMENTAL MONITORING PROGRAM

PROJECT PARTNERS

Rosemont Neighborhood Council

LAMC

University of South Carolina

SECOORA

EJ STRONG

University of Maryland Center for Environmental Science Integration and Application Network

AIR QUALITY INDEX

Air Quality Index (AQI) Values	Levels of Health Concern
0 to 50	Good
51-100	Moderate
101-150	Unhealthy for Sensitive Groups
151-200	Unhealthy
201-300	Very Unhealthy
301 to 500	Hazardous

Community Partnerships to Address Quality of Life Issues
BROADER IMPACTS!!

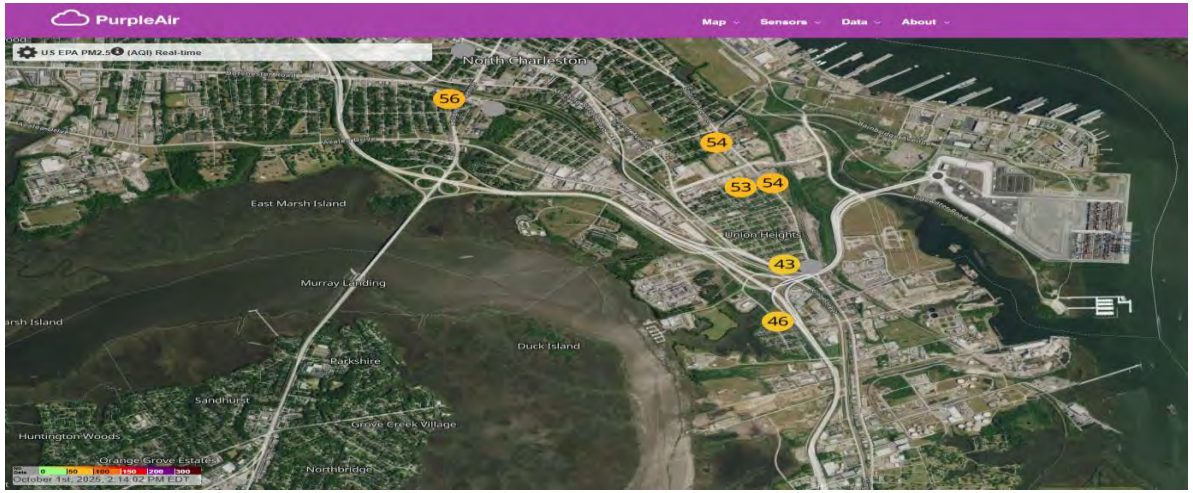
And hot off the press ….

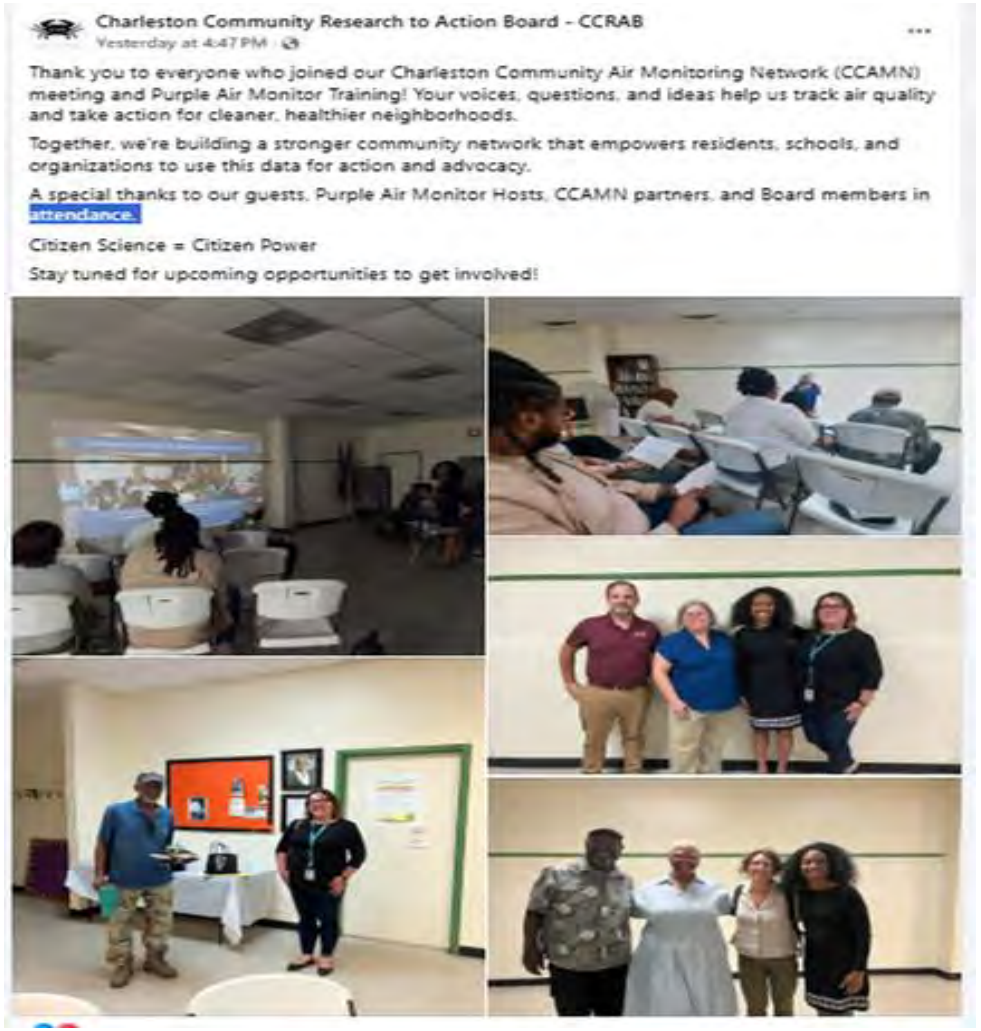
EPA – EJ STRONG: Practicing Risk Reduction Education through Partnership in South Carolina

EPA – EJ STRONG: Resilience in the Southeast

SC General Assembly – EJ STRONG: Citizens Earning and Learning

Charleston Community Air Monitoring Network





Success of Community Engagement Efforts

- Using sound science to make noise
  - Examples that this approach can work, and these things are thematically and geographically transferrable
- Overcoming the parachuting scientist: Maintaining a long-term relationship with communities

SYMPOSIUM EVALUATION

UNIVERSITY OF South Carolina

South Carolina Alzheimer's Disease Research Center

2025 STATEWIDE AGING AND ALZHEIMER'S DISEASE RESEARCH SYMPOSIUM

Symposium Adjourned, Thank you!

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THANK YOU!

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