Multimodal deep learning for dementia assessment

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Disclosures

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a2 COLLECTIVE

Gates Ventures

Visterra

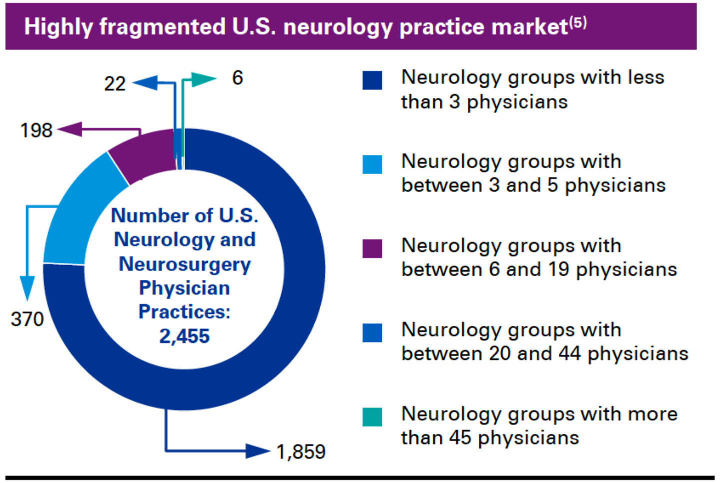
Multidisciplinary team

- Trainees in our lab
  - Chonghua Xue, Michael Romano, Shangran Qiu, Prajakta Joshi, Xiao Zhou, Lingyi Xu, Matthew Miller, Cody Karjadi, Joyce Lee, Akshara Balachandra, Diala Lteif, Yi Zheng, Varuna Jasodanand, Lindsey Claus, Yichi Zhang, Olivia Zhou, Rushin Gindra, Shreyas Puducheri, Anika Walia, Meagan Lauber, Meysam Ahangaran, Sahana Kowshik, Piyush Kathuria, Osman Berke

- PhD students and postdocs in computer science
- MD students, residents and clinical fellows
- Trainees with background in neuroscience
- Background in more than a single discipline

Assistive tools for neurology practice

- Problem: Supply of US neurologists may have grown by 11% between 2013 and 2025, demand will have grown by 16%.
  - *A. Burton, Lancet Neurology, 17(6), P502-503, 2018*



- Solution: Develop AI approaches using routinely collected clinical data that can serve as screening tools for dementia.
  - Leverage multimodal data in native formats.
  - Clinical and demographic data, patient history, bedside cognitive tests, neuropsychological tests, neuroimaging
  - Focus on comprehensive evaluation
    - *Computational validation*
    - *Expert-level comparison*
    - *Post-mortem evidence*

Access to real-world data

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THE NIA ALZHEIMER'S DISEASE RESEARCH CENTERS PROGRAM
National Alzheimer's Coordinating Center

NACC UNIFORM DATA SET
Researchers Data Dictionary
Version 3.0, March 2015

Total n = 4822

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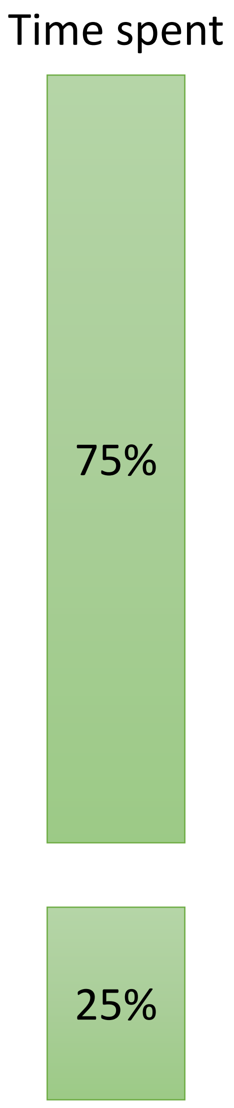
NC [*n*=2524]	69.82 ± 9.93^	871 (34.51%)	15.92 ± 2.95^	(2120, 303, 55, 31, 2, 0)^	599 (29.95%)^	28.98 ± 1.31^	0.06 ± 0.16^	26.80 ± 2.44^
MCI [*n*=1175]	74.01 ± 8.74^	555 (47.23%)	15.36 ± 3.35^	(965, 160, 25, 17, 1, 0)^	322 (38.66%)^	26.79 ± 2.51^	0.46 ± 0.18^	22.68 ± 3.41^
AD [*n*=948]	74.97 ± 9.13^	431 (45.46%)	14.64 ± 3.64^	(816, 85, 23, 11, 0, 0)^	346 (52.19%)^	20.48 ± 5.69^	1.02 ± 0.60^	15.39 ± 5.44^
nADD [*n*=175]	69.35 ± 10.84^	110 (62.86%)	14.86 ± 3.60^	(161, 10, 2, 1, 0, 0)^	34 (25.95%)^	22.23 ± 6.14^	1.07 ± 0.70^	17.53 ± 6.35^
p value	1.145e-56	1.130e-22	1.846e-25	5.349e-2	8.026e-49	<1.0e-200	<1.0e-200	<1.0e-200

Modeling pipeline

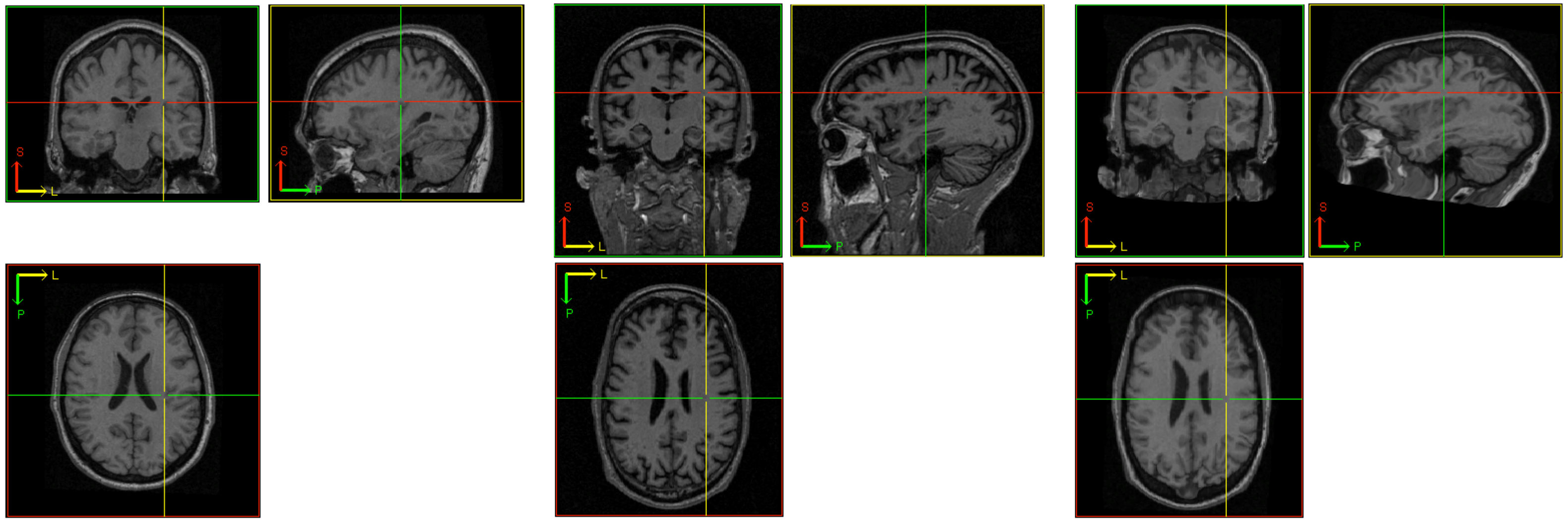
- Data collection
- Data processing/normalization/harmonization
- Image processing
  - Registration
  - Normalization
  - Segmentation
  - ROI selection and removal of unwanted regions
  - Bias correction (For multimodal imaging)
  - Image quality check

DEEP LEARNING APPROACHES



Developing an image processing pipeline

Volumetric registration



a) Source Image (256x256x198) b) Target Image (180x256x256) c) Registered Image (S2T)

Skull stripping

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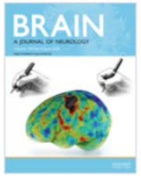

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Article Contents

Abstract

JOURNAL ARTICLE

Development and validation of an interpretable deep learning framework for Alzheimer's disease classification

Shangran Qiu, Prajakta S Joshi, Matthew I Miller, Chonghua Xue, Xiao Zhou, Cody Karjadi, Gary H Chang, Anant S Joshi, Brigid Dwyer, Shuhan Zhu, Michelle Kaku, Yan Zhou, Yazan J Alderazi, Arun Swaminathan, Sachin Kedar, Marie-Helene Saint-Hilaire, Sanford H Auerbach, Jing Yuan, E Alton Sartor, Rhoda Au, Vijaya B Kolachalama

Author Notes

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Multimodal deep learning for Alzheimer's disease dementia assessment

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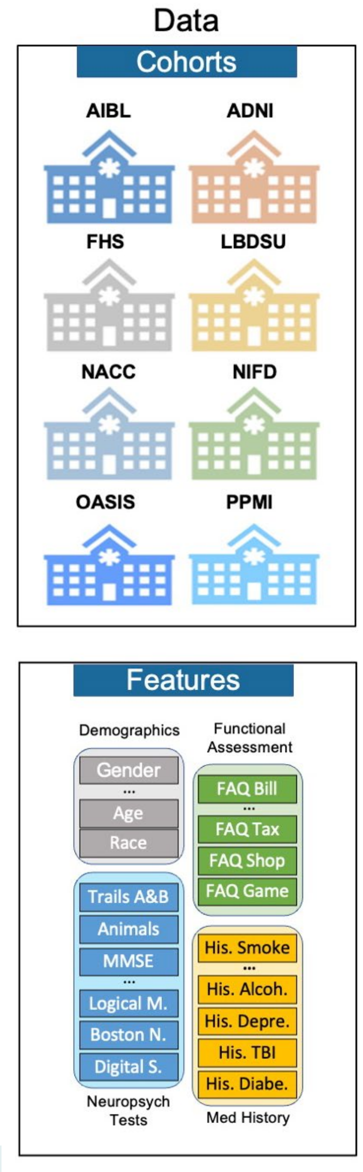
Learning from multiple forms of data

Study population



Multimodal data

1) Demographics
2) Patient history
3) Functional assessments
4) Neuropsychological testing
5) MRI scans

- 4550 with normal cognition
- 2412 participants with mild cognitive impairment
- 1606 participants with Alzheimer's disease dementia
- 348 participants with dementia due to other causes

Dataset (group) [subjects]	Age mean ± std
ADNI	
NC [n = 481]	74.26 ± 6.00
MCI [n = 971]	72.84 ± 7.71
AD [n = 369]	74.91 ± 7.84
p value	2.565e-6
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NC [n = 2524]	69.82 ± 9.93^
MCI [n = 1175]	74.01 ± 8.74^
AD [n = 948]	74.97 ± 9.13^
nADD [n = 175]	69.35 ± 10.84^
p value	1.145e-56
NIFD	
NC [n = 124]	63.21 ± 7.27
nADD [n = 129]	63.66 ± 7.33
p value	6.266e-1
PPMI	
NC [n = 171]	62.74 ± 10.12
MCI [n = 27]	68.04 ± 7.32
p value	1.006e-2
AIBL	
NC [n = 480]	72.45 ± 6.22
MCI [n = 102]	74.73 ± 7.11
AD [n = 79]	73.34 ± 7.77
p value	5.521e-3
OASIS	
NC [n = 424]	71.34 ± 9.43
MCI [n = 27]	75.04 ± 7.25
AD [n = 193]	76.01 ± 8.01
nADD [n = 22]	72.64 ± 8.77
p value	5.896e-8
FHS	
NC [n = 212]	73.37 ± 9.63
MCI [n = 75]	76.23 ± 6.83
AD [n = 17]	78.82 ± 7.20
nADD [n = 9]	79.44 ± 4.17
p value	4.755e-3
LBDSU	
NC [n = 134]	68.77 ± 7.62
MCI [n = 35]	70.16 ± 8.41
nADD [n = 13]	73.42 ± 7.81
p value	1.033e-1

Multimodal deep learning

Multimodal data

1) Demographics
2) Patient history
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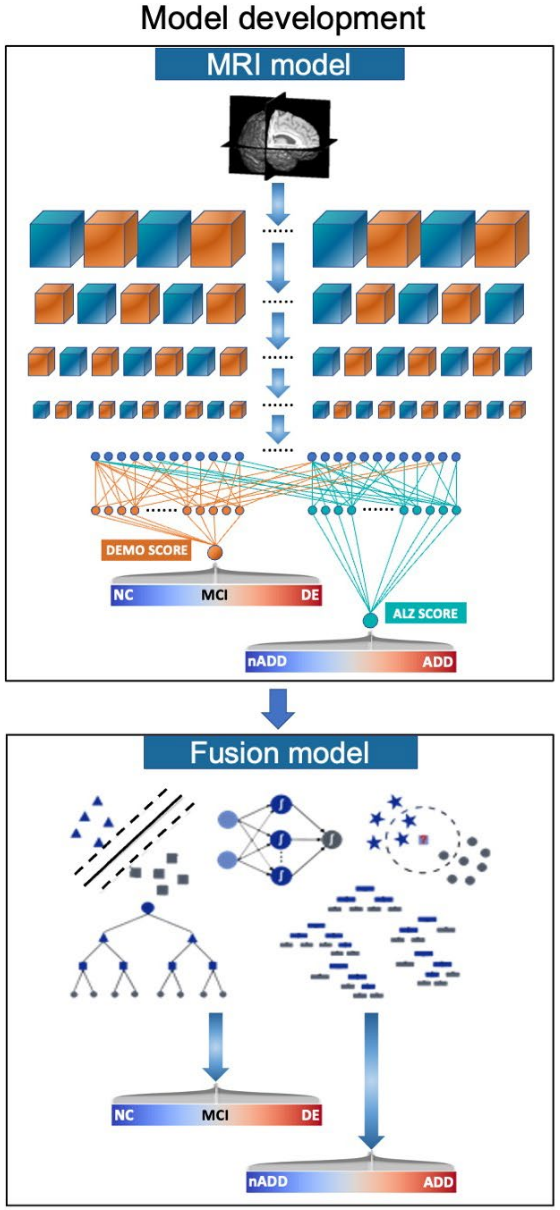
5) MRI scans



Convolutional neural network

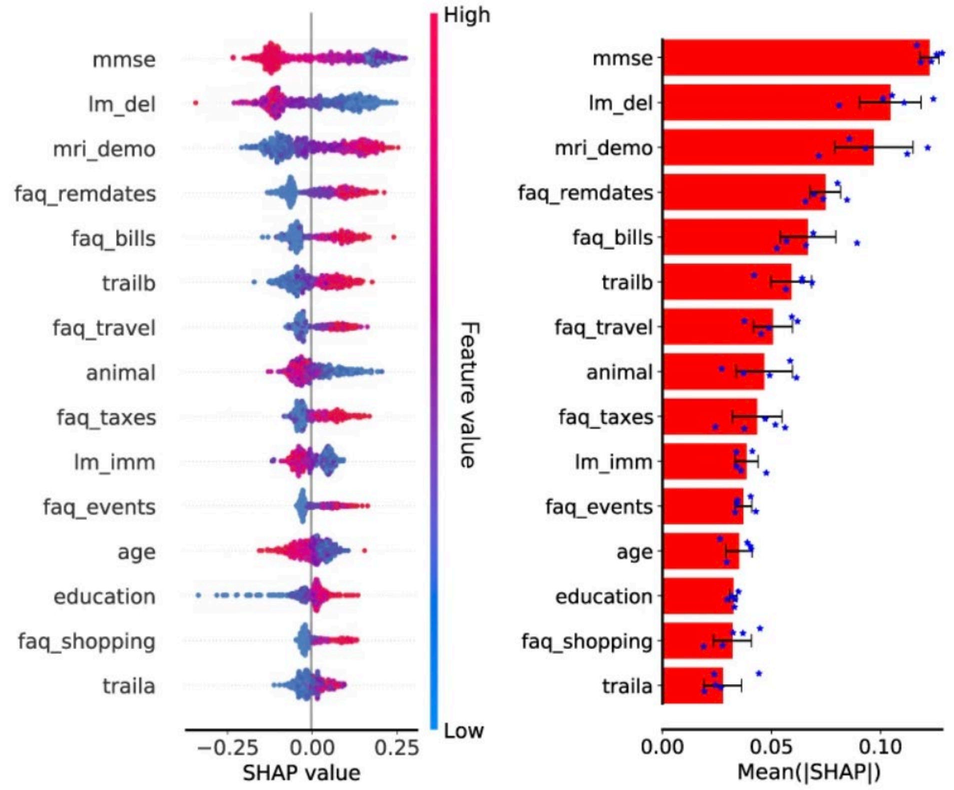
Hierarchical learning strategy that processes voxel-level information

Multilayer perceptron

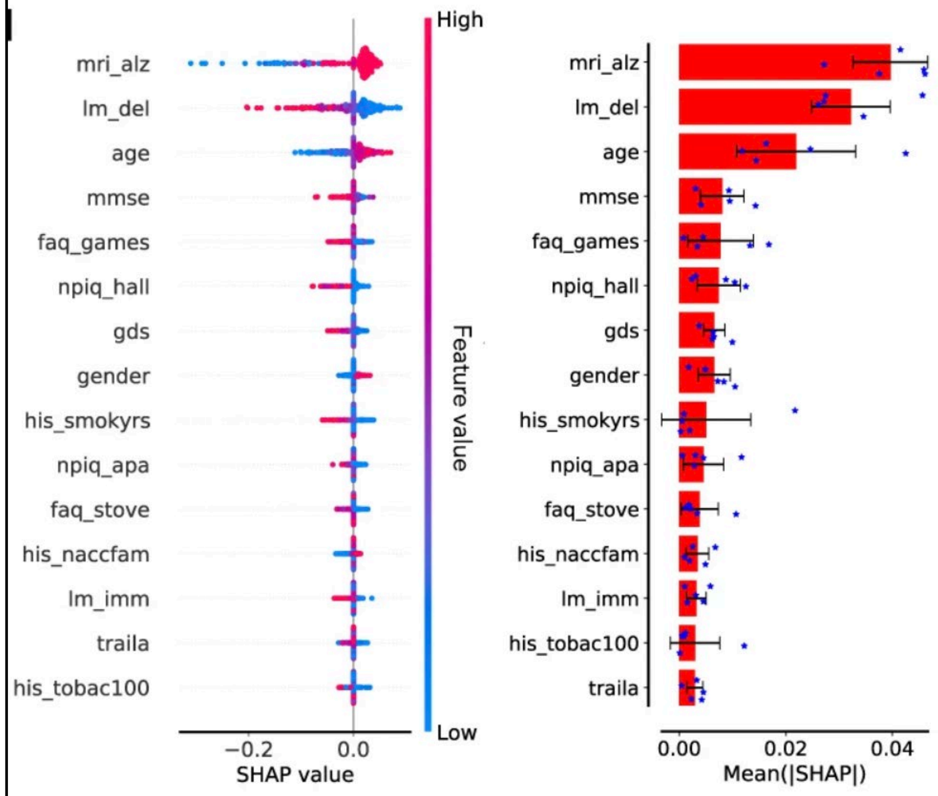
A framework for combining vectorized (imaging and non-imaging) features

Important factors contributing to prediction

NC vs MCI vs Dementia



AD vs non-AD Dementia



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Qiu et. al., Nat Commun. 2022 Jun 20;13(1):3404.

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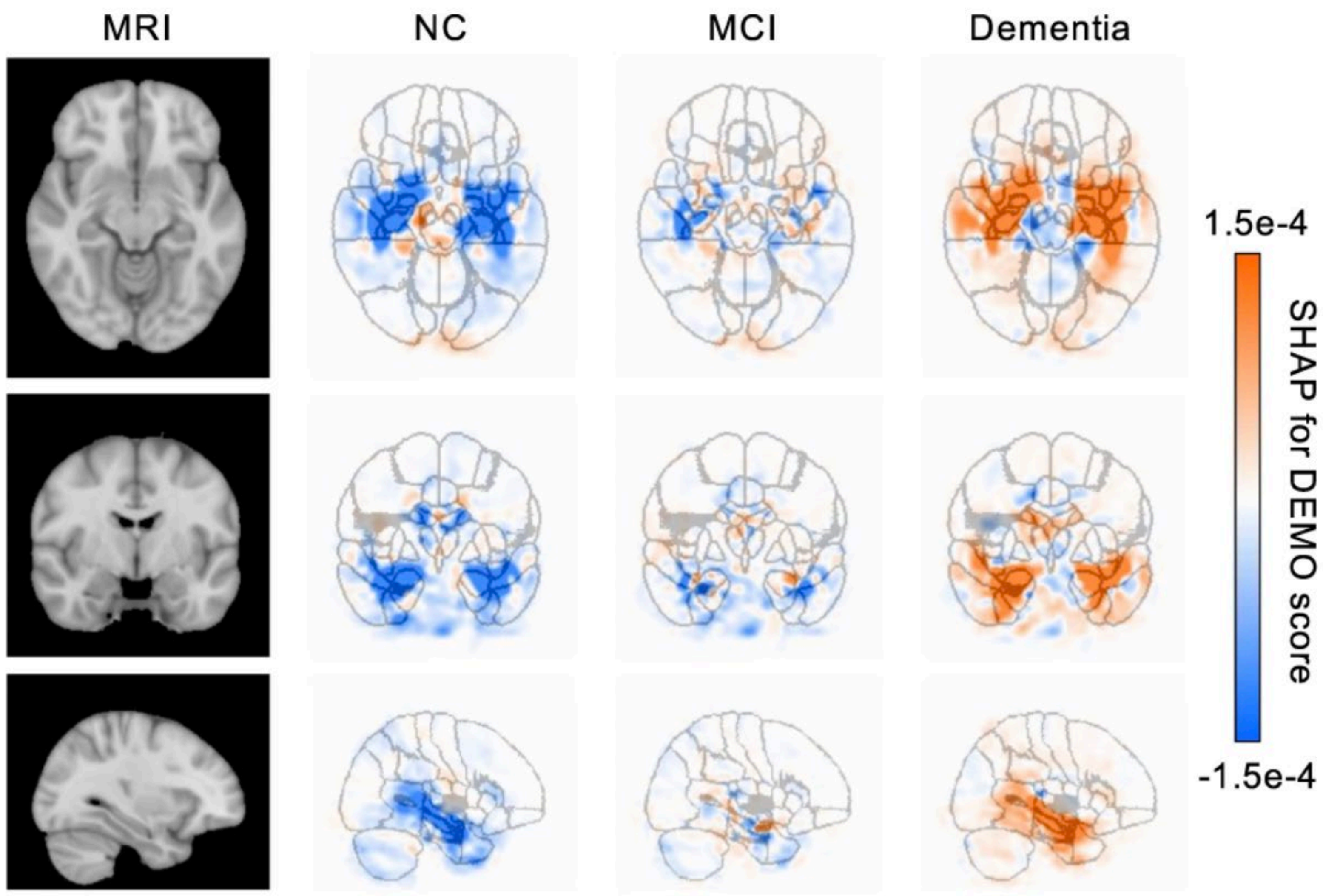
Model interpretability



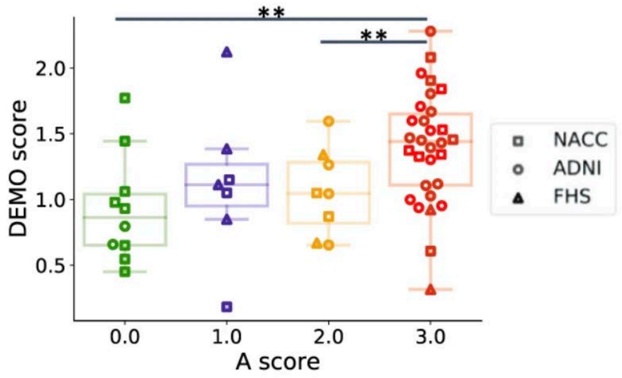
Qiu et. al., Nat Commun. 2022 Jun 20;13(1):3404.

Neuropathologic validation

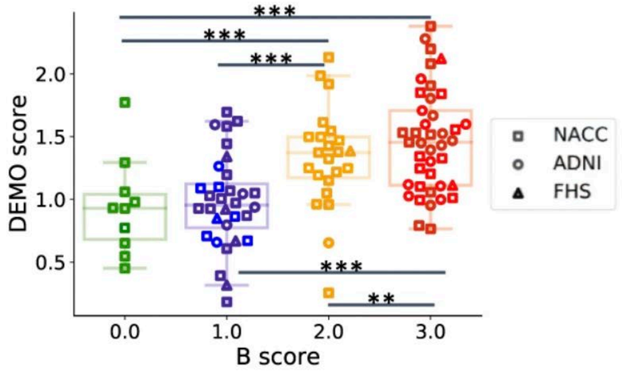
NACC (*n* = 74), ADNI (*n* = 25) and FHS (*n* = 11)

p < 0.05 as *; *p* < 0.001 as **, and *p* < 0.0001 as ***

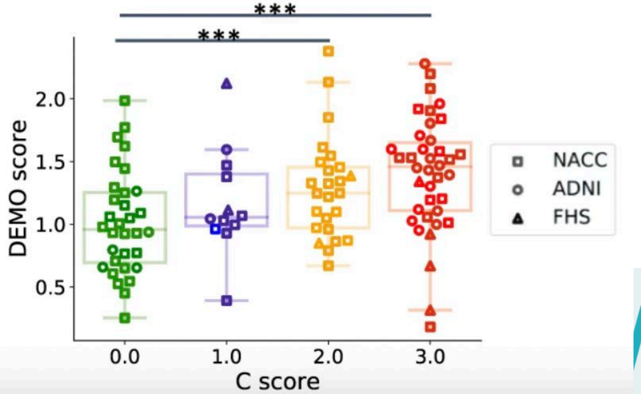
Thal phase for Aβ (A score F-test: F(3, 51) = 3.665, p = 1.813e-2)



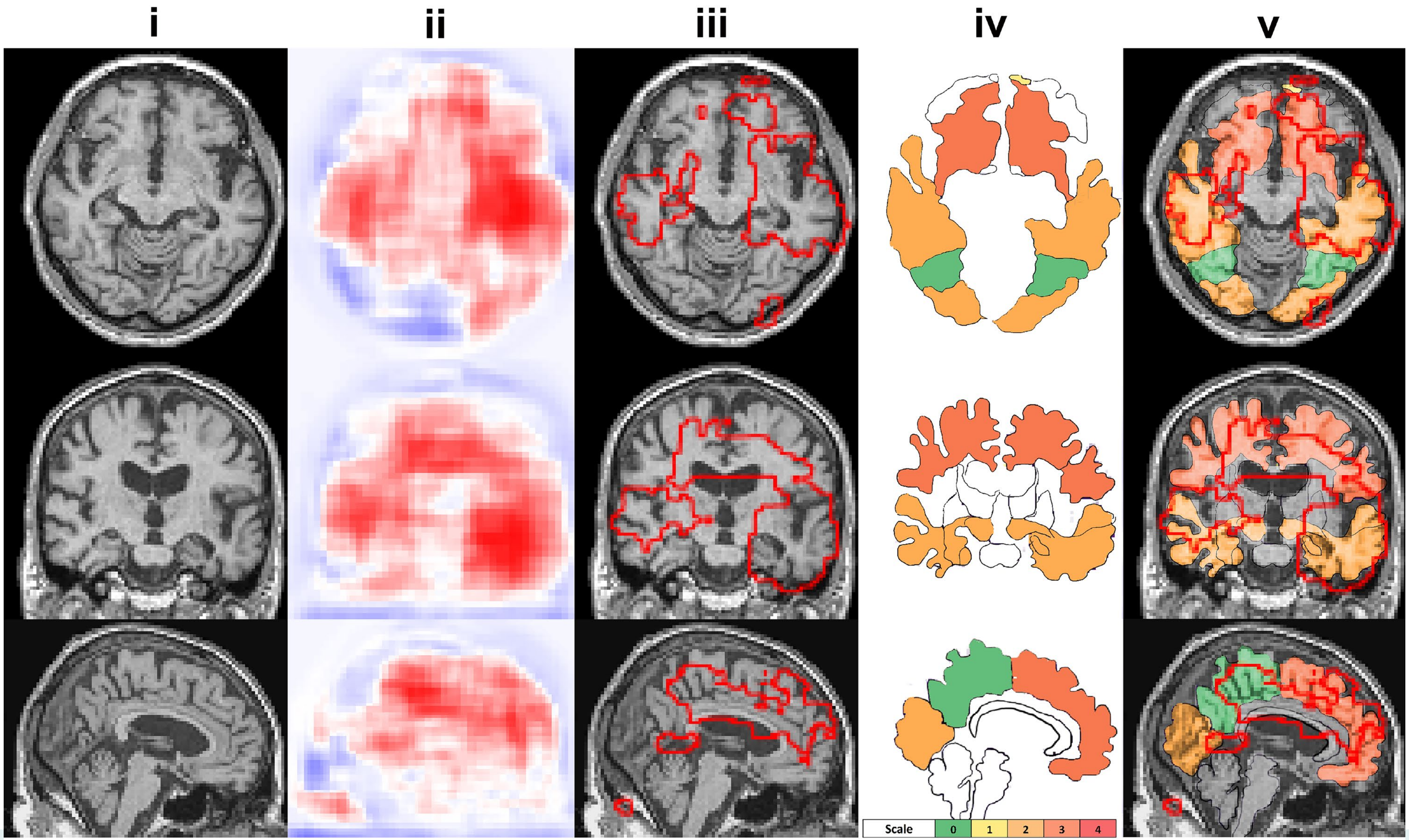
Braak & Braak for neurofibrillary tangles (NFTs) (B score F-test: F(3, 102) = 11.528, p = 1.432e-6)



CERAD neuritic plaque scores (C score F-test: F(3, 103) = 4.924, p = 3.088e-3)



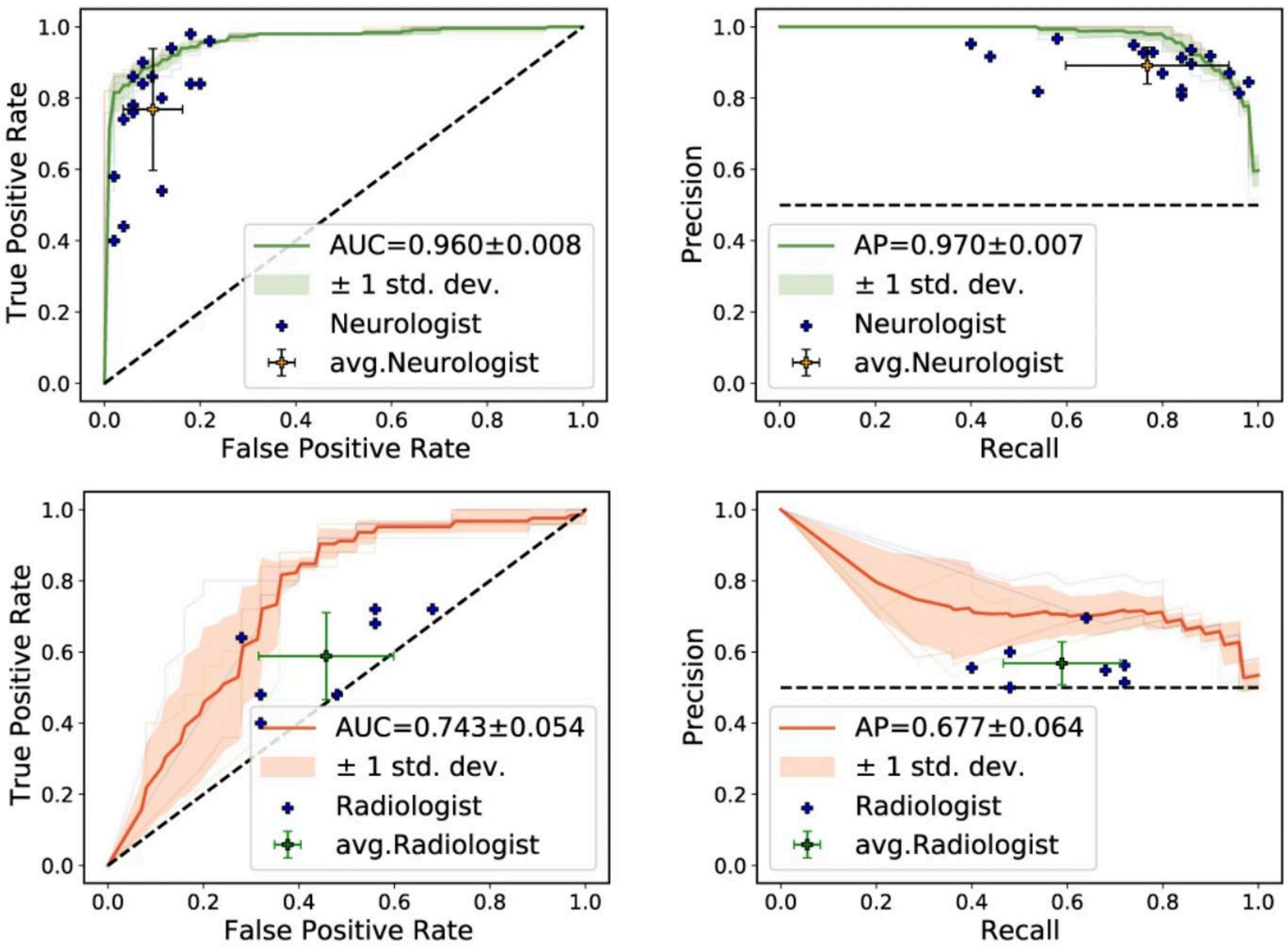
Neuropathologic validation



Qiu et. al., *Brain*, 143(6), 2020, 1920-33.

Expert-level validation

Neurologists



Neuroradiologists

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Summary

- We have developed and validated a deep learning framework that processes routinely collected clinical data to perform dementia assessment – the goal is to assist practitioners in neurology clinics
  - The NACC cohort has allowed us to achieve this goal

- We are currently developing a web-based software that can provide real-time assistance
  - Please reach out if you are interested to test the tool (vkola@bu.edu)

- Partnering with multiple clinical centers around the globe:
  - Boston Medical Center, Mass General, Brigham & Women’s, Lahey Clinic, Stanford, Emory, Beijing, and Nebraska

Thank you!