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IMAGING IN NORMAL BRAIN AGING

MRI signatures of Brain Age in the Alzheimer's disease continuum

Jay Shah[1,2] | Valentina Ghisays[3] | Yinghua Chen[3] | Ji Luo[3] | Baoxin Li[1,2] | Eric M. Reiman[2,3] | Kewei Chen[2,3] | Teresa Wu[1,2] | Yi Su[1,2,3]

[1]ASU-Mayo Center for Innovative Imaging, Tempe, AZ, USA

[2]Arizona State University, Tempe, AZ, USA

[3]Banner Alzheimer's Institute, Phoenix, AZ, USA

Correspondence
Jay Shah, ASU-Mayo Center for Innovative Imaging, Tempe, AZ, USA.
Email: jgshah1@asu.edu

Abstract

Background: Age is the biggest risk factor for Alzheimer's disease (AD). Substantial efforts to extract age signatures from magnetic resonance imaging (MRI) of the brain have achieved impressive accuracy and demonstrated these signatures were altered by neurological disorders including AD. In this work, we develop a deep learning model to characterize brain age signatures and examine their variation over the AD continuum.

Method: A 3D deep ResNet model was implemented to learn the structural signatures of brain age in predicting the chronological age of the participants. The model was trained on 7372 T1-weighted MRI scans from a combined lifespan cohort of 5848 cognitively normal participants (age: 8- 95 yrs) using a 10-fold cross validation procedure. The model was then applied to the independent ADNI cohort (N=1175, 50-98 yrs) to examine MRI derived brain age signatures variation in the AD continuum. The difference (Δ_{age}) between model predicted age and chronological age was used as the independent variable for group comparison using univariate ANCOVA tests, controlling for sex, education, and APOE4 gene dose, among five clinical groups: normal control (NC), normal to MCI converters (NC-MCI), stable MCI (MCIs), MCI to AD converters (MCI-AD), and AD patients.

Result: The ResNet model achieved an MAE=3.76 yrs and R^2=0.93 across 10 folds in the lifespan cohort. In the baseline data of the ADNI cohort, model derived Δ_{age} increased along the AD continuum as expected: NC (-1.2yrs) < NC-MCI (-0.7yrs) < MCIs (-0.3yrs) < MCI-AD (0.7yrs) <AD (1.5yrs) (F=11.24, p<0.0001). Post-hoc pairwise comparison results are summarized in Table 1/Figure 2. Although the difference between NC and NC-MCI did not reach significance (p=0.24) for the baseline data, comparison between the two groups using data from all visits was significant (p=0.0009), suggesting more subtle differences.

Conclusion: A ResNet model was developed that captures the MRI signatures of brain age with high accuracy in age prediction. The model detected group level differences along the AD continuum in the expected direction. Subtle changes in brain signatures were observable in normal participants who later developed cognitive impairment. Our technique provides a novel approach to investigate the relationship between aging and AD.

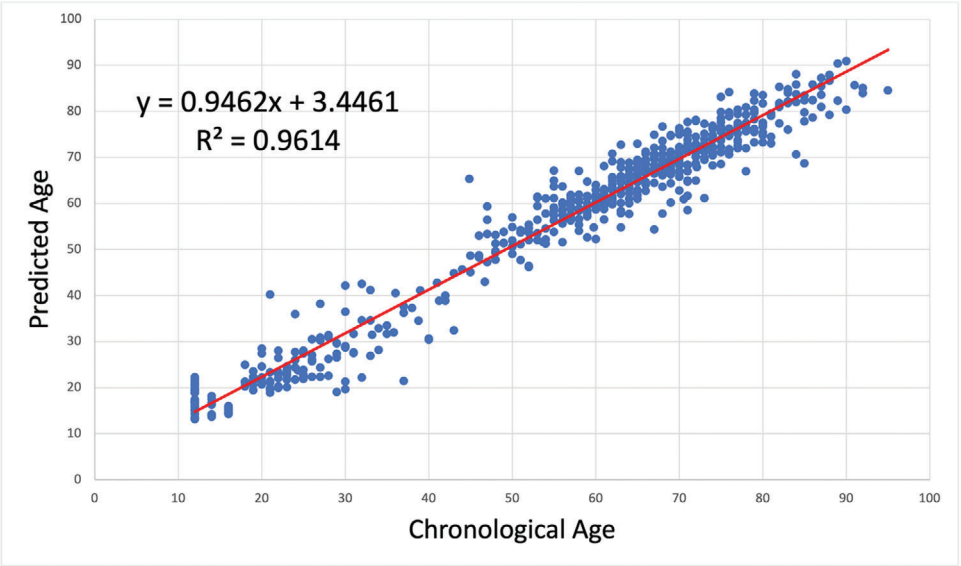

Figure 1 Comparison between chronological and predicted age of participants using our model from one of the 10 test-sets of lifespan cohort

	NC (678)	NC-MCI (179)	MCIs (432)	MCI-AD (139)	AD (155)
Age (range)	72.6 (55-90)	73.9 (56-90)	73.1 (55-98)	74 (55-90)	76.5 (58-87)
Δ_{age} ±SE	-1.22 ±0.19	-0.74 ±0.37	-0.29 ±0.24	0.73 ±0.42	1.52 ±0.41
Sex (M/F)	290/388	97/82	243/189	78/61	93/62
APOE4 (NC/HT/HM)	462/182/14	112/60/6	262/141/29	50/68/21	57/65/30
Education ±SD	16.6 ±2.5	16.4 ±2.5	16.1 ±2.8	16.0 ±2.7	15.7 ±2.6

Table 1 Group comparison using univariate ANCOVA tests, Δ_{age} is the independent variable and controlling for sex, education, and APOE4 gene dose, among five clinical groups

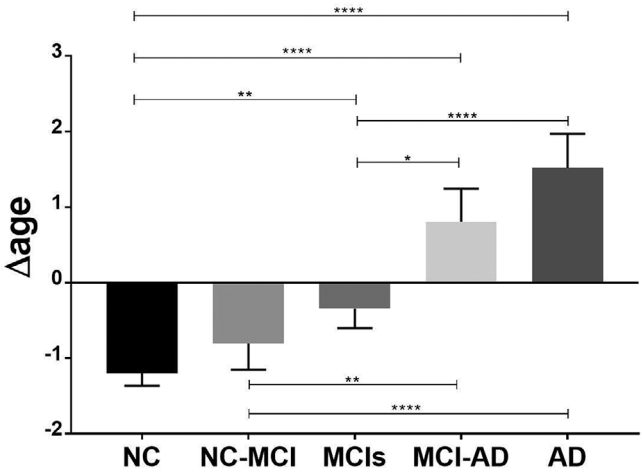

Figure 2 Pairwise comparison of model derived Δ_{age} among five clinical groups along the AD continuum