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Deep Learning-Derived Brain Age from 40,000+ MRI Reveals Disease-Specific Aging

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Background
Brain age is the estimated biological age of an individual's brain predicted from structural MRI.

Methods
Population
We assembled a large population with over 40,841 T1-weighted MRI scans from more over than 46 independent cohorts and 27,190 individuals. A multi-label tag-based diagnostic framework allowed representation of comorbidity and disease. OASIS-3 and Cam-CAN datasets are held out for independent testing. 80% of the rest are used for training and the other 20% for validation.

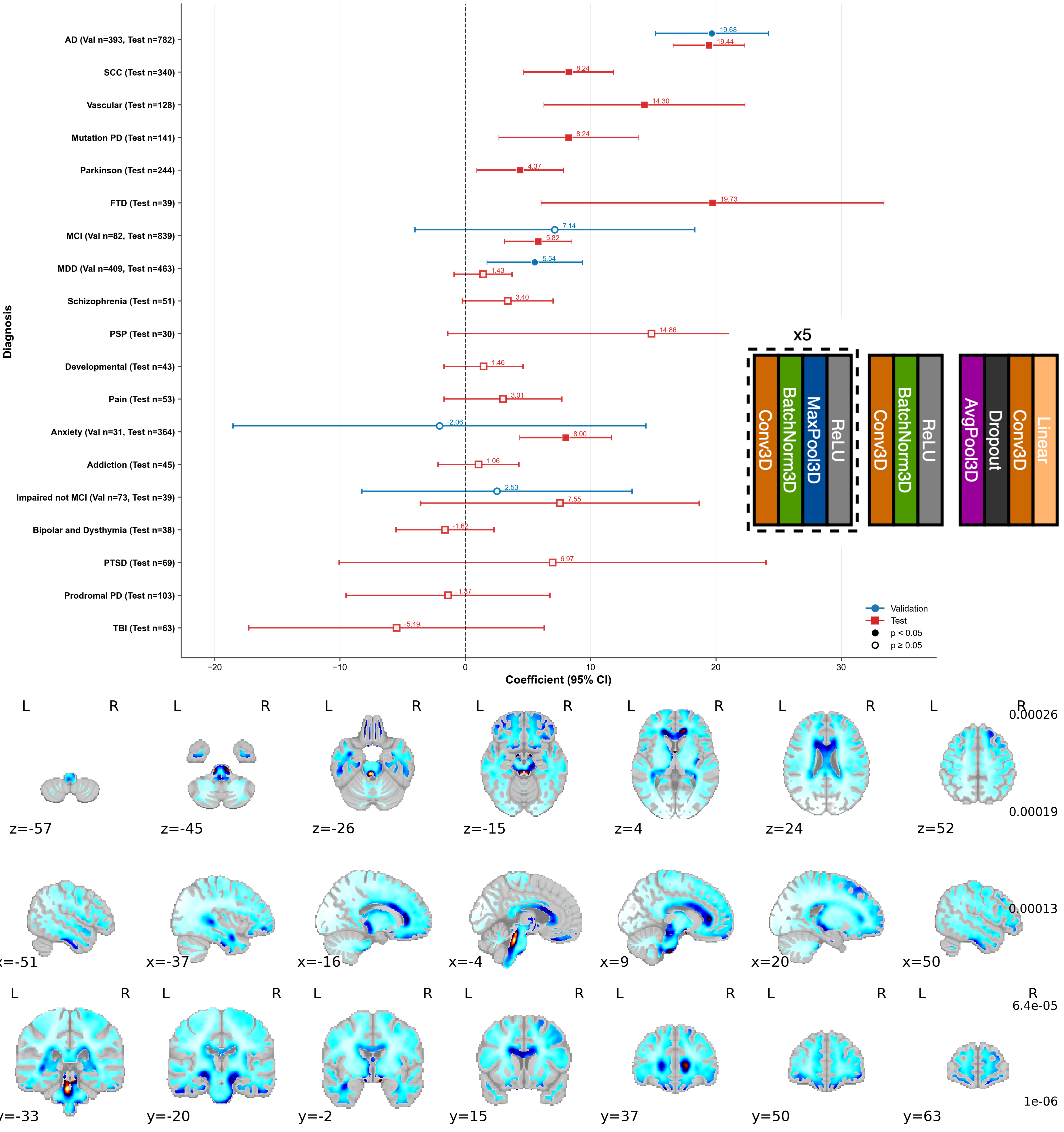
Preprocessing
We applied the same pipeline to each scan starting with a bias field correction of the field bias with ANTS then a rigid spatial registration to a standardized image space. Critically, we did not do spatial normalization – just rigid alignment. Pre-processed scans of IXI were used to train a histogram normalization. We rescaled intensities to a range of 0-1, ignoring the bottom and top 0.5% values and applied the trained histogram normalization. We applied a head mask (excluding face). Optionally, an augmentation was applied (flip, blur, noise, motion, ghosting or spike).

Model Architecture
We adapted the Simple Fully Convolutional Network. The last layers are modified to do a regression instead of classification. The batch size was fixed to 16 with an accumulation gradient of 9 and we used a half precision. Best option is learning rate is 0.04, dopout is 0.4, initial channel of 32 and SGD optimizer.



What if a **single brain scan** could tell you how fast you're **neurologically aging**?

We trained an AI on over **40,000 MRIs** across 46 cohorts to estimate **brain age** – and discovered that some **neurological** and **psychiatric** diseases age the brain by more than 10 years beyond what's expected.



Performances
We achieved a prediction performance MAE of 0.83 for training, 3.14 for validation and 3.65 for test sets in healthy population.

Diagnosis effect
Significantly overestimated age for neurological diagnosis are Alzheimer disease, Vascular dementia, Parkinson, Frontotemporal dementia, Suggestive and Mild Cognitive Impairment and Parkinson mutation.

Only anxiety disorders are significantly associated with overestimated ages.

Explainable Model
Absolute mean Shap value maps revealed distributed contributions for the whole image. Tissue importance order is cerebrospinal fluid, eye muscles, gray matter and white matter. Gray matter map show higher importance in orbito-frontal, temporal and subcortical regions. The white matter map show importance in mamillary body, hippocampus entorhinal and medial geniculate body. The pattern is symmetric.

Discussion
These findings establish deep learning-derived brain age as a scalable and disease-sensitive imaging biomarker with translational relevance for population neuroscience and clinical research.

Suggestive and Mild cognitive impairment showed smaller but significant elevations, aligning with its clinical position between healthy aging and dementia.

Psychiatric disorders exhibited more heterogeneous and generally smaller deviations, consistent with prior work suggesting that psychiatric illness can be associated with accelerated brain aging but with substantial variability across individuals, illness stages, and comorbidities.

Shap value further reinforced biological plausibility, indicating that predictions were driven by distributed cortical and subcortical regions known to be sensitive to aging and neurodegeneration, with minimal contribution from non-brain regions.

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