Brain age

Brain age refers to a concept in neuroscience and biomedical research that estimates the biological age of the brain, which may differ from a person's chronological age. This estimate is derived from brain imaging and computational models, offering insights into the brain's structural, functional, or metabolic health.

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How Brain Age is Estimated 1. **Neuroimaging Techniques:**

1. **Magnetic Resonance Imaging (MRI):** Analyzes structural aspects like cortical thickness, brain volume, and white matter integrity.
2. **Functional MRI (fMRI):** Examines brain activity and connectivity patterns.
3. **Diffusion Tensor Imaging (DTI):** Assesses white matter tracts and microstructural properties.
4. **PET Scans:** Evaluates metabolic activity or amyloid deposition.

2. **Machine Learning Models:**

1. Brain imaging data is input into algorithms trained to predict brain age based on features derived from healthy individuals across various age groups.
2. Commonly used features include gray matter volume, hippocampal size, and white matter hyperintensities.

3. **Brain Age Gap (BAG):**

1. The difference between **predicted brain age** and **chronological age**.
   1. **Positive BAG:** Brain appears older than the person’s chronological age, potentially linked to neurological or systemic health risks.
   2. **Negative BAG:** Brain appears younger, possibly indicating better resilience or health.

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Applications of Brain Age 1. **Neurological and Psychiatric Disorders:**

1. Early detection of neurodegenerative diseases (e.g., Alzheimer’s, Parkinson’s).
2. Understanding conditions like schizophrenia, depression, or traumatic brain injury, where brain aging might accelerate.

2. **Aging Research:**

1. Identifying factors that contribute to healthy versus pathological aging.
2. Studying interventions that could slow brain aging (e.g., lifestyle, medication).

3. **Personalized Medicine:**

1. Monitoring brain health to tailor interventions, such as cognitive training or pharmacological treatments.

4. **Risk Stratification:**

1. Using brain age as a biomarker to predict risks for cognitive decline, dementia, or other age-

related conditions.

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Factors Influencing Brain Age 1. **Genetics:**

1. APOE status and other genetic factors influence brain aging.

2. **Lifestyle:**

1. Physical activity, diet, education, and sleep can slow brain aging.

3. **Medical Conditions:**

1. Hypertension, diabetes, and obesity are associated with accelerated brain aging.

4. **Mental Health:**

1. Chronic stress, depression, and anxiety may negatively impact brain health.

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Limitations of Brain Age Analysis 1. **Model Variability:**

1. Machine learning models depend on the dataset used for training, potentially limiting generalizability.

2. **Data Requirements:**

1. High-quality neuroimaging data is necessary, which may not always be feasible in clinical settings.

3. **Interpretation Challenges:**

1. A higher or lower brain age is not always diagnostic of a specific condition; it must be interpreted in the context of other clinical findings.

4. **Causal Ambiguity:**

1. It is often unclear whether an observed brain age gap is a cause, consequence, or coincidental finding.

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Emerging Trends 1. **Integration with Genomics and Biomarkers:**

1. Combining brain age analysis with genetic and fluid biomarkers for more precise risk assessment.

2. **Artificial Intelligence:**

1. Enhanced predictive accuracy using deep learning algorithms.

3. **Longitudinal Monitoring:**

1. Repeated measurements of brain age over time to track progression or improvement.

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Conclusion Brain age is a powerful concept that bridges neuroscience, imaging, and computational modeling to provide insights into brain health. While promising as a biomarker, its application must be carefully contextualized, and further research is needed to enhance its clinical utility and interpretive accuracy.

A total of 2913 healthy controls (HC), with 1395 females; 331 multiple sclerosis (MS); 189 neuromyelitis optica spectrum disorder (NMOSD); 239 Alzheimer's disease (AD); 244 Parkinson's disease (PD); and 338 cerebral small vessel disease (cSVD).

Field strength/sequence: 3.0 T/Three-dimensional (3D) T1-weighted images.

Assessment: The brain age was estimated by our previously developed model, using a 3D convolutional neural network trained on 9794 3D T1-weighted images of healthy individuals. Brain age gap (BAG), the difference between chronological age and estimated brain age, was calculated to represent accelerated and resilient brain conditions. We compared MRI metrics between individuals with accelerated (BAG ≥ 5 years) and resilient brain age (BAG ≤ -5 years) in HC, and correlated BAG with MRI metrics, and cognitive and physical measures across neurological disorders.

Statistical tests: Student's t test, Wilcoxon test, chi-square test or Fisher's exact test, and correlation analysis. $P < 0.05$ was considered statistically significant.

In HC, individuals with accelerated brain age exhibited significantly higher white matter hyperintensity (WMH) and lower regional brain volumes than those with resilient brain age. BAG was significantly higher in MS (10.30 ± 12.6 years), NMOSD (2.96 ± 7.8 years), AD (6.50 ± 6.6 years), PD (4.24 ± 4.8 years), and cSVD (3.24 ± 5.9 years) compared to HC. Increased BAG was significantly associated with regional brain atrophy, WMH burden, and cognitive impairment across neurological disorders. Increased BAG was significantly correlated with physical disability in MS ($r = 0.17$).

Healthy individuals with accelerated brain age show high white matter hyperintensity (WMH) burden and regional volume reduction. Neurological disorders exhibit distinct accelerated brain aging, correlated with impaired cognitive and physical function [1)]

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Chai L, Sun J, Zhuo Z, Wei R, Xu X, Duan Y, Tian D, Bai Y, Zhang N, Li H, Li Y, Li Y, Zhou F, Xu J, Cole JH, Barkhof F, Zhang J, Zheng H, Liu Y. Estimated Brain Age in Healthy Aging and Across Multiple Neurological Disorders. J Magn Reson Imaging. 2024 Nov 26. doi: 10.1002/jmri.29667. Epub ahead of print. PMID: 39588683.