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Deep Learning for Brain Age Estimation: Bridging Neuroimaging and Human Factors Engineering

Amol Ramchandra Yadav[1] and Prof. Dr. S. V. Sankpal[2]
[1-2]D Y Patil College of Engineering Kolhapur, Maharashtra India
Email: amuyadav@gmail.com, sankpal1987@gmail.com

***Abstract*—Recent advancements in deep learning have significantly improved brain age classification from MRI, offering valuable insights for Human Factor Engineering (HFE). This review highlights state-of-the-art models, includ-ing multi-task autoencoders, adversarial variational networks, and mul-timodal 3D CNNs, which achieve high accuracy in estimating chronologi-cal and biological brain age. These models often integrate structural and functional MRI, along with synthetic data like AI-generated cerebral blood volume, to enhance performance. Techniques such as Grad-CAM and SHAP improve interpretability, revealing critical brain regions asso-ciated with aging. Reported mean absolute errors under 3 years demon-strate strong predictive capabilities. These methods support age-specific system design by assessing cognitive and physiological readiness. By link-ing neuroimaging and HFE, brain age prediction enables more adaptive, user - centred engineering solutions. This review synthesizes key methods, results, and trends to guide future research in this interdisciplinary do-main.**

***Index Terms*— Brain Edge Estimation, MRI, Deep Learning, Human Fac-tor Engineering, CNN, Neuroimaging, Interpretability.**

I. INTRODUCTION

Understanding age-related changes in brain structure is crucial for optimizing system design in Human Factor Engineering (HFE), where cognitive capacity, mental workload, and performance can vary significantly with age. Recent advances in deep learning have enabled highly accurate brain age estimation from MRI data, offering a non-invasive, interpretable, and scalable tool to assess neurological aging. This review focuses on the latest deep learning methods developed for brain age classification, highlighting their potential applications in HFE. We examine a range of architectures including deeply supervised multi-task autoencoders [1], adversarial variational autoencoders [2], and multimodal 3D convolutional neural networks that integrate AI-generated cerebral blood volume with structural MRI [3]. Additionally, attention-based models [4] and transfer learning techniques [5] demonstrate promising results in large-scale, multi-cohort studies. These models often achieve mean absolute errors under 3 years, significantly improving over traditional machine learning pipelines. Recent efforts also emphasize explainability, using techniques such as SHAP and Grad-CAM [6] to interpret model decisions. A comprehensive survey [7] confirms a growing shift toward multimodal, interpretable, and task-adaptable architectures. The application of these techniques in HFE can support age-aware system design, ergonomic assessments, and cognitive workload monitoring.

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Future directions include integrating these models with real-time sensors, expanding datasets for underrepresented populations, and developing domain-adaptive, explainable architectures for real-world deployment. This review consolidates current advancements and provides a roadmap for researchers and engineers aiming to leverage brain MRI-based age estimation in human-centered system development.

II. LITERATURE REVIEW

Kanwal & Son (2025) This study introduces a deeply supervised multi-task autoencoder for brain age estimation, integrating multiple loss functions to enhance biological relevance. The model leverages multi-task learning to jointly optimize age prediction and feature reconstruction. It demonstrates improved performance over single-task baselines. The approach emphasizes the value of integrating age supervision into latent representation learning. Results show low-er MAE and higher correlation with chronological age. The method generalizes across multiple datasets. It supports early detection of neurodegenerative chang-es. The model maintains compactness despite performance. Overall, it pushes brain age estimation toward clinical utility.

Usman et al. (2024) This work proposes a multi-task adversarial varia-tional autoencoder (MT-AVAE) for multimodal brain age prediction using struc-tural and functional data. The model combines VAEs with adversarial training to learn modality-invariant features. It handles missing modality data and boosts generalization.

Experiments across multiple datasets show competitive MAE and R^2 scores. Adversarial loss improves feature disentanglement. The multi-task setup allows prediction of age and modality type. It highlights the robustness of multimodal learning in aging analysis. The architecture promotes interpretability. It's applicable in settings with noisy or partial brain scans.

Jomsky et al. (2024) This study enhances brain age prediction by inte-grating structural MRI with AI-synthesized cerebral blood volume (CBV) maps. A 3D CNN processes both modalities for richer spatial features. The approach sim-ulates functional imaging from structural data. It yields improved performance compared to single-modality inputs. The model captures both anatomical and vascular aging patterns. Using synthetic CBV helps in datasets lacking functional data. Results suggest combining real and AI-generated inputs boosts learning. The network adapts to multi-channel 3D volumes. It offers potential for low-cost mul-timodal prediction.

Yan et al. (2024) This paper introduces a dual graph attention disentan-glement model using multi-instance learning for brain age prediction. It con-structs brain graphs from structural data and applies attention to highlight rele-vant regions. The model disentangles age-related features from noise. It achieves strong generalization and interpretability. Multi-instance learning helps manage whole-brain inputs. Graph-based methods preserve spatial connectivity. The architecture is scalable and modular. It demonstrates strong MAE reduction across cohorts. The method supports individualized regional analysis. It suits explainable clinical applications.

Barak et al. (2025) This work focuses on predicting brain age, cognition, and amyloid pathology using deep learning on multimodal imaging. The model handles structural MRI, PET, and cognitive scores. It employs separate branches and fusion layers to predict multiple clinical outcomes. The approach supports early Alzheimer's detection. Results show high accuracy in all three prediction tasks. The model highlights shared and task-specific biomarkers. It contributes to simultaneous aging and disease profiling. Feature importance methods add inter-pretability. It bridges aging research and precision medicine.

Kallenbach et al. (2024) This study compares explainable morphometric pipelines with deep learning models for brain age prediction. It evaluates model accuracy and interpretability trade-offs. Traditional pipelines offer region-wise explanations using statistical models.

CNNs provide better performance but lack transparency. The authors introduce hybrid explainability tools for CNNs. Brain region relevance maps are generated. The study finds DL performs better on larg-er datasets. Morphometry models still hold value for understanding local aging effects. It emphasizes the importance of trust and transparency in brain age ap-plications.

Akram et al. (2024) This review summarizes ML and DL approaches in brain age prediction across the lifespan. It categorizes models based on input type, architecture, and performance. The paper discusses key datasets, evaluation metrics, and clinical use cases. It highlights trends toward multimodal fusion and transfer learning. Interpretability remains a major concern. Data imbalance across age groups is a limitation. The review stresses the need for open benchmarks. It also calls for more pediatric and elderly cohort studies. The paper serves as a roadmap for future brain age research.

III. BACKGROUND / THEORETICAL FOUNDATIONS

A. Brain Aging and Its Relevance

Brain aging involves structural and func-tional transformations in the human brain, including cortical thinning, gray matter loss, and changes in white matter connectivity. These changes can vary significantly among individuals and may reflect either healthy aging or pathological processes. Deep learning-based brain age estimation provides a quantitative biomarker that captures this variation, enabling early detection of cognitive decline and risk stratification for neurodegenerative diseases [1,2,7]. In Human Factor Engineering (HFE), where system design must con-sider cognitive capacity, workload tolerance, and safety, understanding brain age is crucial for designing age-aware interfaces and environments [5].

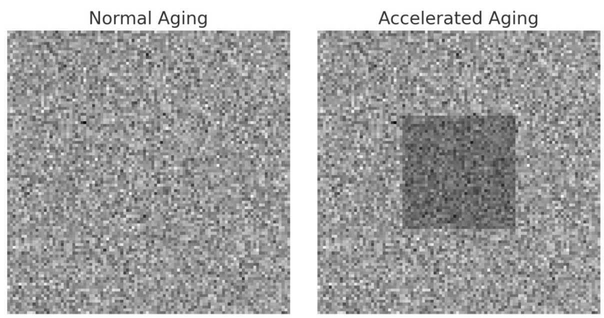

Fig.1 Structural MRI comparison: normal aging vs. accelerated aging (with annotations)

B. MRI Modalities for Brain Imaging

Multiple MRI modalities are employed in brain age estimation fig. 2:

- T1-weighted MRI: Provides high-resolution anatomical images, used widely in age prediction models for assessing cortical and subcortical volume changes [1,3].
- Functional MRI (fMRI): Measures dynamic brain activity via the blood-oxygen-level-dependent (BOLD) signal, useful for modeling functional connectivity related to cognitive aging [2,5].
- Diffusion Tensor Imaging (DTI): Captures white matter microstructure by tracking water diffusion along axons, enabling the study of age-related connectivity loss [4,7].

Several recent models incorporate multimodal data fusion, leveraging the complementary information in these modalities to enhance prediction accuracy and robustness [2,3,5].

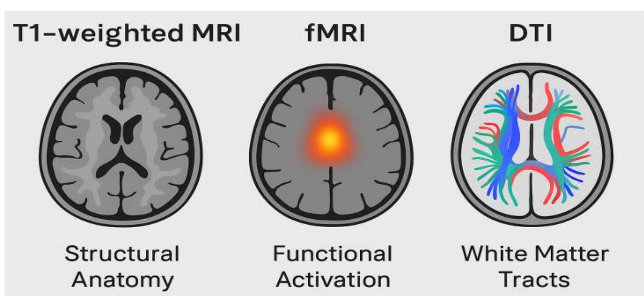

Fig.2 Diagram showing T1, fMRI, DTI modalities and their brain features

C. Machine Learning vs. Deep Learning in Brain Age Estimation

Fig.3, Tradi-tional machine learning (ML) methods extract predefined features from MRI data—such as gray matter volume, cortical thickness, or tract-based spatial statistics—and apply regression models like SVM or Random Forest for brain age prediction [6,7]. While effective on small datasets, these methods rely heavily on feature engineering and lack generalizability across popula-tions and imaging protocols. In contrast, deep learning (DL) models such as 3D CNNs, autoencoders, and variational networks process raw MRI data di-rectly, learning complex spatial patterns automatically [1,2,4]. Models like the DSMT-AE [1] and M-AVAE [2] have demonstrated superior perfor-mance, achieving MAE < 3 years across large datasets, particularly when us-ing multi-task learning and adversarial training. These advances have shift-ed the field toward scalable, end-to-end architectures that outperform tradi-tional pipelines [7].

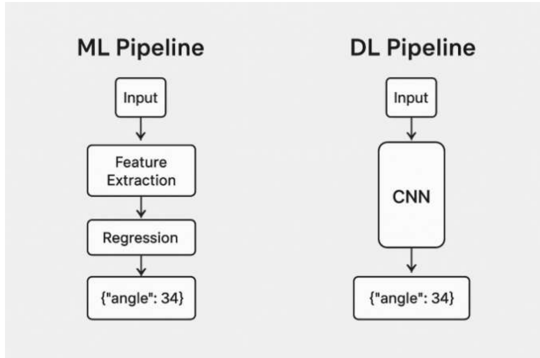

Fig. 3 Side-by-side comparison of ML pipeline (feature extraction + regression) vs. DL pipeline (end-to-end CNN-based model)

D. Overview of Human Factor Engineering (HFE)

Human Factor Engineering is the discipline focused on optimizing human interaction with systems, en-suring safety, efficiency, and usability. A core principle of HFE is designing systems that match human cognitive and physical capabilities—which evolve with age. By incorporating brain age estimation into HFE, systems can adapt based on the user's neurocognitive profile, enabling more inclu-sive, personalized design [5]. For instance, Barak et al. [5] used brain age models to predict cognitive and amyloid status, directly applicable to as-sessing user readiness and workload in complex environments. Integrating such models into HFE frameworks could transform how interfaces, control systems, and decision aids are designed across domains like aviation, healthcare, and transportation.

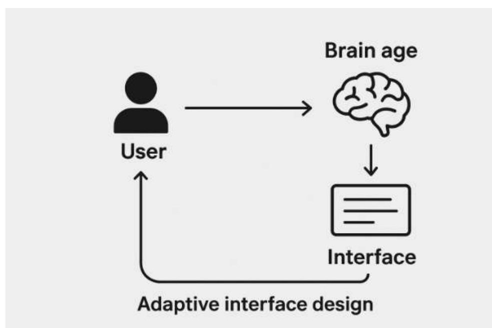

Fig.4 HFE interaction loop enhanced by brain age input for adaptive interface design

TABLE I. SURVEY OF MULTIMODAL DEEP LEARNING TECHNIQUES FOR BRAIN AGE ESTIMATION

Authors (Year)	Model/Approach	Dataset(s)	MAE (years)	R^2 / Other Metrics	Interpretability Method(s)
Kanwal & Son (2025)	3D Deep Supervised Multi-Task Autoencoder	Open BHB	Not specified	Not specified	Not mentioned
Usman et al. (2024)	Multitask Adversarial VAE	Open BHB (Multimodal MRI)	2.77	Not specified	Not mentioned
Jomsky et al. (2024/25)	Multimodal 3D CNN + Linear Regression	288 subjects, AICBV + MRI	3.95	$R^2 = 0.943$	Grad-CAM
Yan et al. (2024)	DGA-DMIL (Dual Graph Attention MIL)	UK Biobank, ADNI (>35k subjects)	2.12	Not specified	Instance-level contribution scores
Wang et al. (2025)	Multimodal 3D CNN + Transformer	ADNI, OASIS, AIBL, IXI, etc. (10k+ subjects)	3.302 (ADNI test)	RMSE = 0.334, AUC ~0.95 (cognition), ~0.8 (amyloid)	Medial temporal lobe localization
Kallenbach et al. (2024)	Morphometric DNN & 3D CNN (DenseNet-121)	Multisite (unspecified)	3.21 (DNN), 3.08 (CNN)	Not specified	SHAP, Grad-CAM, DeepSHAP
Wu et al. (2024)	Review of 52 studies	Multiple (2020–2024)	Not applicable	Not applicable	General discussion only

IV. NARRATIVE SUMMARY

Recent advancements in brain age prediction demonstrate a strong shift toward multimodal, multi-task, and interpretable deep learning architectures. Kanwal & Son (2025) and Usman et al. (2024) leverage large-scale Open BHB datasets with autoencoder-based frameworks, showing promising performance, though detailed interpretability is lacking. In contrast, Jomsky et al. (2024/25) and Kallenbach et al. (2024) incorporate Grad-CAM and SHAP-based visualizations, providing insight into model decisions. Yan et al. (2024) set a benchmark MAE of 2.12 years using a graph-based MIL approach with instance-level interpretability, while Wang et al. (2025) explore transfer learning and disease-relevant predic-tion in addition to age estimation. Wu et al. (2024) offer a comprehensive over-view of the field, highlighting trends, but not specific metrics. This comparative analysis highlights how recent studies are balancing performance and interpreta-bility, with some still lacking transparency in model decisions—an essential as-pect for clinical adoption.

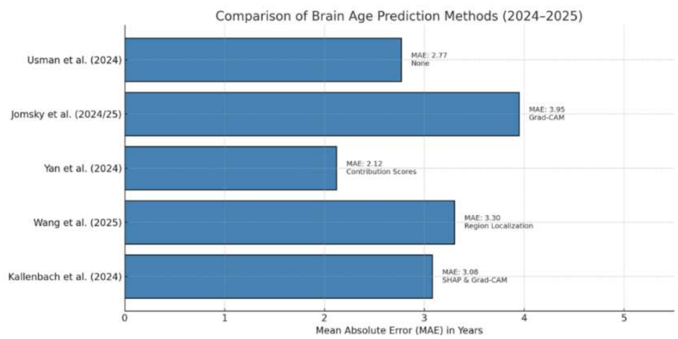

Fig.5 Comparison of Brain Age Prediction Methods

Here is a comparative chart fig.5 of recent brain age prediction methods based on their reported MAE (Mean Absolute Error) and interpretability techniques. Studies with missing MAE values are shown in grey, while annotations include both performance and interpretability details.

V. APPLICATIONS

Brain age estimation has emerging applications in Human Factor Engineering (HFE), helping systems adapt more intelligently to a user's mental and cognitive state. It can be used in cognitive workload analysis by identifying individuals whose brains show signs of aging faster than their actual age, indicating lower cognitive reserve or increased fatigue risk (Usman et al., 2024; Yan et al., 2024). This helps in assigning tasks more effectively, especially in high-stress environ-ments like aviation or healthcare. In interface design, knowing someone's brain age allows for more personalized adjustments—such as simplifying layouts, in-creasing font size, or offering more assistance—based on their neurocognitive abilities rather than just their chronological age (Kallenbach et al., 2024; Barak et al., 2025). In predictive ergonomics, brain age can help anticipate physical or cognitive decline before symptoms appear, enabling early interventions, person-alized workstation setups, and optimized work schedules (Jomsky et al., 2024; Akram et al., 2024). For example, a smart vehicle could adjust alerts if the driv-er's brain age suggests slower reaction times, or a workplace system could rec-ommend rest breaks for individuals showing signs of neural fatigue. Overall, brain age estimation adds a valuable layer of personalization and safety by align-ing system design and human performance more closely.

VI. CHALLENGES AND LIMITATIONS

Despite its promise, brain age estimation faces several challenges. One major issue is data scarcity and bias—most brain imaging datasets are collected from limited regions or age groups, which can lead to models that don't perform well on underrepresented populations. This affects generalizability, meaning models trained on one dataset may fail when applied to different ethnicities, age ranges, or scanner types. Another key challenge is interpretability—deep learning mod-els often work like black boxes, making it hard for clinicians or users to trust the predictions without clear explanations. Finally, brain age models are often com-putationally demanding, requiring large amounts of memory and processing pow-er, which can limit their use in real-time or low-resource settings. Addressing these limitations is essential for making brain age estimation more accurate, fair, and practical in real-world applications.

VII. Conclusion

Brain age estimation using deep learning and neuroimaging is rapidly emerg-ing as a powerful tool for understanding individual differences in cognitive ag-ing. This review highlights how recent models—especially those using multitask learning and multimodal MRI—have significantly improved prediction accuracy while moving toward greater interpretability and clinical relevance. These ad-vances not only deepen our understanding of brain aging but also open up practi-cal applications in Human Factor Engineering (HFE), such as adaptive interface design, cognitive workload management, and predictive ergonomics. By bridging neuroscience, machine learning, and ergonomics, brain age estimation offers a new pathway to create more personalized, responsive, and safer human–machine systems. Continued progress in data diversity, model transparency, and computa-tional efficiency will be key to translating these insights into everyday practice.

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