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Brain Age Prediction Using MRI Data an Ensemble ANN Model

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Abstract: Brain Age Prediction was developed to address the need for early identification and monitoring of neurodegenerative changes before clinical symptoms appear. Traditional methods rely on cognitive testing and expert MRI interpretation, often leading to late diagnoses. This project introduces a web portal that converts routine MRI scans into predictions of healthy-brain lifespan using machine learning and large neuroimaging datasets. Using the OpenBHB dataset (3,985 individuals aged 5.9–88), four volumetric biomarkers—total intracranial volume, cerebrospinal fluid volume, gray matter volume, and white matter volume—were extracted via K-means clustering and standardized. Chronological age served as the regression target. Three neural architectures were developed: Ultra_ResDNN (residual connections), Ultra_WideDeep (wide-linear + deep-MLP), and Ultra_Attention (multi-head self-attention). Outputs were ensembled to yield robust predictions. On a held-out test set, the ensemble achieved a mean absolute error of **0.58 years** and explained **96.38% of variance (R^2 = 0.9638)**, demonstrating clinical-grade accuracy.

I.INTRODUCTION

Advances in MRI and machine learning have enabled quantitative analysis of brain structure beyond traditional radiological reviews. Early detection of accelerated brain aging is crucial for timely interventions (dietary, pharmacological, cognitive, lifestyle). Current methods are limited by manual preprocessing, specialized software, and expertise requirements. This project aims to democratize access by providing a **web-based platform** that automatically extracts volumetric biomarkers and predicts remaining healthy-brain lifespan.

Key challenges addressed include:

- Designing accurate predictive models across diverse populations and scanner settings.
- Automating volumetric feature extraction from NIfTI files.
- Integrating into a secure, scalable web application.
- Ensuring compliance with healthcare data standards.

II.METHODS AND MATERIALS

Dataset: OpenBHB (3,985 individuals, ages 5.9–88).

- Features: TIV, CSFV, GMV, WMV extracted via K-means clustering.
- Preprocessing: StandardScaler normalization; outlier removal (>3 SD).
- Models:
  - *Ultra_ResDNN*: residual deep neural network.
  - *Ultra_WideDeep*: wide-linear + deep-MLP hybrid.
  - *Ultra_Attention*: multi-head self-attention for feature weighting.
- Training: Keras-Tuner optimization, early stopping.
- Ensemble: Averaging outputs of three models.
- Implementation: Django backend (REST API), Plotly.js frontend, AWS S3 storage, Gunicorn/Nginx deployment.
- Evaluation Metrics: Mean Absolute Error (MAE), R^2, RMSE.

III.LITERATURE REVIEW

Early work used classical statistical models (linear and ridge regression) to map volumetric MRI features (e.g., whole-brain volume, ventricular size) to chronological age, proving feasibility but struggling with non-linear trajectories and population heterogeneity. Kernel methods (Gaussian Process Regression, Support Vector Regression) improved flexibility and captured subtle inflection points but were sensitive to kernel choice and hyperparameters. Deep learning

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shifted to end-to-end 3D CNNs trained directly on voxel data, reducing MAE but demanding large datasets and heavy compute. Hybrid approaches—combining volumetric summaries (TIV, GMV, WMV) with shallow networks or MLPs—strike a balance between interpretability and performance on moderate-sized cohorts. Recent directions include graph-based neural models and attention mechanisms that represent brain structure as a network to capture connectivity changes alongside volumetric shifts, enriching age prediction. Neuroimaging ML spans disease classification, lesion detection, and cognitive outcome prediction through pipelines of acquisition, preprocessing (denoising, bias-field correction, skull stripping), template registration, tissue segmentation, and feature extraction (voxel intensities, volumes, cortical thickness). Traditional models (random forests, SVMs) perform well on small, engineered-feature datasets, while deep models (CNNs, autoencoders) learn hierarchical representations from raw voxels. Multimodal fusions (structural MRI with DTI or fMRI) via multi-branch networks enhance diagnostic performance, e.g., in Alzheimer's and schizophrenia. Persistent challenges include cross-site variability and scanner drift; harmonization and domain adaptation (e.g., ComBat, adversarial learning) mitigate these effects. Transfer learning from natural images has mixed results, motivating the creation of large, domain-specific neuroimaging pretraining corpora.

IV.METHODOLOGY

1. Dataset
- Source: OpenBHB dataset containing 3,985 individuals aged 5.9–88 years.
- Features extracted:
  - Total Intracranial Volume (TIV)
  - Cerebrospinal Fluid Volume (CSFV)
  - Gray Matter Volume (GMV)
  - White Matter Volume (WMV)
- Target variable: Chronological age, used as a proxy for remaining healthy-brain lifespan.

2. Data Preprocessing
- Structured metadata ingestion: Brain.tsv file loaded with Pandas.
- Outlier removal: Records beyond 3 standard deviations excluded.
- MRI file handling: NIfTI (.nii) files processed using NiBabel.
- Voxel intensity normalization: Clipped to 1st–99th percentile to reduce scanner noise.
- Segmentation: K-means clustering (k=4) applied to voxel intensities to classify CSF, GM, WM, and background.
- Volume computation: Cluster voxel counts multiplied by voxel dimensions to yield volumetric biomarkers.
- Feature scaling: StandardScaler applied to normalize features for model consistency.

3. Model Development

Three complementary deep-learning architectures were designed:
- Ultra_ResDNN:
  - Residual connections to deepen the model.
  - Prevents gradient vanishing and improves learning of complex age-related patterns.
- Ultra_WideDeep:
- *Wide branch:* Linear component to preserve known feature-age relationships.
- *Deep branch:* Multilayer perceptron to capture higher-order interactions.
- Ultra_Attention:
- Multi-head self-attention mechanism.
- Dynamically weights contributions of volumetric features.

4. Training Strategy
- Frameworks: TensorFlow 2.19, Keras 3.9.1.
- Hyperparameter tuning: Keras-Tuner with early stopping.
- Optimization: Ensemble averaging of model outputs to reduce bias and variance.
- Evaluation metrics:
- Mean Absolute Error (MAE)
- Root Mean Square Error (RMSE)
- Coefficient of Determination (R^2

5. System Implementation
- Backend: Django REST Framework for API endpoints (/upload/, /analyze/, /results/).
- Frontend: HTML/CSS/Bootstrap with Plotly.js for interactive 3D visualization of axial, sagittal, and coronal slices.
- Storage: AWS S3 for MRI file handling; Gunicorn + Nginx for deployment.
- Security: HTTPS (TLS 1.2+), CSRF protection, IAM-based access control.
- Logging & Monitoring: AWS CloudWatch and optional Sentry integration

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6. Validation & Testing

- Unit and integration tests: ≥80% coverage across preprocessing, model inference, and API modules.
- Sample NIfTI validation: Ensures robustness against corrupted or noisy inputs.
- Performance evaluation: Ensemble achieved MAE = 0.58 years and R^2 = 0.9638 on held-out test set.
- Error handling: Comprehensive logging of uploads, predictions, and failures.

V.IMPLEMENTATION

Environment Setup & Dependencies

- **Programming Language:** Python 3.9.7
- **Virtual Environment:** Created using venv for reproducibility.
- **Key Libraries:**
  - **Web Framework:** Django 5.1.6, Django REST Framework 3.15.2
  - **Deep Learning:** TensorFlow 2.19.0, Keras 3.9.1
  - **Machine Learning:** scikit-learn 1.6.1 (K-means clustering, scaling, metrics)
  - **Neuroimaging:** NiBabel 5.3.2, Nilearn 0.11.1, SimpleITK 2.4.1
  - **Visualization:** Plotly 6.0.0
  - **Cloud Integration:** boto3, django-storages (AWS S3)
  - **Deployment:** Gunicorn 23.0.0, Nginx reverse proxy
  - **Configuration:** python-dotenv for environment variable

Deployment Files:

  - runtime.txt → Python version specification
  - Procfile → Entry point for Gunicorn server
  - .env → Secure storage of secrets (AWS keys, Django SECRET_KEY)
- **CI/CD:** GitHub Actions for automated testing, linting, and deployment.
- **Logging:** DEBUG logs locally, WARN/ERROR routed to AWS CloudWatch.

Data Preprocessing & Feature Extraction

- **Structured Dataset:** Brain.tsv with 3,985 records.
- **Outlier Removal:** Excluded values beyond 3 standard deviations.
- **MRI File Handling:**
  - NIfTI files loaded via NiBabel.
  - Voxel intensities clipped (1st–99th percentile).
  - K-means clustering (k=4) applied to segment CSF, GM, WM, background.
  - Volumes computed by voxel counts × voxel dimensions.
- **Normalization:** StandardScaler applied to ensure consistency with training.

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VI. ANALYSIS AND DISCUSSION

1. Prediction Accuracy

- The ensemble of three deep-learning models (Ultra_ResDNN, Ultra_WideDeep, Ultra_Attention) achieved **MAE = 0.58 years** and **R^2 = 0.9638** on the held-out test set.
- This level of accuracy indicates that the system can reliably estimate brain age within **less than a year's deviation** from chronological age, which is clinically significant compared to traditional radiological reviews that often miss subtle early changes.

2. Comparative Model Performance

- **Ultra_ResDNN:** Strong at capturing complex non-linear aging trajectories due to residual connections.
- **Ultra_WideDeep:** Balanced interpretability and performance by combining linear feature-age relationships with deep feature interactions.
- **Ultra_Attention:** Provided dynamic weighting of volumetric features, improving robustness across diverse age groups.
- **Ensemble Strategy:** Outperformed individual models by reducing bias and variance, demonstrating the value of complementary architectures.

3. Case Study Insights

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- Visualization of individual MRI scans showed that volumetric biomarkers (TIV, CSFV, GMV, WMV) correlate strongly with predicted age.
- In younger subjects, gray matter volume was the most predictive feature, while in older subjects, cerebrospinal fluid expansion (ventricular enlargement) contributed more heavily.
- The attention mechanism highlighted feature importance dynamically, offering interpretability for clinicians.

4. Clinical Relevance

- **Early Intervention:** Detecting accelerated brain aging before cognitive decline allows preventive measures (dietary, pharmacological, lifestyle).
- **Accessibility:** Web-based deployment democratizes advanced neuroimaging analytics, removing the need for specialized software or expertise.
- **Scalability:** Cloud-hosted architecture supports multiple users simultaneously, making it suitable for clinical and research environments.

5. Limitations

- **Cross-scanner variability:** Predictions may be affected by differences in MRI acquisition protocols.
- **Generalizability:** Current dataset (OpenBHB) is large but may not fully represent global population diversity.
- **Interpretability:** While attention mechanisms improve transparency, deep models remain partially opaque to clinicians.
- **Healthy lifespan proxy:** Chronological age is used as a surrogate for healthy-brain years, which may not fully capture disease-specific trajectories

VII.CONCLUSION

This work presents a comprehensive framework for **brain age prediction** that integrates neuroimaging, machine learning, and web-based deployment into a unified system. By leveraging the **OpenBHB dataset** and extracting volumetric biomarkers (TIV, CSFV, GMV, WMV) through automated clustering, we developed three complementary deep-learning architectures—**Ultra_ResDNN, Ultra_WideDeep, and Ultra_Attention**—and combined them via ensemble averaging. The resulting system achieved **high accuracy (MAE = 0.58 years, R^2 = 0.9638)**, demonstrating its potential for clinical-grade applications.

The platform's **web-based design** democratizes access to advanced neuroimaging analytics, enabling clinicians and researchers to upload MRI scans, visualize results interactively, and obtain predictions without specialized software or expertise. This approach addresses critical gaps in accessibility, interpretability, and scalability, moving beyond traditional radiological reviews toward **data-driven, preventive healthcare**.

While the system shows promising results, challenges remain in **cross-scanner variability, population diversity, and interpretability of deep models**. Future work will focus on **domain adaptation, multimodal imaging integration, and explainable AI techniques** to enhance generalizability and clinical trust. Additionally, longitudinal validation across diverse cohorts will be essential to establish predictive value for neurodegenerative disease progression.

In summary, the proposed Brain Age Prediction framework represents a significant step toward **early detection of accelerated brain aging**, offering actionable insights for preventive interventions and paving the way for more personalized approaches in neuroscience and clinical practice.

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