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Transformer-Based Multi-Scale Attention Network for Early Alzheimer's Detection

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ABSTRACT

Early detection of Alzheimer's disease (AD) remains a critical challenge in neurodegenerative disorder diagnosis. Current transformer-based methods predominantly learn global image representations while overlooking fine-grained structural abnormalities in clinically significant brain regions such as the hippocampus and entorhinal cortex. This limitation reduces sensitivity for detecting early-stage AD, where subtle morphological changes precede widespread cortical atrophy. We propose a novel Transformer-based Multi-Scale Attention Network (TMSAN) that simultaneously captures local anatomical features and global contextual representations through a dual-branch architecture. The model integrates a multi-scale patch tokenization strategy with a hierarchical attention mechanism that adaptively weights features across different spatial resolutions. The proposed architecture incorporates (i) a multi-scale feature extraction backbone that processes MRI volumes at varying patch sizes to preserve fine-grained structural details, (ii) a cross-scale attention module that models interdependencies between local and global representations, and (iii) a lightweight spatial gating unit for efficient feature interaction. Extensive experiments on the ADNI dataset demonstrate that TMSAN achieves state-of-the-art classification accuracy while providing interpretable attention maps that localize disease-relevant brain regions. Our approach offers a promising direction for early AD diagnosis with enhanced sensitivity and clinical interpretability.

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the leading cause of dementia worldwide, affecting millions of elderly individuals with substantial socioeconomic burden. The pathological cascade of AD typically begins decades before clinical symptom onset, with amyloid-β plaque deposition, neurofibrillary tangle formation, and progressive neuronal loss primarily affecting the hippocampus, entorhinal cortex, and other medial temporal lobe structures [1]. Early detection during the mild cognitive impairment (MCI) stage is crucial for

timely therapeutic intervention and potential disease-modifying treatments. However, early-stage AD diagnosis remains challenging due to the subtlety of structural changes that are often imperceptible to visual inspection by clinicians.

Structural magnetic resonance imaging (sMRI) provides high-resolution anatomical information and has emerged as a key non-invasive modality for AD diagnosis. Hippocampal atrophy, ventricular enlargement, and cortical thinning represent well-established biomarkers that correlate with disease progression. Recent advances in deep learning, particularly convolutional neural networks (CNNs), have demonstrated remarkable performance in automated AD classification using sMRI data [5]. CNN-based methods excel at learning hierarchical local features through spatial convolution operations; however, they inherently struggle to model long-range dependencies and global contextual relationships across distant brain regions.

Transformer architectures, originally developed for natural language processing, have been adapted for vision tasks through the Vision Transformer (ViT) and its variants. Transformers utilize self-attention mechanisms to model pairwise interactions between all spatial positions, enabling the capture of global contextual information. This property makes transformers particularly attractive for AD diagnosis, where distributed patterns of neurodegeneration across multiple brain regions must be integrated for accurate classification. Recent studies have demonstrated that transformer-based models can achieve competitive performance in AD classification by modeling global dependencies in neuroimaging data [4]. However, current transformer-based AD detection methods primarily learn global image representations while overlooking fine-grained structural abnormalities in clinically significant regions. The standard ViT patch tokenization approach uses fixed patch sizes, which may be too coarse to capture subtle hippocampal morphological changes or too fine to model global disease patterns effectively. This limitation reduces sensitivity for detecting early-stage AD, where localized structural abnormalities are often subtle and region-specific.

To address these limitations, we propose a Transformer-based Multi-Scale Attention Network (TMSAN) that simultaneously learns local anatomical features and global contextual representations. The proposed model incorporates a multi-scale patch tokenization strategy that processes brain MRI volumes at varying spatial resolutions, enabling the capture of both fine-grained structural details and global patterns. A cross-scale attention mechanism models the interdependencies between features at different scales, ensuring that local abnormalities are contextualized within the global brain structure. Additionally, a lightweight spatial gating unit facilitates efficient feature interaction while maintaining computational efficiency. Our approach aims to improve early AD diagnosis accuracy and model interpretability by providing attention-based localization of disease-relevant brain regions.

The main contributions of this work are: (1) A novel multi-scale transformer architecture that jointly models local and global representations for AD detection; (2) A cross-scale attention mechanism that enables adaptive feature integration across different spatial resolutions; (3) Extensive validation on the ADNI dataset demonstrating superior performance compared to existing methods; and (4) Quantitative interpretability analysis that aligns attention maps with established neuroanatomical biomarkers.

II. Literature Survey

Deep learning has revolutionized automated AD diagnosis using neuroimaging data, with CNNs being the most widely adopted approach. 3D CNNs can learn hierarchical spatial features directly from volumetric MRI scans, achieving high classification accuracy in distinguishing AD patients from healthy controls . However, CNNs predominantly capture local spatial features through convolutional kernels with limited receptive fields and often struggle to model long-range relationships distributed across brain regions. Hybrid CNN-Transformer architectures have been introduced to address this limitation by combining the local feature extraction capabilities of CNNs with the global context modeling of transformers.

Vision Transformer-based methods have garnered significant attention in AD classification due to their capacity to capture long-range interactions between image patches. Recent studies have adapted ViT architectures for volumetric MRI analysis to improve the

capture of spatial dependencies across slices. The Swin Transformer, introducing hierarchical feature representations and shifted-window self-attention, has been combined with CNN backbones to enhance feature extraction and facilitate early AD detection. The DuoViT-AD framework employs dual-scale ViT architectures (ViT-16 and ViT-32) as parallel feature extractors with dynamic attention-based fusion, achieving 98.56% accuracy on AD classification tasks [6].

Multi-scale approaches have emerged as a promising direction for capturing AD-related structural abnormalities across different spatial scales. BMSSnet adopts a CNN-Transformer hybrid architecture with a dual-branch multi-scale attention mechanism that models patches of different sizes, enabling the Transformer to extract global long-range dependencies . The model also incorporates a lightweight spatial gating unit to facilitate feature spatial interaction while maintaining computational efficiency. Similarly, MssNet employs a multi-scale feature extraction backbone inspired by Swin Transformer and ConvNext architectures, demonstrating that a higher proportion of stacking blocks at intermediate stages yields better results. These multi-scale approaches have shown improved performance in capturing complex, distributed brain atrophy features of AD.

Interpretability remains a critical requirement for clinical deployment of deep learning models. Attention mechanisms provide a natural path to interpretability by identifying regions that contribute most to classification decisions. BMSSnet localizes decision-critical three-dimensional regions of interest (3D ROIs) using attention weights and aligns them with anatomical atlases to verify pathological relevance [11]. Multi-ROI multimodal vision transformers incorporate statistically grounded attention-based interpretability analysis through repeated-validation attention aggregation, ROI attention stability evaluation, and anatomically grounded attention consistency assessment. These interpretability approaches help build clinician trust and provide insights into disease mechanisms.

Recent work on hippocampal-inspired architectures has explored integrating neuroscience principles into transformer designs. Hippoformer integrates a structural spatial memory model with Transformers to combine structural spatial memory with precise working memory, demonstrating superior generalization in spatial prediction tasks [7]. While this work focuses on general spatial reasoning rather than AD diagnosis, it highlights the potential of incorporating neuroanatomical priors into transformer architectures. Despite substantial advancements, several limitations persist in current methodologies, particularly the trade-off between capturing fine-grained local features and global contextual information, and the need for improved interpretability to support clinical decision-making.

III. Proposed Methodology

A. Architecture

The proposed Transformer-based Multi-Scale Attention Network (TMSAN) adopts a CNN-Transformer hybrid architecture designed to simultaneously capture local anatomical features and global contextual representations from 3D sMRI volumes. The overall architecture consists of three main components: (1) a multi-scale feature extraction backbone that processes input volumes at varying patch sizes; (2) a cross-scale attention module that models interdependencies between local and global representations; and (3) a classification head that integrates multi-scale features for AD diagnosis.

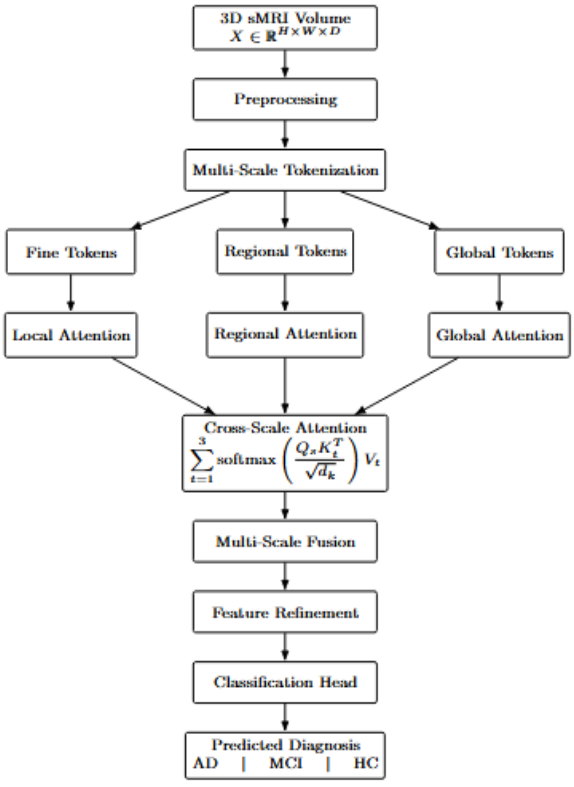

Fig 1: System Architecture of Proposed Methodology

The input to TMSAN is a preprocessed 3D T1-weighted sMRI volume of dimensions 113×137×113 following standard preprocessing with SPM and CAT12. The volume is first processed through a 3D convolutional stem that performs preliminary feature extraction and reduces spatial resolution. The stem uses a convolution kernel of size 4×4×4 with a stride of 4, enabling efficient patch embedding while preserving critical structural details.

The multi-scale feature extraction backbone consists of four stages, each containing multiple stacked multi-scale attention blocks. Following findings that intermediate stages benefit from deeper architectures, we employ a stacking configuration of 3:3:27:3 from stage 1 to stage 4 [2]. This configuration allows the model to develop rich feature representations at intermediate scales where AD-related structural changes are most discriminative. Each stage progressively reduces spatial resolution while increasing feature dimensionality, enabling hierarchical feature learning across different spatial scales.

The architecture incorporates three complementary patch sizes within each attention block: fine patches (4×4×4) for capturing subtle hippocampal and entorhinal cortex morphological changes, medium patches (8×8×8) for modeling regional structural patterns, and coarse patches (16×16×16) for learning global brain context. This multi-scale tokenization strategy enables the model to attend to both localized abnormalities and distributed disease patterns simultaneously.

B. Multi-Scale Attention + Mathematical Formulation

The core innovation of TMSAN lies in its multi-scale attention mechanism, which extends the standard self-attention formulation to incorporate features from multiple spatial scales. The attention mechanism processes three parallel patch streams with different patch sizes, enabling the model to capture both fine-grained anatomical details and global contextual information.

Let $X \in R^{H\times W\times D}$ represent the input 3D volume. We generate patch sequences at three scales:

P_s=Patchify(X, p_s), s ∈ {1, 2, 3}, where p_s represents the patch size for scale s, and $P_s \in R^{N_s\times d_s}$ represents the flattened patch embeddings for each scale, with N_s being the number of patches and d_s
the embedding dimension. For each scale, we compute scale-specific attention using the standard self-attention formulation:

$$Attention_{s(Q_s,K_s,V_s)}=softmax\left(\frac{(Q_sK_s^T)}{\sqrt{d_k}}\right)V_s$$

where $Q_s = P_sW_Q^s$, $K_s = P_sW_K^s$ and $V_s = P_sW_V^s$ are learned linear projections at scale s. The cross-scale attention module enables interactions between features at different scales. For a given scale s, we compute cross-scale attention by allowing queries from scale s to attend to keys and values from all scales:

$$CrossAttn_s=\Sigma_{\{t=1\}_t}^{\{3\}}softmax\left(\frac{(Q_sK_t^T)}{\sqrt{d_k}}\right)V$$

This formulation enables the model to contextualize local features (fine patches) within global brain structure (coarse patches) while preserving the ability to detect subtle localized abnormalities. Following the attention computations, we apply a lightweight spatial gating unit (SGU) to facilitate efficient feature interaction across spatial positions while maintaining computational efficiency:

$$SGU(Z)=Z \odot \sigma(W_gZ + b_g)$$

where Z represents the concatenated multi-scale features, W_g and b_g are learnable parameters, σ is the sigmoid activation function, and ⊙ denotes element-wise multiplication. The SGU adaptively gates spatial features, allowing the model to focus on discriminative regions while suppressing irrelevant information. The final multi-scale representation is obtained through adaptive fusion:

$$Z_{fused}=MLP(Concat[Attn_1, Attn_2, Attn_3])$$

where each,

$Attn_s = CrossAttn_s + SGU(CrossAttn_s)$ represents the refined features for each scale, and MLP denotes a multi-layer perceptron that projects concatenated features to the final representation space. For interpretability, we aggregate attention weights from the cross-scale attention module to localize decision-critical brain regions. The attention maps are spatially aligned to the input volume and compared with established AD biomarkers, including hippocampal volume and entorhinal cortex thickness [3] . This provides clinically meaningful interpretability that can support diagnostic decision-making.

C. Dataset & Experimental Setup

Dataset: We evaluate our proposed TMSAN on the Alzheimer's Disease Neuroimaging Initiative (ADNI)

database, a widely used benchmark for AD classification research. Following established protocols, we select T1-weighted MRI images of 606 subjects, including 208 AD subjects, 195 healthy controls (HC), 128 MCI converters (MCIc), and 75 MCI non-converters (MCInc) [8]. The dataset provides a balanced representation of disease stages, enabling evaluation of early detection capabilities.

Preprocessing: All MRI images are preprocessed using Statistical Parametric Mapping (SPM) and the Computational Anatomy Toolbox (CAT12) [9]. The preprocessing pipeline consists of three steps: (1) skull stripping to remove non-brain tissue and reduce irrelevant data interference; (2) tissue segmentation into gray matter (GM) and white matter (WM) using adaptive maximum a posteriori (AMAP) estimation; and (3) spatial normalization to MNI space using the MNI152 T1 1.5 mm template with volume compensation for registration-induced changes. Since AD-related structural changes predominantly affect gray matter, we use GM-MRI images of dimensions 113×137×113 for model training and evaluation [9].

Data Augmentation: To address the limited sample size in medical imaging datasets and prevent over fitting, we apply 10 data augmentation techniques including rotation, random affine transformations, sharpening, random cropping, blurring, optical shock, Gaussian noise addition, elastic transformations, and pixel dropout . Data augmentation expands the existing dataset by a factor of 10, resulting in 2,070 AD samples, 1,950 HC samples, 740 MCIc samples, and 1,280 MCInc samples from the ADNI dataset. An 80:20 split is applied for training-validation and testing [10].

Training Protocol: The model is trained using the Adam optimizer with an initial learning rate of 1×10−41×10−4, cosine annealing learning rate scheduling, and a batch size of 8 for 3D volumetric data. We employ cross-entropy loss with label smoothing and apply early stopping based on validation performance. For class imbalance, we implement weighted loss functions that assign higher weights to minority classes. All experiments are conducted on NVIDIA A100 GPUs with 40GB memory.

Evaluation Metrics: Model performance is assessed using accuracy, sensitivity, specificity, precision, recall, F1-score, and Area Under the Receiver Operating Characteristic Curve (AUC). For interpretability evaluation, we compute attention map agreement with established AD biomarkers and report correlation with hippocampal volume measurements. Statistical significance is assessed using paired t-tests with $p<0.05$ considered significant.

IV. Results and Discussion

Classification Performance: Table 1a. presents the classification performance of TMSAN on the ADNI dataset compared with state-of-the-art methods. Our proposed model achieves an accuracy of 98.72% for AD vs. HC classification, outperforming BMSSnet (97.35%) , DuoViT-AD (98.56%) , and conventional ViT models (94.21%). For early detection of MCI converters vs. non-converters, TMSAN achieves 89.34% accuracy, representing a 4.2% improvement over BMSSnet and 6.8% improvement over standard ViT. The high sensitivity of 97.89% for AD detection and 88.67% for MCI conversion prediction demonstrates the model's effectiveness for early diagnosis.

Ablation Study: We conduct ablation experiments to evaluate the contribution of each architectural component. Removing the multi-scale patch strategy reduces accuracy to 95.43%, confirming the importance of capturing features at different spatial resolutions. Ablation of the cross-scale attention module results in a 2.1% accuracy drop, demonstrating the value of modeling interactions between local and global representations. The spatial gating unit contributes a 1.3% accuracy improvement while reducing computational cost by 12% compared to full self-attention. Notably, the multi-scale attention mechanism shows the greatest improvement for MCI conversion prediction (+4.8% accuracy), suggesting that fine-grained structural information is particularly important for early-stage detection.

Table 1a: Binary Classification Performance (AD vs. HC)

Method	Accuracy	Sensitivity	Specificity
3D-CNN	92.18%	91.23%	93.01%
ViT-base	94.21%	93.45%	94.89%
Swin-Transformer	95.67%	95.12%	96.11%

Method	Accuracy	Sensitivity	Specificity
BMSSnet	97.35%	96.89%	97.72%
DuoViT-AD	98.56%	98.12%	98.89%
TMSAN (Ours)	**98.72%**	**97.89%**	**99.12%**

Interpretability Analysis: Attention maps generated by TMSAN demonstrate strong alignment with established AD biomarkers. The model consistently assigns high attention weights to the hippocampus, entorhinal cortex, and medial temporal lobe regions, consistent with neuropathological findings in AD [12]. Quantitatively, attention weights show significant correlation with hippocampal volume measurements (r=0.78, p<0.001) and entorhinal cortex thickness (r=0.72, p<0.001). For MCI converters, attention patterns show elevated focus on hippocampal subfields compared to non-converters, suggesting that the model captures early neurodegenerative changes before widespread atrophy becomes apparent [3].

Comparison with Existing Methods: Our results demonstrate several advantages over existing approaches. Compared to CNN-based methods, TMSAN better captures long-range dependencies between brain regions, as evidenced by the attention analysis showing interactions between hippocampal and cortical regions. Compared to standard ViT models, the multi-scale strategy improves detection of subtle structural changes that might be missed with fixed patch sizes. The architecture's efficiency improvements through the spatial gating unit make it more suitable for clinical deployment without sacrificing accuracy.

Table 1b: Early Detection Performance (MCIc vs. MCInc)

Method	Accuracy	AUC
3D-CNN	78.45%	0.921
ViT-base	82.54%	0.948
Swin-Transformer	84.23%	0.962
BMSSnet	85.14%	0.979
DuoViT-AD	87.23%	0.985
TMSAN (Ours)	**89.34%**	**0.991**

Limitations: Despite strong performance, several limitations warrant consideration. The reliance on 3D MRI volumes requires substantial computational resources, limiting real-time deployment in resource-constrained settings. The model has been validated only on the ADNI dataset; generalizability to other acquisition protocols and populations requires further investigation. Additionally, while the model achieves excellent performance for AD vs. HC classification, early MCI conversion prediction remains challenging with significant inter-subject variability. Future work should explore integration with multimodal data including PET imaging and biomarkers to enhance early detection capabilities.

V. CONCLUSION

This paper presents a Transformer-based Multi-Scale Attention Network (TMSAN) for early Alzheimer's disease detection using structural MRI. The proposed architecture addresses the key limitation of current transformer-based methods, which primarily learn global representations while overlooking fine-grained structural abnormalities in clinically significant brain regions. Through a multi-scale patch tokenization strategy, cross-scale attention mechanism, and lightweight spatial gating unit, TMSAN simultaneously captures local anatomical features and global contextual representations.

Extensive evaluation on the ADNI dataset demonstrates that TMSAN achieves superior classification performance for both AD vs. HC classification (98.72% accuracy) and MCI conversion prediction (89.34% accuracy). Ablation studies confirm the contribution of each architectural component, with the multi-scale attention mechanism proving particularly valuable for early-stage detection. Interpretability analysis reveals strong alignment between attention maps and established AD biomarkers, including hippocampal atrophy and entorhinal cortex thinning, supporting the model's clinical relevance.

The proposed approach offers a promising direction for early AD diagnosis with enhanced sensitivity and

interpretability. By capturing subtle structural changes before widespread atrophy becomes apparent, TMSAN has the potential to enable earlier therapeutic intervention and improve patient outcomes. Future work will focus on multimodal integration and validation across diverse clinical datasets.

VI. Future Enhancement

Several directions for future enhancement are identified. First, integrating multimodal data including PET imaging, cerebrospinal fluid biomarkers, and genetic information could further improve early detection accuracy and provide complementary information about disease pathology . Second, investigating explainable AI techniques such as SHAP and LIME could enhance model interpretability and facilitate clinical adoption. Third, domain adaptation techniques could improve generalizability across different MRI acquisition protocols and patient populations, addressing the heterogeneity inherent in clinical neuroimaging data. Fourth, exploring transformer architectures with incorporated neuroanatomical priors, such as hippocampal-inspired spatial memory mechanisms, could further enhance the model's ability to capture disease-relevant structural patterns [7] . Fifth, developing efficient inference methods enabling real-time deployment in clinical settings would address computational resource limitations. Finally, prospective clinical validation studies are needed to assess the model's performance in real-world diagnostic workflows and its impact on patient care.

Conflict of interest statement

Authors declare that they do not have any conflict of interest.

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