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AN EVALUATION OF CNN AND GNN APPROACHES FOR ANALYSING THE DEVELOPING BRAIN

***[1]Ms.A. Kamatchi, [2]Dr. V. Maniraj**

[1]Research Scholar, Department of Computer Science, A.V.V.M.Sri Pushpam College(Autonomous),Poondi, Thanjavur (Dt),Affiliated to Bharathidasan University, Thiruchirappalli, Tamilnadu.

[2]Associate Professor, Research Supervisor, Head of the Department,Department of Computer Science, A.V.V.M. Sri Pushpam College(Autonomous),Poondi,Thanjavur(Dt),Affiliate to Bharathidasan University, Thiruchirappalli, Tamilnadu.

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***Corresponding Author: Ms. A. Kamatchi**
Research Scholar, Department of Computer Science, A.V.V.M.Sri Pushpam College(Autonomous),Poondi, Thanjavur (Dt),Affiliated to Bharathidasan University, Thiruchirappalli, Tamilnadu.

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ABSTRACT

In this work, we introduce a novel analysis framework for studying and comparing brain MRI data from non-standard animal models, such as sheep, without the use of predefined neuroanatomical priors. The proposed pipeline integrates automated MRI segmentation with graph neural networks (GNNs) to address the shortcomings of conventional approaches. Traditional neuroimaging methods typically rely on fixed anatomical atlases and struggle to generalize to developing brains or atypical species. By deriving regions of interest directly from MRI data and representing the brain as a graph, our method reduces template-induced bias and increases adaptability. Experimental results demonstrate that the GNN-based pipeline achieves higher accuracy in an age prediction task (63.22%) than a standard convolutional neural network (CNN) model (59.77%). In addition to improved performance, GNNs enhance model interpretability and effectively capture complex relationships between brain regions. These findings highlight the potential of the proposed framework as a flexible, unbiased, and interpretable solution for brain MRI analysis in developmental and non-conventional animal studies.

KEYWORDS: Graph, Machine Learning, MRI, Segmentation.

INTRODUCTION

Automated approaches have greatly advanced brain MRI analysis, particularly in human studies and widely used laboratory animals (Kaur and Gaba, 2021; Park and Friston, 2013). Nevertheless, equivalent tools remain scarce for investigations involving immature brains or less common animal models such as sheep. Consequently, brain structure delineation in these contexts often relies on manual annotation or automated segmentation driven by signal intensity and existing templates, when such resources exist (Nitzsche et al., 2015; Ella et al., 2017). These strategies are heavily reliant on prior anatomical knowledge and atlas quality, which may inadequately represent inter-individual variability or pathological alterations. The problem is further compounded in developing brains, where low tissue contrast, heterogeneous maturation, and incomplete structural visibility pose significant challenges (Li et al., 2019). Moreover, the use of predefined anatomical regions can restrict exploratory analyses and hinder the identification of previously unrecognized brain features associated with disease.

In this study, we introduce a processing framework designed to mitigate both segmentation-related biases and the inherent limitations of convolutional neural networks. Our approach constructs regions of interest (ROIs) without the use of predefined neuroanatomical information. Specifically, voxel intensity–based information is leveraged to produce segmented images using two distinct segmentation techniques. Furthermore, we employ graph neural networks (GNNs) to detect and analyse anatomical patterns by representing the brain as a network of interconnected patches, thereby enabling the modeling of complex inter-regional relationships (Cui et al., 2021; Li et al., 2021; Ravinder et al., 2023). By eliminating dependence on anatomical atlases, this strategy supports a more adaptable, data-driven investigation of brain organization.

RELATED WORKS

2.1 CLASSICAL APPROACHES USED ON BRAIN MRI

The literature primarily focuses on two major objectives: image or brain segmentation (Coupeau et al., 2022) and image or brain classification (Srinivasan et al., 2024; Kaur and Gaba, 2021; Poriya, 2023). In both contexts, machine learning methods particularly convolutional neural networks (CNNs) and graph convolutional networks (GCNs) offer robust frameworks capable of automatically learning the most informative features. Regardless of whether CNNs or GNNs are employed, several essential steps are required, including image pre-processing and patch extraction. MRI pre-processing procedures such as denoising and intensity normalization aim to standardize voxel intensity distributions and improve comparability across datasets. Images are typically resampled to achieve uniform voxel resolution, and registration may be applied to align scans within a common anatomical space, often using a reference template. In addition, non-brain structures such as the skull and scalp are removed through cropping and skull-stripping to isolate brain tissue for subsequent analysis.

2.1.1. SEGMENTATION

The purpose of segmentation is to define and label anatomical regions of interest (ROIs) within brain MRI scans, with the resulting segmented images serving as the basis for constructing graph-based representations. This process can be carried out through manual annotation or by using atlas-based methods derived from individual brain images or standardized templates (Van Essen and Drury, 1997; Yang et al., 2020; Fil et al., 2021). Such approaches enable the identification and delineation of multiple brain regions and structures, and they also provide reference frameworks for registering individual MRI scans into a shared spatial coordinate system. This alignment supports consistent and reliable comparisons across subjects.

2.1.2.CNN DESIGN

A convolutional neural network (CNN) is generally composed of stacked layers such as convolutional, pooling, and fully connected layers. The adoption of sophisticated CNN architectures, including AlexNet (Krizhevsky et al., 2012) and ResNet (He et al., 2016), has substantially improved the ability to capture complex image features and achieve strong performance across a range of MRI analysis tasks, such as classification and clustering. The integration of biological knowledge through the use of brain atlases can further enhance these approaches by increasing robustness, accuracy, and reproducibility in MRI studies. In the specific context of brain age estimation, multiple CNN-based models have been introduced, notably VGG, ResNet, and DenseNet architectures (Cole et al., 2017; Jiang et al., 2020). More recent developments incorporate attention mechanisms to strengthen feature representation and further improve predictive accuracy (Lam et al., 2020; Cheng et al., 2021).

2.1.3.GRAPH DESIGN

In graph-based brain representations, nodes are most often defined at the regional scale, with each node corresponding to a specific brain area. The choice of regions depends strongly on the objectives of the study and may represent elements ranging from individual neurons and voxels to broader anatomical structures or tissue types. From an anatomical perspective, node attributes can encode spatial information such as centroid coordinates and orientation, as well as morphological characteristics including volume and shape metrics. Signal intensity–based features are also commonly used to describe tissue composition. In addition, graph-theoretical measures, such as centrality or node strength, can be incorporated to further characterize regional importance. Edges can be constructed in multiple ways and parameterized according to the study's goals, with three main categories typically considered: structural, functional, and effective connectivity (Fedorov et al., 2012). Edge attributes may include measures such as Euclidean distance, tract length, or connection cost (Bullmore and Bassett, 2011; Sporns, 2018). Defining edges is often the most challenging step in building brain networks. While fully connected graphs are possible, achieving an interpretable and computationally efficient representation generally requires reducing edge density to retain only meaningful connections. This is commonly done by applying thresholds to eliminate weak or irrelevant edges, although determining appropriate thresholding strategies whether statistical, expert-driven, or customized remains an open research problem.

2.1.4. GNN DESIGN

After representing the brain as a graph, graph neural networks (GNNs) are applied to learn from these structures and to model complex interactions and variability in brain organization (Li et al., 2021; Ravinder et al., 2023; Srinivasan et al., 2024; Coupe au et al., 2022). In the context of brain age estimation, GNN-based models have been introduced to more effectively leverage inter-regional dependencies, such as architectures that analyze diffusion MRI based connectivity while accounting for the local topology of brain networks (Sporns, 2007). More advanced approaches, including multi-hop graph attention mechanisms and graph Transformer models, typically depend on well-defined graph structures, such as tractography-derived networks, or on the alignment of multi-modal imaging data to a common reference space using standardized brain templates (Lim et al., 2024; Cai et al., 2023).

2.2. APPROACHES FOR BRAIN IN DEVELOPMENT AND NON-CONVENTIONAL ANIMAL MODEL

Analyzing developing brains or brains from non-traditional animal models presents a number of challenges that differ substantially from those encountered in adult human neuroimaging studies. Key difficulties include pronounced anatomical variability, the absence of standardized atlases and analysis tools, and the frequent limitation of small sample sizes. In many non-conventional animal models, brain segmentation is still performed manually—a labor-intensive process that requires specialized neuroanatomical knowledge and is prone to significant operator-dependent bias due to inter-observer variability (Fedorov et al., 2012). Atlas-based registration offers an alternative approach, whereby a representative template is constructed by aligning and normalizing multiple MRI scans into a shared space using affine transformations. The template is then segmented and the resulting labels are propagated back to individual scans (De Vico Fallani et al., 2017). Although this strategy facilitates the simultaneous processing of large datasets, additional post-processing steps are often necessary to ensure accurate alignment with individual anatomical features. More recently, automatic and incremental segmentation methods incorporating biological priors have been proposed as complementary solutions (Galisot et al., 2022).

3.THE PROPOSED PIPELINE

3.1. FROM 3D MR IMEGES TO GRAPHS

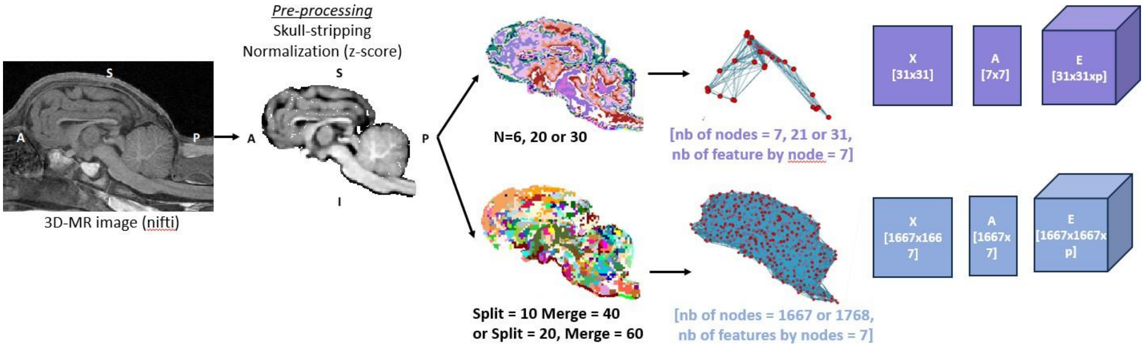
We introduce a general-purpose framework for converting 3D brain MR images from developing brains and non-conventional animal models into graph representations. The goal of this approach is to construct graphs that retain as much relevant information as possible from the original images, allowing the graph neural network to autonomously identify and exploit the most informative features during learning.

3.2. PREPROCESSING

The pre-processing stage consists of skull stripping and z-score intensity normalization. Z-score normalization is commonly preferred in brain MRI studies, especially for machine learning applications, as it preserves the relative alignment of intensity distributions corresponding to white matter, grey matter, and cerebrospinal fluid (Schmid, 2023). Following pre-processing, graph construction proceeds in two main steps: the definition of nodes and the establishment of edges.

3.3. NODES AND EDGES CREATION

Node creation is based on the segmentation of regions of interest (ROIs) (Figure 2). To analyze developing brains of non-conventional animal models, we employ a segmentation strategy that does not rely on biological priors, treating the MRI data purely as conventional images rather than pre-labeled brain structures. For this study, we tested two approaches: a histogram-based clustering algorithm and a “split and merge” algorithm. The histogram-based method divides the intensity range into N equal segments, with the challenge being the selection of optimal parameters depending on the study goals and the desired level of detail. This approach is illustrated in Image 1. The second method, the “split and merge” algorithm (Gonzalez and Woods, 2017), functions in two phases. During the split phase, the image is recursively divided into smaller, more homogeneous regions (“cubes”) according to a user-defined homogeneity criterion and a minimum region size, where homogeneity is measured by the intensity range within the region. In the subsequent merge phase, adjacent regions are combined if their union satisfies a separate homogeneity criterion.



3.4.GRAPH ANALYSIS AND CLASSIFICATION

As previously noted, graph neural networks (GNNs) are particularly effective for analyzing brain MRI data because they can capture complex relationships between distinct brain ROIs. Unlike convolutional neural networks, which primarily extract features from local voxel neighborhoods, GNNs operate at a higher organizational level, where nodes correspond to brain regions or subregions and edges represent the connections between them. This relational modeling enables predictions that are often both more accurate and easier to interpret. In our experiments, the proposed GNN architecture leverages these strengths to estimate the age of sheep brains by framing the problem as a graph classification task across K discrete age categories.

3.4.1.GRAPH CONVOLUTION LAYERS

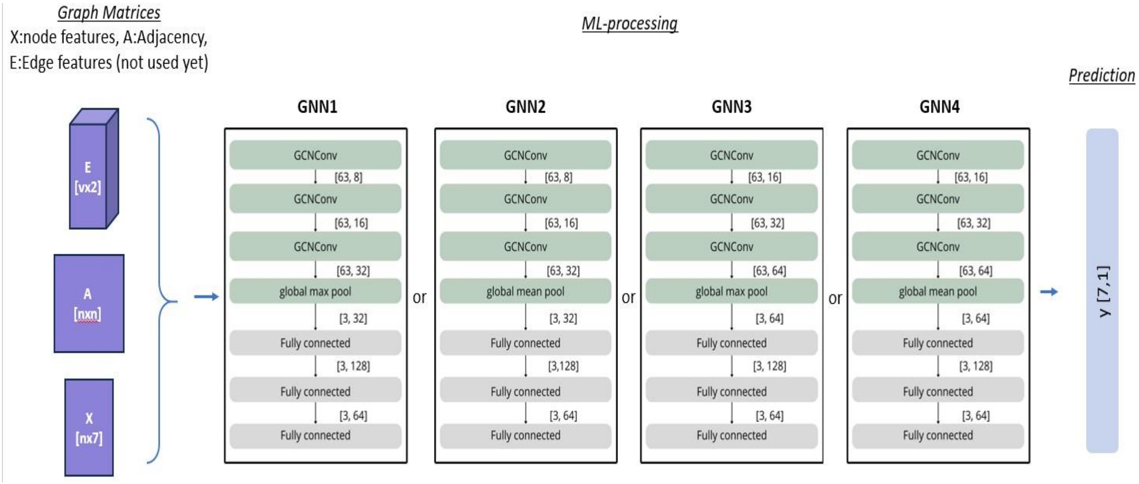
To enable information flow across the graph, we employ a sequence of three graph convolutional layers. Although many convolutional architectures are available, our dataset is relatively limited, containing around 200 graphs. Therefore, implementing a highly complex network with large or intricate layers would be unsuitable and could lead to overfitting.

- **First set of parameters**: The model begins by transforming the 7 initial features into 8 features using the first GCNConv layer. This output is then passed to a second GCNConv layer, which further transforms it to 16 features. Finally, a third GCNConv layer transforms the features to 32 dimensions. Each layer applies a learned linear transformation followed by an activation function (ReLU in our case), enabling the network to progressively capture complex patterns in the data.

- **Second set of parameters**: Instead of incremental changes, the model starts with 7 features and dou- bles the number of dimensions at each layer: from 7 to 16, then to 32, and finally to 64. This more aggressive dimensionality increase aims to test the model's ability to learn richer representations.

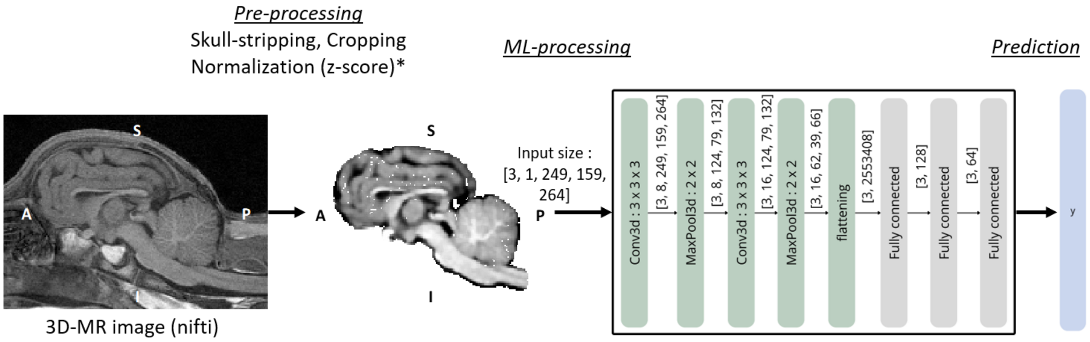
3.4.2. POOLING AND FULLY CONNECTED LAYERS

A global mean pooling and a global max pooling were tested to capture interesting information while taking into account the small amount of data. The pooled features are then passed through three fully connected (FC) layers (fc1, fc2 and fc3) to per- form the classification



4. EXPERIMENTS AND RESULTS

We performed a series of experiments testing various CNN and GNN architectures to determine which models are most effective for predicting the age of brains from non-conventional animal models, such as sheep. The experiments were carried out on a system with an Intel Core i7-11850H CPU at 2.50 GHz, 32 GB of RAM, and an NVIDIA GeForce RTX A3000 Laptop GPU. All analyses and computations were implemented using Python.



5. CONCLUSION AND PERSPECTIVES

In this study, we propose a novel pipeline to predict the brain age of nonconventional animal models without relying on neuro-anatomical pri- ors to not bias the analysis. We provide an open access generic graph generation tool from 3D images available at this URL: https://scm.univ- tours.fr/projetspublics/lifat/3dbrainminer. Our pro- posed GNN pipeline provides better results in terms of accuracy than a traditional CNN pipeline. The process starts with automatic MRI segmentation, fol- lowed by graph transformation and analysed using a GNN model. We compared 2 segmentation algo- rithms with different parameters and GNN architec- tures.

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