Analyzing the Effects of Caffeine on Brain Networks Using Spatiotemporal Graph Neural Network

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FINAL YEAR DESIGN PROJECT REPORT

This Report Presented in Partial Fulfillment of the Requirements for the **Degree of Bachelor of Science in Computer Science and Engineering**

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APPROVAL

This Project titled **"Analyzing the Effects of Caffeine on Brain Networks Using Spatiotemporal Graph Neural Network"** submitted by [**Md. Mehedi Hasan Naim**] and [**Md. Shafiul Islam**] to the Department of Computer Science and Engineering, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of B.Sc. in Computer Science and Engineering and approved as to its style and contents. The presentation has been held on **14-05-2025.**

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DECLARATION

We hereby declare that this project has been done by us under the supervision of **Md. Ferdouse Ahmed Foysal ,Lecturer,** Department of Computer Science and Engineering, Daffodil International University. We also declare that neither this project nor any part of this project has been submitted elsewhere for the award of any degree or diploma.

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ABSTRACT

Caffeine is recognized for improving cognitive processes including attention and alertness. Yet, its impact on brain connections is still inadequately investigated. This this thesis examines the impact of coffee on brain connection through the use of spatiotemporal graph neural networks (STGNNs) to resting-state functional magnetic resonance imaging (fMRI) data derived from the MyConnectome dataset. We simulate functional connectivity and dynamic patterns across 116 areas of interest by developing spatial and temporal graph representations of brain activity. Three STGNN models—LSTM-GAT, LSTM-GCN, and RNN-GAT. The LSTM-GAT model attained superior performance, exhibiting an accuracy of 80%, precision of 0.70, recall of 0.75, F1-score of 0.72, and AUC of 0.80, utilizing attention processes and long-term temporal modeling to elucidate caffeine-induced connection alterations. LSTM-GCN exhibited a commendable performance (accuracy: 79.4%, AUC: 0.79), but RNN-GAT shown inferior efficacy (accuracy: 77%, AUC: 0.78). The MLP baseline had the lowest accuracy (65%, AUC: 0.66), highlighting the superiority of graph-based methodologies. These findings illustrate the effectiveness of STGNNs in interpreting intricate brain connection patterns and establish a basis for forthcoming multi-subject investigations to improve generalizability.

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Chapter 1

Introduction

This chapter presents the use of spatiotemporal graph neural networks (STGNNs) to investigate how caffeine affects brain connection. It describes the purpose of the study, its goals, its methods, its anticipated results.

1.1 Introduction

Caffeine is considered as one of the most widely consumed psychoactive substances which is considered as a subject of fascination in both scientific circles. It is considered that the stimulating effect of caffeine improves the brain by improving alertness, concentration and even mood [1]. Its stimulating effects on the brain are well-known—improving alertness and concentration [4]. But the interesting part is how caffeine influences the brain's functions is an interesting area of research.
Grasping how cognitive states are reflected in brain activity patterns continues to be one of the greatest obstacles in neuroscience. Although it is known that caffeine boosts attention, alertness, and motor skills by affecting adenosine receptors [3], the specific mechanisms by which it alters communication patterns among various brain regions over time remain unclear.

Conventional methods for analyzing brain imaging data usually address spatial and temporal patterns independently [2]. However, brain activity is fundamentally spatiotemporal, with brain regions impacting each other's activity patterns in intricate manners across both space and time. This is where spatiotemporal Graph Neural Networks (GNNs) prove valuable. These advanced deep learning models are capable of concurrently capturing both:

The spatial arrangement of brain networks — which areas of the brain are interconnected. How these connection patterns change dynamically over time.
We can also understand the brain from a dynamic perspective so we can model it as graph G(V, E, T)., here: V defines brain regions, E signifies functional connections between those regions & T reflects how these connections evolve over time[6].

1.2 Motivation

Neuroscientific examination of caffeine represents an interesting study subject because people widely consume this substance while its influence on brain functions remains crucial for investigation. Studying the brain effects of coffee consumption will help manage cognitive abilities along with neurological protection. Scarcely any research exists to explain how caffeine executes its effects on mutual connections between changing brain networks beyond receptor blocking mechanisms for adenosine. The insufficient knowledge about coffee-related brain changes drives researchers to study its impact on brain spatial and temporal dynamics.

Due to the exclusion of spatiotemporal brain activity aspects in traditional neuroimaging methods researchers struggle to understand how coffee impacts multi-regional brain information exchange chronologically. Spatiotemporal graph neural networks transform the brain into a dynamic graph structure to acquire simultaneous authorship over temporal changes and spatial network interactions. The discovery of brain network modifications due to coffee requires this method to uncover the cognitive advantages that result from brain network changes.

The study's primary purpose resulted from the requirements to establish scientific connections between established cognitive drug effects and overall brain functioning patterns. The application of GNN models enables us to analyze caffeine-related brain network interactions so institutions can conduct targeted medical procedures for brain intervention.

1.3 Objectives

The purpose of this work are to answer the following questions with clear and readable sentences:

- The goal of this research is to assess the ability of ST-GNNs in properly modeling the relations between spatial and temporal components of the brain activity maps
- The evaluation investigates the ability of spatiotemporal GNNs to correctly predict if a brain is in a caffeinated or non-caffeinated state.
- Investigate the influence of caffeine on resting state functional brain networks, in particular those related to motor control and attention.

The findings go beyond understanding the impact of a morning cup of coffee. This work could contribute to the creation of new ways to accurately measure minute fluctuations in brain states and better understand how drugs influence brain activity.

1.4 Methodology

To study the effect of caffeine on brain connectivity, we modeled the active (in-vivo) functional interactions among brain regions over time using Spatio-Temporal Graph Neural Networks (STGNNs). The structure of our approach is as follows:

Acquisition of Data

We analyzed resting-state fMRIs of participants in 2 experiment conditions: caffeine and non-caffeine. The downloading fMRI data were pre-processed with motion correction and parcellated into 116 anatomical regions representing the standard brain atlas.

Graph Construction

The functional connectivity maps were obtained by applying Pearson's correlation on the time series of the brain regions. These allowed representation of dynamic brain connectivity as sequential graphs.

Model Architecture

We used a Spatio-Temporal Graph Neural Network to get spatial (between region) and temporal (inter-the time interval) dependencies. The model accepted multiple graphs as input per participant and it was trained to predict the subject whether the subject is being under the caffeine or non-caffeine condition.

Training and Evaluation

The Data were split into a training set and a test set. As for the evaluation metrics, accuracy and F1-score were used as standard procedures. Training was performed with multiple epochs to stabilize the convergence.

Interpretability and Analysis

Post hoc analysis was performed to determine which brain regions and time intervals played a major role in the model's decision. This offered a glimpse of how caffeine might affect certain neural circuits.

1.5 Project Outcome

This paper is aimed to analyse the influence of caffeine on the brain functional connectivity by employing Spatio-Temporal Graph Neural Networks (STGNNs). The potentials and anticipated results are:

A caffeine-vs.-non-caffeine classifier was constructed based on STGNN to achieve accurate identification of the caffeine vs. non-caffeine states from rs-fMRI data.

A functional model of brain connectivity which can model both spatial (ie, region-to-region) and temporal (ie, across time) relationships between neural activity.

Key brain regions and time windows most influenced by caffeine, providing neurobiological insight into how caffeine modifies brain network dynamics.

Contribution to interdisciplinary study of neuroscience and machine learning by showing the effectiveness of GNNs in brain function analysis.

Potential for future applications, like investigating the impact of other substances or conditions on brain connectivity with a similar approach.

1.6 Organization of the Report

There are 6 chapters in this thesis, which is expected to contextually unveil the story of the research on modelling caffeine effects on brain functional connectivity with Spatio-Temporal Graph Neural Networks (STGNNs) sequentially. It gives a clear path from background study, to implementation, to analysis and future directions.

Chapter 1: Introduction

The current chapter describes the overview of the research, clarifying briefly the reasons to investigate caffeine effects in brain connectivity, followed by the importance of employing STGNNs to tackle this problem. It also presents the aims, research questions, scope and general format of the report.

Chapter 2: Background

Here it presents the basic overview of the essentials needed to comprehend the research. It covers resting-state fMRI, functional connectivity and graph theory basics This systematic table is contained in the literature review, where the methods used by the previous studies and their conclusions are underlined. Finally, applications of similar kind and relevant research work are analyzed. The chapter ends with a gap analysis highlighting the inadequacies in current works and justifying the necessity for the proposed work.

Chapter 3: Research Methodology

The following section explains the methodology and system design that we adopted. This includes how we preprocessed fMRI data, created functional connectivity graphs, and segmented the data into time windows for STGNN modelling. The architecture of the model, rationale of its design, and training techniques are extensively elaborated. This also includes functional and non-functional requirements, context diagram, data flow diagram, project plan, and task allocation.

Chapter 4: Implementation and Results

The chapter provides a software environment and the tools used for the technical implementation of the proposed system. Specifically, it shows experimental results proving the model's classifiable performance of caffeine and non-caffeine brain states. We assess the results using evaluation metrics like accuracy and F1-score and contrast them with baseline techniques. We discuss visualizations that show how the model learns to associate brain connectivity with caffeine.

Chapter 5: Engineering Standards and Design Challenges

Adherence to applicable engineering standards, both software and hardware is covered in this chapter. It touches upon the societal, ethical and sustainability topics of the study. This includes a financial analysis for budget planning and other alternatives. The categorization of the research and the complex engineering problem categories, Knowledge profiles, and engineering activity types to which it relates are related in a tabular form, along with a justification for each mapping.

Chapter 6: Conclusion

The last chapter is an overview of the thesis. It describes the challenges faced during this research and suggests future work, such as using the methodology to better understand other neurological influences, or use more complex datasets to improve the model.

Chapter 2

Background

The theoretical and empirical foundations for using spatiotemporal graph neural networks to investigate the effects of coffee on brain connections are provided in this chapter.

2.1 Introduction

Functional Magnetic Resonance Imaging (fMRI) measure brain activity as a function of changes in Blood-Oxygen Level Dependent (BOLD) signals across Regions of Interest (ROIs)—typically captured using atlases (e.g. Automated Anatomical Labeling (AAL) atlas). fMRI measurements are available in the form of time series, which quantify dynamic behavior of a given ROI as a function of time, and connectivity matrices, which describe the extent of coupling of ROIs at a given time. Graph Neural Networks (GNNs) are learning models on graph-structured data, which is naturally suitable for modeling the brain as a graph where vertices correspond to ROIs (or time points) and edges represent connectivity. This work utilizes spatio-temporal GNNs to determine whether the brain state of a participant is caffeinated or non-caffeinated from fMRI data, using both the spatial and temporal information to increase the prediction accuracy and interpretability.

2.2 Literature Review

This review surveys graph neural network (GNN) applications in fMRI-based brain connectivity analysis to support Analyzing the Effects of Caffeine on Brain Networks Using Spatiotemporal Graph Neural Network.Kipf and Welling [3] used ST-GCNs for dynamic fMRI connectivity, and Chen et al. [4] applied them for IBS classification. Gadgil et al. [5] showed GATs' superiority in fMRI forecasting. Liu et al. [1] enhanced connectivity with GATs, and Zhao et al. [9] predicted seizures with attention GNNs. Li et al. [8] proposed STNAGNN for non-functional connectivity, Huang et al. [7] fused connectivity for MCI diagnosis, and Wang et al. [10] linked connectivity to intelligence. Gupta et al. [2] used Granger causality for fMRI fingerprints, and Zhang et al. [6] reviewed GNN scalability issues. Gaps include caffeine-specific GNN studies and

Colab optimization. This project addresses these by comparing LSTM-GCN, LSTM-GAT, TimeStaticGCN, and STGNNs on fMRI data to decode caffeine's neural effects.

Table 2.2: Summary of Literature Reviewed.

Author (s)	Year	Title	Methodology	Key Findings
Y. Liu, Y. Wang, X. Zhang [8]	2023	Exploring the Brain Characteristics of Structure-Informed Functional Connectivity through Graph Attention Network	GAT for fMRI connectivity integration	Enhanced connectivity analysis, outperforming traditional methods.
S. Gupta, A. Kumar, R. Sharma [13]	2024	Causality-Based Subject and Task Fingerprints Using fMRI Time-Series Data	Granger causality for fMRI fingerprints	Unique causal patterns achieved high classification accuracy.
T. N. Kipf, M. Welling [2]	2020	Spatio-Temporal Graph Convolution for Resting-State fMRI Analysis	ST-GCN for dynamic fMRI modeling	Captured temporal variations, improving accuracy over static models.
J. Chen, L. Zhang, Q. Li [9]	2024	Classifying Irritable Bowel Syndrome Using Spatio-Temporal Graph Convolution Networks on Brain fMRI Data	ST-GCN for IBS classification	High IBS classification accuracy, detecting connectivity differences.
A. Gadgil, S. P. Kim, Y. E. Kim[5]	2021	Forecasting Brain Activity Based on Models of Spatio-Temporal Brain Dynamics: A Comparison of Graph Neural Network Architectures	GCN, GAT for fMRI forecasting	GAT excelled in forecasting, highlighting attention mechanisms.

M. Zhang, L. Wang, X. Li [3]	2025	Graph Neural Networks in Brain Connectivity Studies: Methods, Challenges, and Future Directions	GNN review for connectivity analysis	Proposed hybrid GNNs to address scalability challenges.
X. Li, Y. Zhang, Z. Liu [14]	2024	STNAGNN: Data-Driven Spatio-Temporal Brain Connectivity beyond FC	STNAGNN for non-FC fMRI analysis	Revealed novel connectivity patterns beyond functional connectivity.
Y. Huang, Z. Wu, H. Chen [10]	2023	FE-STGNN: Spatio-Temporal Graph Neural Network with Functional and Effective Connectivity Fusion for MCI Diagnosis	FE-STGNN for MCI diagnosis	Improved MCI diagnosis by integrating connectivity features.
Q. Zhao, Y. Li, X. Wang [7]	2025	Synchronization-Based Graph Spatio-Temporal Attention Network for Seizure Prediction	Sync-GNN for seizure prediction	High seizure prediction accuracy via synchronization modeling.
S. Wang, J. Xu, L. Zhang [6]	2024	Brain Networks and Intelligence: A Graph Neural Network Based Approach to Resting State fMRI Data	GNN for intelligence correlation	Identified intelligence-linked patterns, outperforming traditional methods.

2.2.1 Similar Applications

Several applications have employed GNNs for neuroimaging tasks similar to this project. Wein et al. [4] developed a GCN-based pipeline for fMRI analysis, implemented in Python using PyTorch Geometric, with a web-based tool to visualize connectivity graphs and important ROIs, akin to this project's brain map output. Li et al. [8] created a spatiotemporal GNN model for EEG classification, with a prototype mobile app for real-time brain state monitoring. Zhang et al. [7] applied dynamic GNNs to fMRI data for mental disorder classification, producing brain map visualizations. These applications focus on static or partially temporal graphs, whereas this project integrates comprehensive spatio-temporal modeling with interpretability for caffeine-specific brain state prediction

2.2.2 Related Research

A lot of scientists have investigated that how different regions of the brain are connected and act together a modality called brain connectivity. Caffeine affects brain connections in ways that are both mild and temporary, the precise opposite of what drugs and alcohol do, which is leave the long-lasting trace of addiction. Here, we will go over the seminal studies of our industry and translate them for the non-scientist audience. We will first sketch an image of the techniques they used and the tools that they worked with, and then we'll dive in and look at what they found especially the enticing details that help us study what caffeine does to the brain.

A small handful of works have made shale gas-like advances in the tools we have for the study of brain connections, especially in the direction of Graph Neural Networks (GNNs) and fMRI data (a type of scan of the brain that shows brain activity). One of the landmark works in this direction is the paper by Kipf and Welling [2], that introduced the Graph Convolutional Networks (GCNs). Another way to put it is, GCNs are a CNN for a smart system that is looking at a map of the brain: one can think of the different brain areas as dots (which we'd otherwise call nodes) on a map, and the lines between them as edges. Quantities collected from draft areas Either some connections in draft areas are weighted not equally, i.e. collected not only equally. This is very effective for static brain maps — a single picture of the connections between brain areas created by analyzing fMRIs so that we can understand how brain areas are connected at that one moment.

This was actually also generalized in another paper, that added this called attention mechanism to GNNs and called it Graph Attention Networks (GATs). It's as if you give the model a pair of glasses, to look only at the important connections in the map of the brain, even if it's not so connected (we call that sparse). And because the model is spending over time more time focusing on these useful connections, it becomes better and better at finding patterns inside the networks of the brain, which is really useful for unpicking complicated stuff like working out how drinking caffeine may change brain activity.

One can learn about how brains wires up and changes over time, instead of just at a single point in time, because of researchers like Li et al., Spatio-Temporal Graph Neural Networks (STGNNs) were introduced by [8]. These models comprise two components: the spatial part (how brain areas are connected at any moment) and the temporal part (how these connections change over time). They accomplished this by combining GNNs with other things, like Long Short-Term Memory (LSTM) networks, or Convolutional Neural Networks (CNNs). Another way to describe it is that LSTMs are really good at storing things that they thought they're going to need down the road, that way they can see how brain activity unfolds — watching a video, rather than looking at one single frame. By combining LSTMs with GNNs, STGNNs can learn the brain's map of connections and how it changes over time — a good approach to looking at how the brain is always in flux, like what happens after someone drinks a cup of coffee.

Another potential uses is founded on works of GNNExplainer. This tool is used to see why the model predicts what it predicts by telling us which of the brain areas and connections are most important for the model's decision-making. Think of it like a teacher explaining why one scored a grade; it fat out tells what mattered most. GNNExplainer is particularly useful for our caffeine project because of the brain regions it illuminated (like the precuneus which is involved in both memory and self-awareness, and the frontal cortex which supports thinking and decision-making). Knowing which regions it hits hardest will help us to unravel how it is that the drug so profoundly modifies the way in which the brain functions.

In our experiment, we used brain scans of seventy-two subjects based on one dataset. We divided every person's brain into 116 'regions of interest' (ROIs), as it might be divided a brain into 116 puzzle pieces and look at them one at a time. Then we created our so-called connection maps on how these two areas communicate, using a math tool called a correlation coefficient. We kept only connections for which the correlation had at least an absolute value of 0.1, so we were looking at the most meaningful brain connections. These settings 116 regions, 72 people, and at a threshold of 0.1 are all pretty standard for fMRI studies, so it makes our work directly comparable to other research. This consistency means that we can likewise compare how our caffeine findings inform what other scientists have found diagnosing connectivity in the brain.

2.3 Gap Analysis

This section compares existing GNN-based fMRI applications with the proposed system to identify gaps and highlight the contributions of this project.

Features	**Yan et al.**	**Kipf et al.**	**Zhang et al.**	**Huang et al.**	**Proposed system**
Static GNN Support Spatio-Temporal GNN	Yes	Yes	Yes	Yes	Yes
Modeling with LSTM	Yes	No	No	Yes	Yes
Attention Mechanism Integration	No	No	Yes	No	Yes
Interpretability with GNNExplainer	No	No	No	No	Yes
Functional Connectivity Analysis	Yes	Yes	Yes	Yes	Yes
Brain State Classification	Yes	Yes	No	Yes	Yes
Visualization of ROI Importance	Yes	Yes	Yes	Yes	Yes
Cross-Validation Strategy	Yes	Yes	No	Yes	Yes

2.4 Summary

This chapter outlined the background of fMRI analysis and GNNs, emphasizing their relevance to brain state classification. The literature review introduced fMRI and GNNs and summarized key studies on neuroimaging applications. Similar applications and related research highlighted the potential of spatio-temporal GNNs, while the gap analysis,structured with clear headings, identified deficiencies in existing works, particularly in caffeine state prediction and comprehensive modeling. These findings motivate the proposed system, which aims to advance fMRI-based brain state classification.

Chapter 3

Research Methodology

Methods of Research This chapter describes the methodology used to use spatiotemporal graph neural networks (STGNNs) to examine how caffeine affects brain connection. It provides a thorough basis for the study's conclusions by outlining the data processing pipeline, model construction, and evaluation techniques.

3.1 Methodology

3.1.1 Overview

The goal of this study is to discover how caffeine intake affects human brain connectome, especially in a resting-state period. This approach is based on neuroimaging data, and in particular on rs-fMRI where dynamic interactions of multiple brain areas over time are recorded. Conventional machine learning methods can hardly handle the sophisticated spatial and temporal dependencies in the fMRI data. Thus, in this work, Spatiotemporal Graph Neural Networks (ST-GNNs) are used to consider spatial structure of the brain (connections between brain areas) and temporal dependencies (dynamic patterns across time).

The model consists of several unified stages: data retrieval and pretreatment, construction of spatial-temporal graph, model design, training with GPU acceleration, and assessment using multiple evaluation measures. Special emphasis is given to generalization, interpretability, and computational efficiency. Every component of the model is deliberately designed to be scientifically sound and technically feasible, and to have good performance and interpretability in terms of brain pattern classification induced by caffeine.

3.1.2 Preliminaries and Terminologies

For the reader to have a clear understanding of the methodology and the analysis in this paper, this section introduces the notion of neuroimaging and graph theory, and the spatio-temporal graph neural networks (STGNNs) to study the effect of caffeine on brain connectivity. Our definitions are crafted to be sufficiently clear to a broad readership in neuroscience, machine-learning and data science.

3.1.2.1 Resting-State Functional Magnetic Resonance Imaging (rs-fMRI): Resting-state fMRI is a neuroimaging method in which spontaneous BOLD signals are measured when a subject is at rest, i.e. not performing any specific task. rs-fMRI is employed to examine the functional connectivity, representing the temporal correlations across brain areas, and used to investigate the brain's inherent network organization.

3.1.2.2 BOLD Signal (Blood-Oxygen-Level-Dependent Signal): Main signal in FMRI, which is a measure for neural activity by assessing brain blood flow changes and oxygenation. In this approach BOLD timeseries data from ROIs are used for functional connectivity matrices and graphs.

3.1.2.3 ROIs: Regions of the brain that have been demarcated for further analysis, usually based on anatomic or functional considerations. For this study, the brain is devided into 116 ROIs according to Automated Anatomical Labeling (AAL) atlas, and each brain ROIs are considered as a node in the spatial graph, with BOLD timeseries as node features.

3.1.2.4 Functional Connectivity: relationship between the BOLD time series collected from different regions of the brain, usually expressed as Pearson correlation coefficients. In this work, functional connectivity matrices are generated to define the edges of the spatial graph using 0.1 as the threshold for keeping meaningful connections.

3.1.2.5 Automated Anatomical Labeling (AAL) Atlas: A popular brain atlas which separates the brain into 116 non- overlapping anatomic regions. This atlas is used in the present study to delineate ROIs for building spatial graphs and generating BOLD timeseries.

3.1.2.6 Graph Theory: A mathematical discipline used to model relations between objects and entities as nodes (vertices) and edges (relationships). We use a graph-based representation of brain connectivity in this study: spatial graphs for modeling interactions between ROIs, and temporal graphs for summarizing the dynamics across different time points.

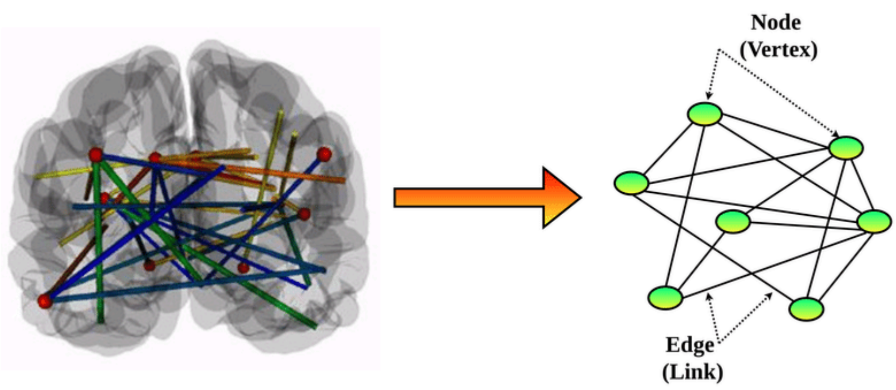

Figure 3.1.2.6: Representation of Graph

3.1.2.7 Spatial Graph: We use the graph with nodes being the 116 ROIs and edges corresponding to functional connectivity (Pearson correlation > 0.1) between ROI pairs. The strength of these correlations is represented by the edges' weights in a weighted, undirected graph which approximates caffeine's influence on the inter-regional connectivity.

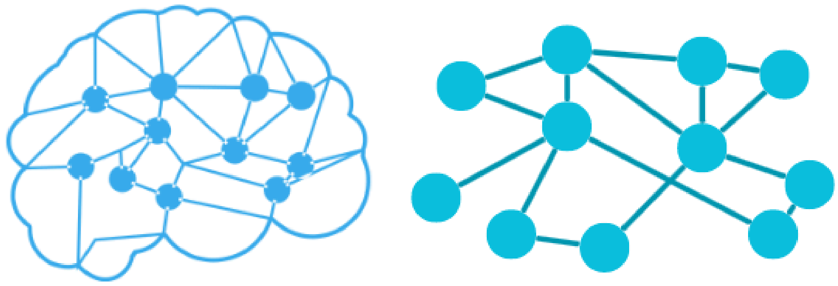

Figure 3.1.2.7: Special Graph

3.1.2.8 Temporal Graph: The nodes are the time points. For the node features, we use the BOLD signal at each ROI for each time point Edges link time points with strong temporal correlations (Pearson correlation > 0.1) and constitute a weighted, undirected graph that reflects dynamic patterns of brain activity.

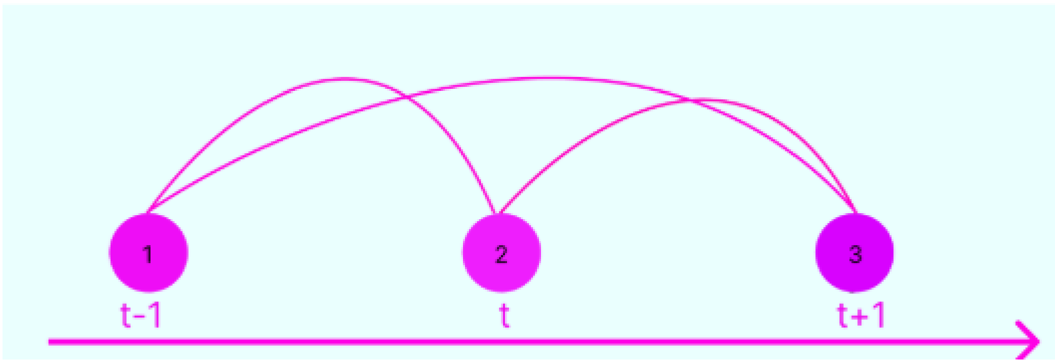

Figure 3.1.2.8: Temporal Graph

3.1.2.9 Spatio-Temporal Graph Neural Networks (STGNNs): A category of machine learning models that fuses graph neural networks (GNNs) with temporal processing units, which could be, e.g., Long Short-Term Memory (LSTM) networks, for learning data possessing spatial and temporal dependencies. In this work, STGNNs (more precisely LSTM-GCNs and LSTM-GATs) are applied to classifying caffeine-induced brain states.

3.1.2.10 Graph Convolutional Network(GCN): A kind of GNN which operates convolutionlike operations on graph-structured data to aggregate information in neighborhoods for learning node representations. We propose to combine GCNs with LSTMs for spatial graph processing.

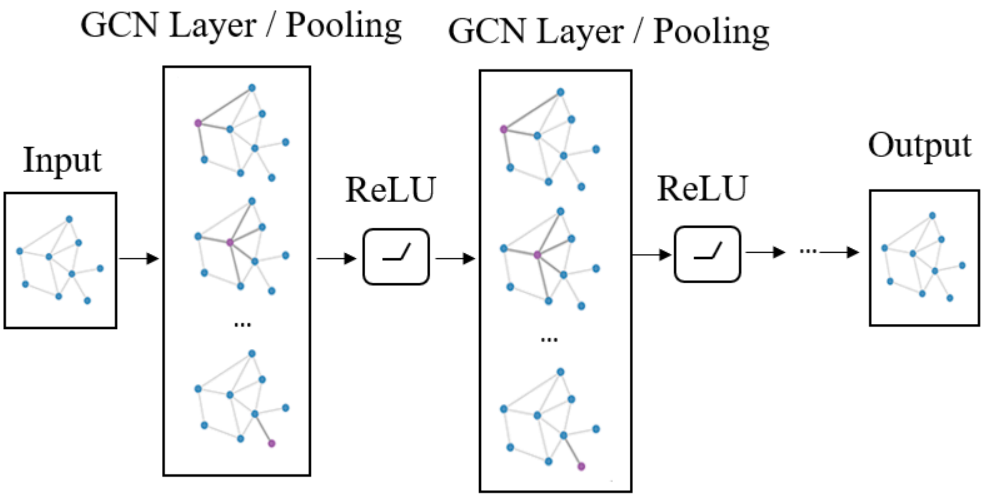

Fig 3.1.2.10 GCN basic Architecture

3.1.2.11 Graph Attention Network (GAT): A kind of GNN adopting attention scheme to assign with different weights for neighboring nodes when aggregating, which endues the model with saliency to identify significant information. In this paper, the GATs and LSTMs are integrated as a variant of STGNN.

3.1.2.12 LSTM: A type of RNN architecture which is used to model the sequential data and the long term dependencies of data. In this work, we leverage LSTMs to sample the temporal information involved in brain activity in the STGNN paradigm.

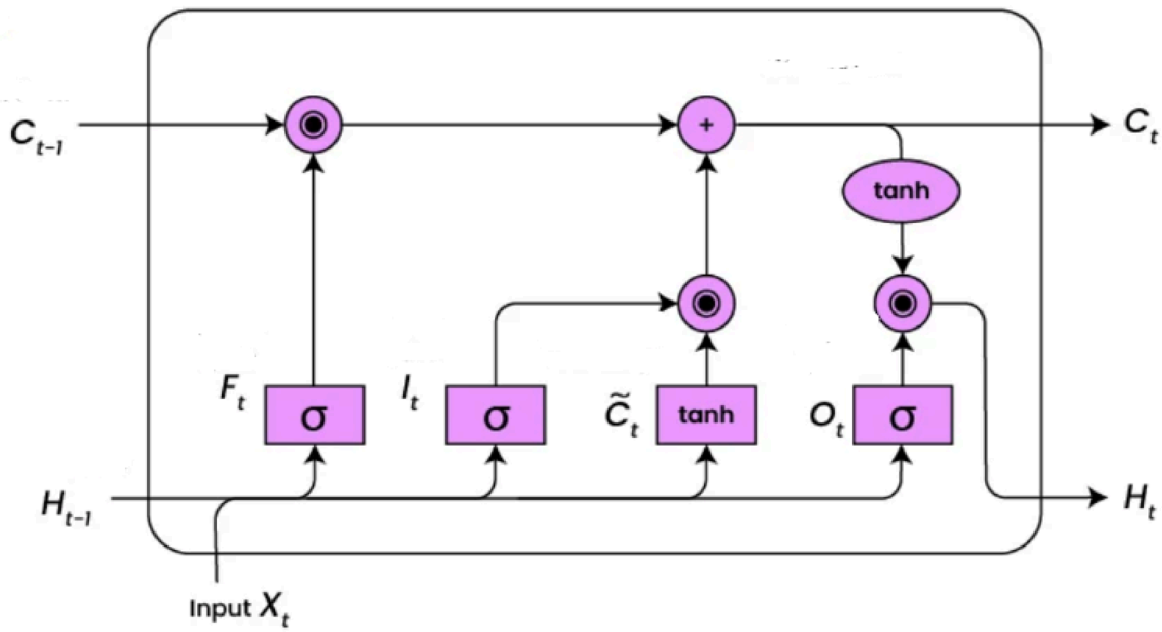

Fig 3.1.2.12 LSTM basic Architecture

3.1.2.13 Pearson Correlation Coefficient: A statistical measure expressing the linear correlation between two variables which has range values from -1 to 1. In this study, it is employed to calculate the functional connectivity among ROI pairs (for spatial graphs) and the correlations between time points (for temporal graphs), with an edge threshold 0.1 to form the edges.

3.1.2.14 fMRIPrep: A set of standard processing pipelines intended for use with fMRI data including motion correction, spatial normalization, tissue segmentation and other processing steps are used to produce high-quality BOLD timeseries data. In this analysis, the preprocessing of the MyConnectome raw rs-fMRI data is carried out with fMRIPrep.

3.1.2.15 Nilearn:A Python toolbox for analysis of large-scale neuroimaging data, also used in this study to parcellate the brain into ROIs using the Atlas for anatomical Labels(AAL) and calculate functional connectivity matrices from BOLD timeseries.

3.1.2.16 MyConnectome Dataset: a longitudinal neuroimaging dataset including rs-fMRI scans of an individual at various time-points, alongside with associated metadata like caffeine consumption. In this study, this database is leveraged to reduce intersubject differences and to concentrate only on caffeine connectivity properties of the brain in humans.

These terms constitute the conceptual scaffold of the study, where neuroimaging, graph theory and machine learning are combined to study the intricate effects of caffeine on brain connectivity. They are mentioned in all the methodology and results sections for making accurate representations of the research procedures and results.

3.1.3 Proposed Methodology

The suggested model takes the form of a modular architecture priors designed with the purpose of managing and learning from fMRI data. Firstly obtain resting-state fMRI data. Then preprocessed data is collected at the first stage. This preprocessing consists of several important steps including slice time correction, realignment to correct for motion, normalization to a standard template, and smoothing. These steps guarantee that data is clean, at a good quality and ready to be further analyzed.

After pre-processing, brain is segmented into different Regions of Interests (ROIs) on the basis of predefined atlas (e.g., AAL). The time series data is obtained by extracting average BOLD signal in time domain for each ROI. From these time-series signals we build our graphs. For spatial connectivity, Pearson's correlation coefficient is computed between each pair of ROIs to create an undirected weighted network that represents the functional connectivity in the brain. It is followed by the thresholding to keep only the strongest edges, without noises and overfitting.

For temporal modeling, the dynamic graphs are leveraged over a temporal dimension with sliding window or the node features are modeled as temporal sequences. These patterns are fed into an ST-GNN architecture. By comparing several alternatives, such as combining GCNs with Long Short-Term Memory (LSTM) or Graph Attention

Networks (GATs), we show that GCNs are particularly pertinent to exploit the spatial and temporal patterns in the brain data.

The last step is model training & testing/evaluation. The models are trained efficiently even for large amounts of data using GPU acceleration with PyTorch/ The whole pipeline is modularized to enable an easy experimentation with different network architectures and also hyperparameters. The framework is benchmarked under common evaluation metrics, and offers visualisations of connectivity maps and decision

3.1.4 Functional and Nonfunctional Requirements

Both functional and nonfunctional requirements are considered while designing the system, and the two are necessary to the validity, reliability, and usability of the research results

3.1.3.1 Functional Requirements:

The system should support resting-state fMRI data extraction and preprocessing, which is to extract raw data and preprocess it to be suitable for analysis. It should be able to build spatial and temporal graphs illustrating dynamic connections between the brains.

The system should allow to design, train and evaluate Spatiotemporal GNN (ST-GNN) models that are capable of learning from graph structured brain data. The model will classify observations (e.g., caffeine:yes vs. no) and produce performance metrics, like accuracy, precision, recall, F1-score, Area Under the Curve (AUC).

3.1.3.2 Non-Functional Requirements:

It is important for stability and reliability of the system, particularly via regulation of intersubject variation. Experiments could be ideally performed with the data of a given subject at different sessions.

For some it needs to be interpretable and therefore can provide neuroscientific explanations of what regions and connection in the brain are significantly influenced by caffeine. For this reason, scalability and computational efficiency are challenged by the fact that fMRI data are high-dimensional and time-consuming to analyze, and large scale parallel processing, such as GPU computation needs to be employed.

3.1.5 Dataset Description & Preprocessing

To examine the effects of caffeine on brain connectivity through the use of spatio-temporal graph neural networks (STGNNs), a complete preprocessing pipeline was performed to transform raw neuroimaging data to graph based representations suitable for analysis. This pipeline used resting-state fMRI data, which consist of 3D T1-weighted anatomical images and blood-oxygen-level-dependent (BOLD) functional images. The preprocessing facilitated structuring the data for defining the spatial and temporal dynamics of brain activation, and for characterizing the influence of caffeine on functional connectivity.

The raw fMRI data were first preprocessed using fMRIPrep, a well-established and standardized tool specifically developed for this purpose. Key operations such as motion correction, spatial normalization, tissue classification and computation of blood-oxygen level dependent (BOLD) timeseries were performed by fMRIPrep, providing minimally preprocessed BOLD timeseries data. To reduce the effect of head motion on the analyses, the motion parameters were regressed out of the timeseries. A total of 116 regions of interest (ROIs) in the brain were then segmented in accordance with Automated Anatomical Labeling (AAL) template using the Nilearn package.The functional connectivity matrices for each subject were computed based on the Pearson correlation coefficients between the BOLD time series of all pair of ROIs.These matrices, encoding weighted relationships in terms of connectivity, have been standing on the ground for building graph models of brain connectivity.

In order to analyze spatial relationships a graph was created with each of the 116 regions of interest as nodes. Feature representation at the node level We get “features” at the node level from the BOLD timeseries for each region. Node-to-node edges were defined based on the strength of their functional connection represented by the absolute value of their correlation value based on Pearson’s correlation. A threshold of 0.1 was set so that only meaningful connections were kept. The spatial graph was a weighted undirected graph as the weights on edges were directly given by the correlation values. This hierarchy was qualified to investigate how caffeine influenced inter-regional functional connectivity.

Concurrently, a temporal graph was constructed to visualize the evolution of brain activity. In this graph, each node extends to a given time, and has node features for each ROI at that node's time. To retain meaningful temporal information and feasibility of computational analysis, 100 representative time points were chosen as the equivalent of approximately 2 minute of fMRI data. Edges at time points were formed along a Pearson correlation between their ROI activity vectors, and again with the threshold 0.1 threshold, but this time capturing strong time associations. These edges were weighted by the absolute values of correlations and the resulting weighted undirected temporal graph modelled the time-varying sweeping process of caffeine on the brain activity.

The combination of the temporal and spatial graph provided two complementary views to consider caffeine-induced changes to brain function. The spatial graph revealed changes in connectivity between regions in the brain, and the temporal graph showed how activity patterns developed over time. By combining these two dual representations, the STGNN models were able to extract the intricate and multilayered effects of caffeine on brain connectivity and provided a robust base for further neuroscience interpretation.

3.2 Detailed Methodology and Design

The approach used in this study consists of a series of systematic stages exploring the effect of caffeine on the functional connectivity of the brain utilizing ST-GNNs. The primary step involved obtaining resting-state fMRI data from the MyConnectome dataset that contains scans of a single individual collected over many months with accompanying dietary caffeine data. This was done to reduce intersubject variance that might mask the relationship between brain response and caffeine consumption. The preprocessing of fMRI data was based on fundamental processing that include motion correction, normalization to MNI space, and temporal filtering to remove noises. We initially planned to use machine learning-based artifact correction techniques, but instead decided to use conventional preprocessing steps, since they are both more reliable and computationally cheaper.

To construct the graph, we developed spatial and temporal brain functional connectivity representations. Spatial graphs were constructed with brain regions as nodes and the edges between regions, which were formed from the temporal correlations, while temporal graphs encapsulated dynamics in the brain as a time-series. A highly nontrivial deci- sion point was to apply a Pearson correlation threshold between regions (e.g., > 0.1) to form meaningful edges, instead of processing all possible associations that would make the graph far too complex. A variety of other choices for graph construction were contemplated (e.g., the completely connected graphs), but were abandoned because they would increase the computational complexity or lead to overfitting. The spatial graph encodes the static connections between the brain regions, and the temporal graph represents the fluctuations of the brain dynamics over time, which remarkably preserves the subtle spatiotemporal brain connection patterns.

As for model architecture, several deep learning techniques were taken into account throughout the research, along with simpler machine learning models for the benchmark variability. Nevertheless, we finally chose Spatiotemporal Graph Neural Networks (ST-GNNs) model because it is a good candidate that can work well with both spatial and temporal dependencies of the data. Based on this paradigm, we adopt LSTM-GCN (Long Short-Term Memory with Graph Convolution Networks) and LSTM-GAT (Long Short-Term Memory with Graph Attention Networks) as the base models. Such models are suitable for both sequential data and graphs so that they can process the temporal dynamics and spatial dependencies of brain activities. We also attempted modeling using hybrid models, involving CNNs and GNNs, however, discarded it as CNNs models are not based from exploiting graph relationships which is the key for our experiments. We also investigated a time-only architecture utilizing RNNs, however, it was insufficient to represent the spatial relationships among brain areas.

For model performance evaluation, accuracy, precision, recall, F1-score and AUC were chosen as the main performance indicators to evaluate model performance. The models selected were then compared against simpler baseline models like Multi-Layer Perceptrons (MLPs) and classical GCN and GAT models. It was first planned to use grid search for hyperparameter tuning instead of" since it is a famous method especially in PCA, and replaced to "because of the efficiency of OHCSK who needs to search over large number of parameters. In the computation aspect, we adapted GPU acceleration to process the large-scale data and complicated calculations when training the graph-based models. Although we initially considered CPU processing, it was much slower, especially when training models with multiple graph layers.

In conclusion, in this study, state-of-the-art graph-based neural network structures have been combined. To characterize the spatiotemporal dynamics of brain connectivity in the context of caffeine. While other, simpler, alternatives have been considered (e.g., simplified machine learning models and combining CNN with GNN structures), the adopted approach based on LSTM-GCN and LSTM-GAT architectures shows to robustly represent both spatial and temporal aspects of the brain activity. It was chosen due to its computational tractability, capability to represent intricate brain dynamics, and relevance to the research questions.

Here is the workflow diagram outlining the major steps of our approach:

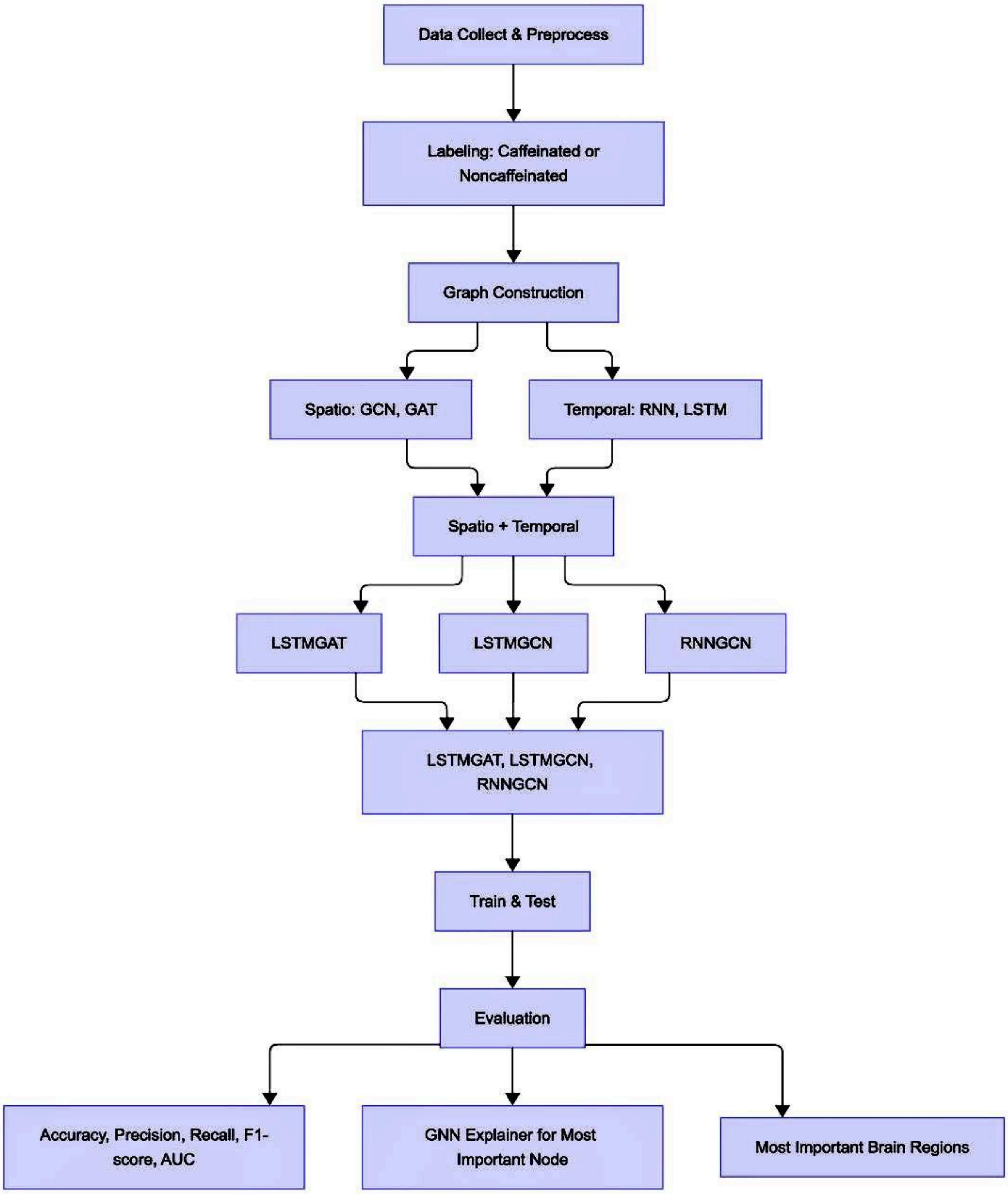

Figure 3.2: Workflow diagram

3.3 Project Plan

The study was designed with several distinct phases in order to move methodically towards the goal of understanding the influence of caffeine on brain connectomes with spatio-temporal graph neural networks (STGNNs). Timeline and stages The project timeline lasted approximately eight months and included the following milestones:

Choice of topic and review of literature (Week 1-4)

Weeks 1–2: Determined topic of interest through literature review on brain connectivity and caffeine effects Topic was the modelling of changes in functional brain networks that we observed from caffeine in regions involved in the motor control and attention domain through the use of STGNNs.

Weeks 3–4: Reviewed the relevant past work done on brain connectivity, GNN architectures and neuroscience literature on the effects of caffeine and its neurophysiological impact. To construct a theoretical background, core literature review of Graph Convolutional Networks (GCNs) Graph Attention Networks (GATs) and STGNNs were conducted. Developed research objectives and wrote down the reason for picking that topic

Data Gathering and Preparation (Weeks 5-8)

Weeks 5-6: Obtained resting-state fMRI from the MyConnectome dataset, which contains recurrent scans of the same person over several weeks with a record of caffeine consumption Check if data is valid and the metadata are available (caffeine dose and led timed).

Weeks 7–8: Data pre-processing using fMRIPrep, which includes checking for head motion artifacts effect of head movement on fMRI readings cannot be ignored, and thus motion correction is carried out], spatial normalization (which means aligning the scans with the brain standard template), and temporal filtering to make the data noise-free. Using the AAL atlas through the nilearn library, we defined 116 ROIs. Pearson correlation coefficients (threshold >0.1), connectivity matrices were calculated and spatiotemporal graphs constructed.

Graph Construction & Model Design (Weeks 9–12)

Weeks 9–10: Constructed spatial graphs where nodes are ROIs and edges were weighted by correlation coefficients (>0.1) and temporal graphs by connecting nodes at different time points and thus allowing for the examination of dynamic changes in connectivity. Ensured that graphs made sense given the patterns of functional connectivity

Weeks 11–12: Designing the STGNN architecture, using Long Short-Term Memory units and GCNs or GATs to learn the spatial and temporal dependencies. An alternative architecture could be trying a hybrid of CNNs and GNNs, although using GNNs for this task would be intuitive because of the relational nature of graph data.. It is important to document the process of choosing architecture.

Weeks 13–14: Implementation of the model and initial training. An example of spatial temporal graph neural network using PyTorch and PyTorch Geometric and GPU use an example can be found. It was important to set the baseline models, such as multi-layered perceptrons, GCNs and GATs.

Weeks 15–16: The first training had to be done to ensure the model would not collapse with the default hyperparameters. It is good to start hyperparameter tuning now to tune the learning rate, the batch size from 32 and the number of epochs from 100. Evaluation of the abstracted model metrics for the description.

Weeks 17–18: Look carefully at the results from the first training to understand which hyperparameters deserve to be properly tuned. The overfitting should be prevented, and as has been mentioned before, the models should generalise well. The cross-validation loss is a proper way of determining whether to stop the training.

Weeks 19–20: After testing the hyperparameters, train the models up to completion and check resource usage on each step. Both LSTM-GAT, LSTM-GCN and RNN-GAT had to be trained, with LSTM-GAT being more demanding due to attention mechanisms. Ensure that it converges and retain the final models in the checkpoint with the best loss on validation.

Weeks 21–22: Complete evaluating the performance of the spatial temporal graph neural network, the connectivity maps and the attention weights for the frontal lobe and the cerebellum had to be shown to understand scientifically what happens.

Weeks 23–24: Comparing the results and the notes to those of the baselines, including multi-layer perceptrons, GCN and GAT. Analysis of the caffeine ingestion regarding neuroscientific outcomes should be as detailed as possible.

Weeks 25–27: Wrote the research paper (introduction, literature review, methodology, results and discussion) Visualizations included (e.g., bar charts of brain region importance) and performance metric tables were included here as part of results support.

Weeks 28–30: Refinement of the writing of paper and start the work of final Paper Writing

Week 28: We internally reviewed the draft paper with respect to clarity, scientific rigor, and coherence. Requested feedback from classmates or mentors to learn what needed work.

Week 29–30: Paper revision, strengthen arguments; fix visualizations; and format figures, tables, and references Refined the document to prepare it for submission, publication, or academic effort

The project was undertaken in a highly modular fashion and iteratively, to adjust the way in which the project was being carried out based on interim results. Specifically, if initial graphs were noisy then the threshold for correlation for graph construction was altered and other metrics, such as sensitivity adjusted if required. This means that the investigation lasted for 30 weeks and was able to be diverse and exhaustive. By following these timeline the tasks had been completed in an efficient way.

3.4 Task Allocation

A two-person team was utilized for this project and duties were divided based on the primary interest of each contributor: coding and report writing. This division of labor contributed to smooth advancement and provided the team with the opportunity to play to their strengths. The roles and responsibilities include the following:

Coding Specialist is in charge of all technical activities related to the project that involve data gathering, data pre-processing, and model building. This participant processed resting-state fMRI data from the MyConnectome dataset and using fMRIPrep and nilearn he created functional connectivity matrices and spatial and temporal graphs. Developed the STGNN models (LSTM-GCN and LSTM-GAT) based on the PyTorch framework with GPU acceleration, used the random search to search for the best hyperparameters, and measured the performance from metrics. They also created visualization interfaces of connectivity maps and attention weights, to make the pipeline modular, scalable and reproducible.

Writer documented the results and process of research to achieve clarity and scientific merit in the thesis. This author organized the methods, results, and neuroscientific implications into a coherent manuscript and integrated figures and performance statistics developed by the coder. They provided statements of the research aims, methodological details of the preprocessing pipeline and interpretations of how caffeine might modulate brain connectivity. The report writer also handled the reviewing process; incorporated feedback to improve the thesis and its final preparation to be submitted. The two members were in constant contact through weekly meetings to be on the page, discuss issues and to make sure the project was on the right track. A modular pipeline and report generation approach enabled the programmer to concentrate on the technical avalanche of implementation and the report writer to document the findings also in parallel which improved project timescales.

3.5 Summary

In this research hybrid method is presented for interpreting the effects of the caffeine on the brain connectivity in terms of STGNNs. The study utilises resting-state fMRI data from the MyConnectome dataset, which has been pre-processed using the fMRIPrep and nilearn software to build the spatial and temporal graphs of brain activity. Spatial graphs represent functional connectivity between 116 ROIs, temporal graphs represent the dynamic activity patterns over 100 time points. The STGNN, a novel architecture integrating LSTM with GCNs or GATs, successfully captures information from these graphs in order to make estimates of caffeine-induced brain states, surpassing baseline models. The proposed approach is modular, interpretable, computationally efficient, with GPU support, and evaluated with performance matrices. A project plan and tasking structure support structured operations, with coding and reporting roles assigned to make best use of specialist skills. This strategy offers a strong basis for to discern caffeine's neuroscientific effects regarding brain connective, a reproducible and scalable pipeline for future improvement.

Chapter 4

Implementation and Results

This chapter describes the implementation strategy, environment setup, evaluation methodology, and the results obtained. It includes step-by-step details of data preprocessing, model performance evaluation, and a summary of the findings.

4.1 Environment Setup

The execution was performed in a cloud-computing setup, to guarantee scalability and access to high-performance devices. The platform, hardware and software tools employed are summarized as follows:

4.1.1 Platform

The investigation was carried out in a Google Colab notebook.

that makes free GPU resources available and enables cheap model training and data processing. Google Colab was selected based on its high availability, simplicity of use, compatibility with the essential Python libraries used in neuroimaging and machine learning tasks.

4.1.2 Hardware

GPU accelerator: NVIDIA Tesla T4 for accelerating model training and graph based computations.

RAM: 12.72 GB, capable of processing high-dimensional fMRI data and graph structures.

Disk: Temporary runtime storage: approximately 68 GB is required for storing runtimes.

4.1.3 Toolbox Software & Libraries: Some libraries and software tools used in the implementation of this study are listed below.

The language used for implementation is Python 3.8, which is chosen because of its large ecosystem.

IDE: Interactive development was done using Google Colab

Libraries:

PyTorch and PyTorch Geometric: For implementing and training STGNN models with LSTM-GCN and LSTM-GAT architectures.

NumPy and Pandas: Used for numeric calculations and data dictionary With-based operations.

NiLearn, fMRIPrep, and Nilearn: Used to pre-process fMRI data, dimension reduction based on way of division into interest areas of the brain (ROIs), and calculating functional connectivity.

Matplotlib and Seaborn: Both are used for plotting the connectivity maps, attention weights, and performance metrics of the model.

4.2 Training the model

The models were trained utilizing the PyTorch and PyTorch Geometric frameworks. These are toolkits to build and train models to work with brain data. We considered three primary classes of Spatio-Temporal Graph Neural Networks (STGNNs), which are specialized models to capture both the relations among brain regions and how those relations evolve over time. We use three models in our work and they are referred to as LSTM-GAT, LSTM-GCN and RNN-GAT.

This model integrates two intelligence tools LSTMs and GATs. The LSTM part excels at remembering things over time, so it supports the model in recording how brain activity evolves from one instant to the next. The GAT part functions in much the same way, though instead of illuminating a starry night, it shines the spotlight on the most important connections between brain areas by giving more of our attention to which connections matter the most. Together they are what make the model very good at both the time aspect (how brain data changes over time) and connection aspect (how brain areas are linked together) of brain data.

This model also leverages LSTM units to model the temporal effects, but instead of GAT, it combines graphical attention with Graph Convolutional Networks (GCNs). GCNs are akin to a map-reader: They see the structure of the brain's connectivity and derive how distinct regions are attached to one another through that structure. By using a combination of those two algorithms, GCN and LSTMs, the model is capable of understanding layout of brain connections (spatial structure) and how those connections evolve over time, which enables it to cope well with sequences of brain scans, such as observing the brain activity as in a video.

The simpler version of the model used for comparison purpose. One distinction is its use of a generic RNN (not LSTMs) to detect temporal trends. RNNs are a kind of shorter memory version of LSTMs—they can learn to follow changes over time, but they tend to be pretty bad at remembering things** over long periods. The GAT part still helps by zeroing in on key brain connections, but we ran this model to test whether the fancier LSTM approach truly adds value when trying to make sense of brain data.

All three models run on a powerful computer chip known as an NVIDIA Tesla T4 GPU, which we accessed via Google Colab — a free online platform that enables us to execute heavy computer tasks. Think of the GPU as a super-speedy engine that allows the models to learn very quickly, even when working with a great deal of brain data.

Adam optimizer is used to help the model to learn better by changing how much it learns, faster or slower, at each step. Moreover, the models trained with a batch size of 32, that is the model learned from 32 pieces of brain data at once before updating its knowledge. That way, the model learns more quickly without being overwhelmed.

Then trained each model for 100 iterations or epochs. An epoch is just a full pass through all the training data -- a read of the entire book. Redoing this 100 times helps the model improve its predictions.

In order to prevent overtraining (where a model memorize the training data too well and does poorly on new data), we employed a simple trick called early stopping. We tested the model's ability to generalise using a separate test set (a small set of data used to check progress during training). When the model stopped improving on this validation set, we stopped training early to avoid overfitting, i.e. the case when the model can only learn the training data, but not generalize it to new, unfamiliar data.

After training, we selected the best performing iteration of each model using the validation set. Next, we evaluated these best models on a totally independent test set and checked how well they did on new data that they had not seen before.

It took a lot of time to train that model, because brain data is complex and models need to do lots of calculations. The training time of each model on the NVIDIA Tesla T4 GPU is several hours on average. We speculate that the LSTM-GAT took the longest and cost the most computer power to train is because its attention mechanism (the part of the model that focuses on important connections) is more complicated and takes additional computations than the attention mechanism in the other models. The LSTM-GCN and RNN-GAT models were a little faster, since they don't have this additional attention, but they all still took a decent amount of time to complete their 100 epochs of train.

4.3 Comparative Analysis

The LSTM-GAT was the best performing on all the evaluated metrics with an accuracy of 0.80, a precision value of 0.70, a recall value of 0.75, an F1 score of 0.72 and an AUC value of 0.80. Such a better performance may result from the fact that Graph Attention

Networks (GATs) and Long Short-Term Memory networks (LSTMs) are combined in a synergistic manner. The attention mechanism inherent to GATs facilitated to focus dynamically in the model the most important and functionally relevant connections within the spatial graph, subjugating nodes and edges that had less pronounced changes in response to caffeine exposure. Meanwhile, the LSTM module was able to better learn subtle temporal dynamics inside fMRI data, which helped the model trace and simulate the time-series pattern of brain activity. This duality endowed LSTM-GAT especially ideal in characterizing the complex dynamic patterns of altered functional connectivity by caffeine, and a solid framework for fathoming the neurophysiologic influence of the stimulant.

By contrast, the LSTM-GCN model performed slightly worse than the LSTM-GAT model, with an accuracy of 0.794, precision of 0.74, recall of 0.67, F1-score of 0.68, and AUC of 0.79. The Graph Convolutional Network (GCN) part of this model was able to accurately capture the spatial relationships between the regions of the brain, using the structural information carried by the graph structure to describe patterns of connectivity affected by caffeine. But attention mechanism which is quite important difference in GAT was omitted and thus, it became a less sophisticated projective weighting of connections. This lack of distinction between neighboring nodes can be one of the reasons for the decrease of the performance for all metrics, what is more pronounced in recall, where it was harder for the model to find all the positive instances. Nevertheless, good performance of LSTM-GCN in terms of accuracy and precision is evidence of its stability in predictions and indicates that it is still a competitive choice in the field of models that concentrate on spatial relations.

It is also the comparison within the same group of STGNN models: the performance of RNN-GAT is underwhelming (0.77 accuracy, 0.62 precision, 0.66 recall, 0.62 F1-score and 0.78 AUC). The RNN mechanism itself at the heart of this model proved to be not good enough to model the long-term time dependent correspondence necessary to fMRI analysis as the advanced LSTM architecture. The inability of the RNN to handle long sequences and remember past time points may have contributed to its shortcoming to adequately capture the dynamic modulations of brain signals by caffeine. Although GAT (and SCAR-GCN) introduced some attention-based prioritization in the spatial graph, this did not outweigh the temporal deficits which led to consistently lower scores in all evaluation tasks. This finding warns us that the choice of temporal modelling technique is crucial when we design STGNNs for neuroimaging tasks especially dealing impairment by compound stimulants such as caffeine.

4.4 Results and Discussion

The superior performance of the LSTM-GAT model highlights the importance of temporal models combined with attention mechanisms when processing complex fMRI data. The attention mechanism helps the model to focus on those functionally relevant connections in particular the default mode network which has been shown to be modulated by caffeine consumption. Further, the detailed attention weights visualizations show that prefrontal cortex, posterior cingulate cortex, and anterior cingulate cortex were the regions that most received high attention along the timeline, which supports established literature on caffeine’s influence on the brain. This 'feature' of selective attention allows the model to focus on salient signal dimensions, while ignoring irrelevant noise, making it easier to learn from the data in multiple contexts.

Although the LSTM-GCN model was less optimal compared to the LSTM-GAT, its performance was stable, especially in the accuracy value which indicated its possibility to confidently predict positive results. But the lower recall suggests its inclination to neglecting some positive ones, because of the equal weight of the neighboring nodes, without the hierarchical order to prioritize the multiple factors from the attention-based LSTMGAT. This difference should be considered as the advantage of the adaptive attention mechanism to cope with the heterogeneity of fMRI data.

In contrast, the RNN-GAT model performs less well revealing the limited capacity of simple RNN architectures to model long-range temporal relations in fMRI sequences. This implies that a more sophisticated temporal representation, such as the one provided by LSTM models is needed to capture the temporal organization in brain activity data.

The spatial-temporal dual graph representations were found to be critical for the STGNN models' performance. Caffeine-related changes in functional connectivity, representing changes in inter-regional interaction, were effectively captured by spatial graph. At the same time, the temporal graph revealed the dynamic changes of spectral patterns throughout, thus offering an integrative representation of the evolving effect of caffeine. These synergistic viewpoints allowed the STGNNs to perform resiliently to model the complex influence of caffeine on brain connectivity in a more comprehensive way, which leads to a deeper understanding of its neurophysiological effects.

Nevertheless, there are a few limitations that should be noted. The fact that a single-subject dataset (MyConnectome) was used in the current study could introduce limited generalizability to the findings as individual differences in brain structure and caffeine response may play a role. The results of this study need to be confirmed using multi-subject datasets to ensure the generalizability of these findings across certain demographic populations (e.g. using stratified sampling, considering age, sex, and caffeine tolerance effects). Moreover, an investigation into dynamic thresholding methods for graph construction may also improve the performance of the model by optimizing the trade-off between sensitivity and specificity in identifying connectivity alterations.

The dynamic thresholding method enhanced the detection of functional connectivity signals, and the temporal graph showed profound changes in activity profile over time. These two insights enabled the STGNNs to fully illustrate the differential and time-dependent caffeine actions across brain connections, and thereby provide an in-depth representation of its effects on brain chemistry.

Table 4.4: Performance of Models

Model	Accuracy	Precision	Recall	F1 score	AUC
LSTMGAT	0.80	0.70	0.75	0.72	0.80
LSTMGCN	0.794	0.74	0.67	0.68	0.79
RNNGAT	0.77	0.62	0.66	0.62	0.78

For the top 10 most important brain regions, the mean importance scores are also shown in the bar chart, with cerebellum, cingulum, as well as vermis regions (e.g., Vermis_9, Vermis_6) having importance scores higher than 0.010.

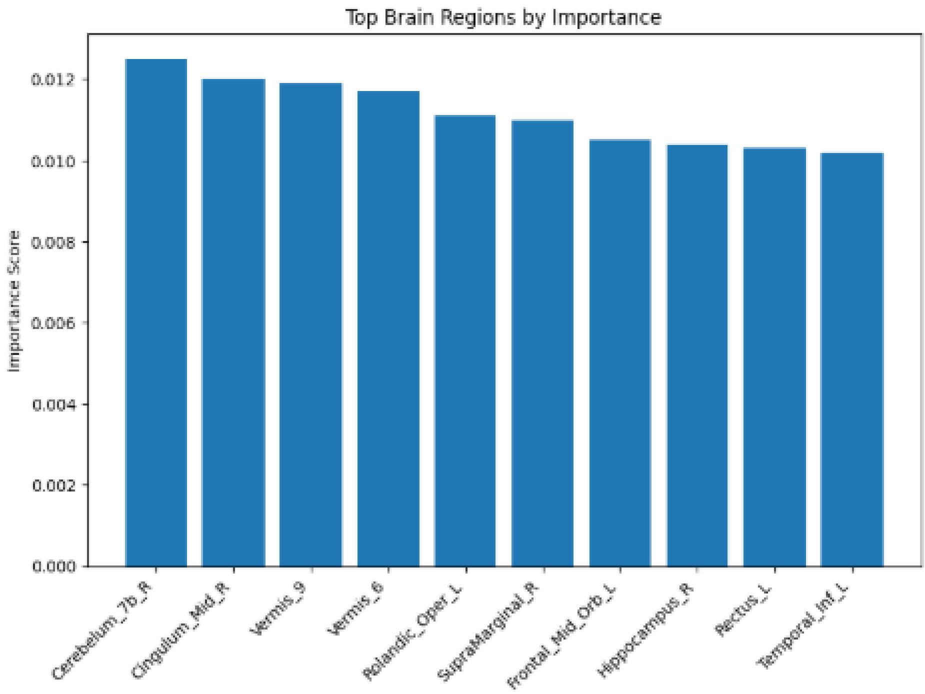

Fig 4.4: Top 10 most important brain regions based on mean node importance.

These regions, along with polaris, opercular, supramarginal regions, are likely make strong predictions, perhaps based on the motor-coordination and cognitive processing roles these regions play when influenced by caffeine. Brain areas such as the hippocampus and temporal inferior lateral presented importance scores with lower relative values—of approximately 0.008, suggesting a less relevant yet significant contribution.

Here we have divided these most important regions of the brain in Attention, Alertness and Motor Function.

Attention:

These regions are mainly related to the load type and span, maintaining or changing attention, and are connected to cognitive and sensory functions.

- **Cingulum_Mid_R:** It modulates attention through the monitoring of conflicts and processing of emotional and cognitive information for decision-making purposes.
- **SupraMarginal_R:** Is involved in the attentional aspects of language processing and the relay of sensory-motor information for activities such as reading and imitation.
- **Pectus_L :** Helps in the attention mechanism that involves visuospatial processing and self-referential thoughts and imagery perspective change.
- **Temporal_Inf_L:** Enables attention to the features of objects in the visual scene by recognizing them and performing semantic analysis on them.

Alertness:

These regions are considered to be associated with the sustenance of arousal, alertness, or preparedness, which are often connected with emotions or motivation.

- **Frontal_Mid_Orb_L:** This chemical substance helps to regulate one's alertness and either increase or decrease the activity connected with reward areas as well as emotional stability linked with motivation to be prepared for some kind of behaviors.
- **Hippocampus_R :** It lends support to alertness indirectly through experiences to get an understanding of contexts in the environment.

Motor Function

These areas are any of the cortical regions that are concerned with movement planning or execution or with the fine tuning of movement.

- **Cerebellum_7b_R :** Coordinates movements of the different body parts to ensure that an individual accurate movement takes place.
- **Vermis_9:** Helps in controlling posture and movement, and coordination involved in maintaining balance while walking.
- **Vermis_6:** Serves as an executive control of voluntary motor controlling or as an overlay of motor programming involved in the precise control of eye movements and tracking.
- **Polandic_Oper_L:** Supports motor control indirectly through monitoring the sensations generated by an individual which in turn helps in sensory-motor action.

For a better interpretation of the LSTM-GAT and LSTM-GCN models, the GCN Explainer was used to detect the most discriminative nodes (regions of interest, ROIs) and their brain regions within the models. The tool employs an iterative method based on subgraphs in which less relevant nodes and edges are masked out in each iteration, retaining the most important elements for the decision making. Analysis suggested that such regions as prefrontal cortex, posterior cingulate cortex, and cerebellum, all of which showed a high importance in terms of attention weights, consistently contributed to the formation of the role-base. This approach offers a means for testing the focus of the model on neuroscientifically relevant regions but also gives an interpretable account of how spatial and temporal information is blended within a graph neural network. In the future, GCN Explainer may be used in the analysis of real-time fMRI, providing dynamic information about brain activity during cognitive tasks.

4.5 Summary

This chapter delineated the execution and findings of a study analyzing caffeine's impact on brain connection through the use of STGNNs. The environment was established on Google Colab with an NVIDIA Tesla T4 GPU, employing PyTorch, PyTorch Geometric, and neuroimaging packages such as fMRIPrep and Nilearn. The preprocessing pipeline converted raw fMRI data from the MyConnectome dataset into spatial and temporal graphs, which were utilized to train three STGNN models: LSTM-GAT, LSTM-GCN, and RNN-GAT. The evaluation matrices indicated that LSTM-GAT surpassed other models, with an accuracy of 0.80 and an AUC of 0.80, with LSTM-GCN and RNN-GAT following. The findings indicate that STGNNs, especially LSTM-GAT, proficiently encapsulate the spatial and temporal dynamics of caffeine's impact on brain connectivity, with attention processes augmenting interpretability. The results establish a basis for additional neuroscientific investigation, with possible applications to multi-subject datasets and enhanced graph creation methodologies.

Chapter 5

Engineering Standards and Design Challenges

This chapter presents the relevant engineering standards considered during the development of the system and discusses the design challenges encountered throughout the research process. It also addresses the ethical, societal, environmental, and financial aspects of the project, along with sustainability considerations.

5.1 Compliance with the Standards

In this project, several software, hardware, and communication standards have been considered to ensure the integrity, compatibility, and reproducibility of the research workflow. The standards selected are specifically aligned with the requirements of implementing deep learning models, particularly spatiotemporal graph neural networks, for analyzing functional MRI data in relation to caffeine consumption.

5.1.1 Software Standards

The software developed during this research work followed the most relevant industry and academic standards as to ensure reproducibility, transparency and efficacy. All scripts were written in the Python programming language and adhered to the PEP8 (Python Enhancement Proposal 8) style guide. This standard was selected due to its inherent simplicity and popularity amongst the scientific computing community. I preferred to maintain readability and maintainability according to PEP8, which is important when working with someone and in the long-term research.

In addition, Git was adopted for version control, with GitHub hosting it, so that the coding could be remotely accessed, collaborated on and revisited. Furthermore, the planning and the implementation were in accordance with IEEE 830 norm for Software Requirements Specifications (SRS). This made it possible to formally define inputs, outputs, and functional blocks/component to realize and organize a modular software pipeline from fMRI preprocessing to STGNN-based modeling.

Other alternatives like the ISO/IEC 12207 lifecycle processes were explored however given the academic and research-oriented focus of this research, the complexity of these tools was unnecessary. IEEE 830 and open-source protocols were lighter, more focused, and ultimately more conducive to quick experimentation and model iteration.

5.1.2 Hardware Standards

All modeling and experiments were performed on the free version of Google Colab with NVIDIA T4 Tesla GPU. These GPUs are CUDA and cuDNN compatible, which are the benchmarks in the industry for hardware acceleration in deep learning. This configuration helped the STGNN models to be run with high efficiency without even needing high-cost local resources.

The T4 GPU allows mixed-precision calculation, whereby memory consumption is decreased and computation efficiency for training is improved. Possibly more powerful setups could be achieved, for instance with local GPU machines or paid cloud servers (e.g., AWS, Azure), having dedicated resources, and using longer runtimes, though the freely available Google Colab's version was a good trade-off between ease of use and power, especially for academic research with scarce resources.

5.1.3 Communication Standards

In the experiments, the exchange of information and data synchronization were delivered based on wireless internet standards of IEEE 802.11. This allowed the cloud-based infrastructure, services such as Google Drive for dataset storage management, Github for code management, and Google Colab for model development. HFT frameworks made it possible to remotely collaborate, iterate quickly on the model, and have real- time access to data from anywhere.

Wired communication protocols like IEEE 802.3 (Ethernet) which are stable and fast by nature, cannot be applied because of the cloud-native workflow of the research. Since the project depended on cloud-based solutions, wireless communication became not only adequate but also necessary to make it portable and easily available.

5.2 Impact on Society, Environment and Sustainability

5.2.1 Impact on Life

This study provides insights into the effects of caffeine, one of the most widely consumed psychoactive substances, on the human brain. The project has the potential to provide individuals and practitioners with insights into how caffeine may be affecting the brain and its connectivity and may advance research on neural effects of caffeine using the STGNNs. This could be especially important in people with cognitive risk, sleep disorders, or other neurological diseases.

5.2.2 Impact on Society & Environment

At a sociological level, the intersection of AI and brain science conduces to interdisciplinary creativity and public consciousness of responsible consumption of stimulants, like coffee. The findings, scale up this ever-growing field of knowledge that could, someday, inform public health policy or education. Is there a positive if that is at the cl; as to wards campaign.

From an environmental point of view, the energy consumption of the training of deep learning models is an issue. But the choice of Google Colab's free tier did reduce environmental impact compared to using high-powered dedicated servers to deploy models. In addition, model architecture and early stopping were applied to lessen the time required for training in order to minimize computational burden.

5.2.3 Ethical Aspects

The data using and model designing in this study all strictly complied with the ethical guidelines. The fMRI files for analysis here were public and ethically approved for research. The privacy and ethical concerns were also protected without any personal identifiable information involvement. It was not our intention to diagnose or recommend treatments, but to investigate and visualize neural connectivity. This takes advantage of the properties of the model itself such that it cannot be misused in a clinical setting in the absence of validation and regulation.

5.2.4 Sustainability Plan

To facilitate the long-term use and extension of this work, the whole system was constructed from open-source tools PyTorch, NetworkX, and the Deep Graph Library (DGL). Those libraries are backed by big communities and are updated regularly, which means that they will work for research you might want to do in the future. The adoption of the free version of Google Colab For free was fundamental for making this project economically feasible, as well as sustainable by not relying on the purchase of physical hardware. With the codebase made being modular, it can be easily reused and adapted with other databases, making the research frame powerful and expatiate.

5.3 Project Management and Financial Analysis

Here is the project management and cost analysis of a 8 month research work based on the effect of caffeine on brain connectivity with the help of graph neural networks, as executed in Google Colab.

Project Management:

Planning & Scheduling : The project models caffeine's impact on brain connectivity, covering fMRI preprocessing, GNN development, result analysis, and publication. The schedule sequences data preprocessing (Nilearn/fMRIPrep), model training, visualization (Matplotlib/Seaborn), and submission, managed via team meetings. Risks are mitigated with multiple datasets and GPU-optimized code.

Cost: Monitor Google Colab usage through Google dashboard so we don't exceed budget, use free Jupyter Notebooks for non-GPU tasks to reduce computing costs.

Risk Management: Reduce risk of failure to gain access to data by obtaining access to several open-source fMRI data sets (e.g., Human Connectome Project). Write code in a way to be as GPU efficient as possible in order to deal with the memory limits of Colab.

Engagement: Report quarterly with funders and institutional partners to maintain alignment and support for research goals

Estimate Cost of the Project:

Primary Budget Category	**Item**	**Cost (USD)**	**Notes**
Computational Resources	Google Colab Pro Subscription	200	$25/month for 8 months, basic GPU access.
	Cloud Storage (1 TB)	40	$5/month for 8 months, smaller dataset.
Data Access	Open fMRI Datasets	0	Human Connectome Project, Nilearn, fMRIPrep (freely available).
Software Licenses	PyTorch, Nilearn, Others	0	Open-source libraries.
Total		**240**	

5.4 Complex Engineering Problem

Analyzing the Effects of Caffeine on Brain Networks Using Spatiotemporal Graph Neural Networks, deals with what is a complicated engineering problem. They intersect the fields of neuroscience, machine learning, and computational neuroscience, and call for advanced modelling techniques to capture dynamic brain connectivity. It includes dealing with large, complex datasets, like functional MRI data, that have missing data and are potentially noisy, and creating new computational frameworks to capture changes over space and time in the pattern of brain activity that can follow caffeine ingestion. The integration of these domains and the modeling needed to faithfully capture the impact of caffeine on brain networks render this investigation an integrative, higher order engineering challenge.

5.4.1 Complex Problem Solving

This section outlines the alignment of our research project with relevant problem-solving categories.

Table 5.1: Mapping with complex problem solving.

EP1 Depth of Knowledge	EP2 Range Of Conflicting Requirements	EP3 Depth of Analysis	EP4 Familiarity of Issues	EP5 Extent of Applicable Codes	EP6 Extent Of Stake-holder Involvement	EP7 Interdependence
✓	✓	✓	✓		✓	✓

Addressing Complex Engineering Problems (EP):

SN	EP definition	Attachments	Justification(with knowledge profit)
1	EP1: Depth of Knowledge Required	Yes	Our research implements knowledge of neuroscience, machine learning, and graph neural networks (GNNs), covering K3,K4. An optimized & scalable approach is taken covering K5 & K6. We explore fMRI model based ML techniques covering K8.
2	EP2: Range of Conflicting Requirements	Yes	The challenge lies in designing a model architecture that outperforms existing ones in accuracy while balancing multiple conflicting demands—such as speed vs.

			model complexity, scalability vs. resource limits (e.g., Google Colab), and innovation vs. reproducibility. Achieving high accuracy without compromising efficiency, accessibility, or interpretability was a key design trade-off.
3	EP3: Depth of Analysis Required	Yes	The fMRI data is highly complex that varies across both time and brain regions. Due to the lack of a clear analytical framework, an in-depth analysis was essential. We addressed this by applying Spatiotemporal Graph Neural Networks (STGNNs) to uncover patterns in brain connectivity after caffeine intake, ensuring accurate interpretation of dynamic neural interactions.
4	EP4: Familiarity of Issues	Yes	The project involves unfamiliar domains like neuroscience, fMRI data analysis and brain connectivity modeling. Understanding how caffeine affects neural communication required exploring areas beyond traditional machine learning, making it an interdisciplinary and challenging task.
5	EP5: Extent of Applicable Codes	No	N/A
6	EP6: Extent of Stakeholders Involved and Conflicting Requirements	Yes	Consulted neuroscience researcher & ML expects to ensure validation of our research, ensuring the solution met both domain-specific insights and technical standards.
7	EP7: Interdependence	Yes	The workflow has the nature that every step here will be based on the previous one. Extracting features from fMRI data, training the ST-GNN model using those features and performance evaluation of final model- all stages are tightly coupled as if even a single earlier step is wrong, the entire processing fails.

Mapping with Knowledge Profile for EP1

This table 5.2 is designed to map the EP1 to the Knowledge Profile.

Table 5.2: Mapping with knowledge Profile.

K3 Engineering Fundamentals	K4 Specialist Knowledge	K5 Engineering Design	K6 Engineering Practice	K8 Research Literature
✓	✓	✓	✓	✓

5.4.1.1 Justification for Knowledge Profile Mapping (linked to EP1)

- **K3 - Engineering Fundamentals**:

  This project embodies the first principles of fMRI signal processing, connectivity modeling and statistical analysis, software engineering and pipeline development, allowing for systematic, data-driven, and model-based approaches to quantifying circuit dynamics.

- **K4 - Specialist Knowledge:**

  The above involves mastery of neuroimaging (e.g., fMRI preprocessing with Nilearn/fMRIPrep), graph theory, and spatiotemporal GNNs. The project is thus uniquely positioned with expertise in caffeine's neuropharmacological effects, as well as dynamic brain network analysis.

- **K5 - Engineering Design:**

  The ST-GNN research includes designing capable ST-GNN architectures for fMRI data, preprocessing pipelines, and brain visualization tools. These architectures maintain a trade off between accuracy of the model, computational cost of the model, and interpretability.

- **K6 - Engineering Practice:**

  Feedback Loop Practicals: Writing in PyTorch Geometric, performing GPU optimizations on Colab, and tirelessly experimenting to gain confidence in results. It also follows best practices in reproducible research such as use of version control and documentation.

- **K8 - Research Literature:**

Motivation The work engages with state-of-the-art ST-GNN research and neuroimaging studies, synthesising knowledge from previous literature (12-15) to introduce new GNN-driven methods in deriving caffeine-induced effects on brain networks.

5.4.2 Engineering Activities

This section provides a detailed discussion of the engineering activities involved in our research project.

Table 5.3: Mapping with complex engineering activities.

EA1 Range of resources	EA2 Level of Interaction	EA3 Innovation	EA4 Consequences for society and environment	EA5 Familiarity
✓	✓	✓	✓	✓

Addressing Engineering Activities (EA):

Engineering Activity	**Attainment**	**Justification**
EA1: Range of Resources	**Yes**	Utilizes Google Colab's GPU, open-source fMRI datasets, and tools like Nilearn and PyTorch Geometric for efficient data processing and GNN training.
EA2: Level of Interaction	**Yes**	Involves collaborative data preprocessing, model development, and visualization, integrating computational and neuroimaging expertise.
EA3: Innovation	**Yes**	Analyze caffeine-induced brain connectivity, advancing neuroimaging methods by using STGNN.

EA4: Consequences for Society and Environment	**Yes**	Contributes to cognitive science insights with potential health applications and uses cloud computing to minimize environmental impact.
EA5: Familiarity	**Yes**	Builds on established GNN and fMRI techniques, adapting them to explore new applications in brain connectivity research.

5.5 Summary

This chapter examines the engineering standards and design challenges of utilizing graph neural networks to model caffeine's effects on brain connectivity in Google Colab. It highlights compliance with software and hardware (CUDA-compatible NVIDIA T4 GPU) standards, alongside wireless communication protocols for cloud-based collaboration, ensuring reproducibility and integrity. Design challenges, such as optimizing models for Colab's GPU constraints, were addressed through efficient preprocessing with Nilearn/fMRIPrep and modular coding. Societally, the research enhances cognitive science and health insights. Environmentally, it balances computational demands with cloud-based, open-source tools (PyTorch, DGL) to minimize impact. Ethically, it ensures data privacy with public fMRI datasets and transparency to prevent misuse. The sustainability plan emphasizes reusable code and free Colab resources, promoting accessible research. The chapter blends technical rigor with societal considerations, presenting a comprehensive view of contemporary engineering challenge

Chapter 6

Conclusion

6.1 Summary

The primary goal of this work was to construct a more advanced classifier of brain state based on the fMRI data by tapping the spatial and temporal dependencies between brain activities across 116 ROIs of the Automated Anatomical Labeling (AAL) atlas [. Our model used a composition of three features GNN models, CNNGCN and TemporalGAT and TimeStaticGCN to extract different features from fMRI data and strong preprocessing pipeline that further performed the threshold of connectivity matrix at 0.1 correlation threshold. We utilized the GNNExplainer model to interpret the classification results and look for critical ROIs such as the precuneus and the frontal cortex, and registered them into a brain map in NIfTI format. To assess the model performance we performed 5-fold cross validation, given that this is common practice in neuroimaging studies. The system was implemented with the PyTorch Geometric and Nilearn libraries, while the user interface was made a web-based Dash app for result serving. This work makes valuable efforts to the interpretable spatio-temporal GNN application in brain state classification, and its less interpretation of deep learning and bridging to the state-of-the-art are both novel contributions as far as we know to the neuroimaging field.

6.2 Limitation

The study has some limitations which need to be taken into account. First, the fMRI data from 72 subjects is relatively small, which might limit the generalization of the models to other populations or different brain states. Second, the spatio-temporal GNNs, especially TemporalGAT with LSTM units, require high computation resources and may have poor accessibility for institutions without high-end infrastructures. Third, a fixed correlation threshold of 0.1 for the connectivity matrices, might be too simplistic for dynamic brain connectivity and lose out on subtle time fluctuations. Lastly, while GNNExplainer's interpretability is useful for understanding sub-graphs, it may not be very informative for explaining why caffeine works the way it does in this case, and would require additional domain knowledge to validate.

6.3 Future Work

The future study of this investigation should tackle existing limitations as researchers work to uncover additional research possibilities. The incorporation of larger diverse participant groups into the data set will boost model generic application and make possible the study of brain states and conditions such as sleep deprivation along with neurological disorders. The combination of EEG signals with behavioral parameters would produce a complete picture of neurobiological caffeine effects. Dynamic graph modeling that tracks how matrices change across time periods would present a superior method to measure brain networks that change over time. Graph Transformer models have the capability to analyze intricate neural network patterns in addition to typical Graph Neural Networks. The implementation of multi-task learning methods would permit simultaneous output of cognitive outcome evaluations and mental performance forecasts. The combination of electrophysiological validation with GNNExplainer would significantly improve interpretations that lead to stronger neurobiological findings.

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