PROJECT SEMESTER REPORT

MEG based classification of Mild Cognitive Impairment in a passive audiovisual task

and

EEG-Audio based multimodal classification of Major Depressive Disorder leveraging emotional attentional deficits

by

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Abbreviation	Full Form
MEG	Magnetoencephalography
MCI	Mild Cognitive Impairment
PSD	Power Spectral Density
ERP	Event Related Potential
AD	Alzheimer's Disease
SRT	Simple Reaction Time
CRT	Choice Reaction Time
CCRT	Cued Choice Reaction Time
MDD	Major Depressive Disorder
EEG	Electroencephalography
PET	Positron Emission Tomography
fMRI	functional Magnetic Resonance Imaging
HC	Healthy Control
ICA	Independent Component Analysis
LASSOCV	Least Absolute Shrinkage and Selection Operator
AAR	Adaptive Autoregressive Coefficients
ZORK	Zero-crossing Rate over Kurtosis
CNN	Convolutional Neural Network
RNN	Recurrent Neural Network
DSM	Diagnostic and Statistical Manual of Mental Disorders
MDLF	Multimodal Deep Learning Framework
CMAN	Cross-Modal Attention Network
DCNN	Deep Convolutional Neural Network
BiLSTM	Bi-directional Long Short-Term Memory
GUI	Graphical User Interface
TFA	Time-Frequency Analysis
PHQ-9	Patient Health Questionnaire-9

1. COGNITIVE ANALYTICS RESEARCH LAB, ULSTER UNIVERSITY, UK

1.1. Overview

The Cognitive Analytics Research Lab (CARL) at Ulster University is a pioneering initiative aimed at establishing a world-class research capability in cognitive analytics. CARL is designed to attract significant local and international industry engagement, along with foreign direct investment, positioning the region as a global leader in this emerging field.

Ulster University has a longstanding reputation for excellence in data analytics, both in terms of developing advanced machine learning algorithms and applying analytical techniques across various domains. The university boasts over 60 academic staff dedicated to this research, contributing across all subject areas. CARL aims to consolidate and expand this expertise, growing into a 200-person center of excellence over the next five years. This unique center is built from the ground up through collaborative consultation with industry and civic stakeholders, focusing on both economic and societal impacts.

Fig 1: Organization Logo

1.2. Research

Ulster University's extensive experience in data analytics is supported by substantial investments in several key facilities and projects. These include:

- **Centre for Stratified Medicine:** A £11 million investment focused on tailored healthcare solutions.
- **Functional Brain Mapping Facility:** A £5 million facility dedicated to understanding brain function.

- **MIDAS (Meaningful Integration of Data, Analytics, and Services):** A €4.5 million project aimed at integrating data analytics services.
- **Capital Markets Collaboration:** A £1 million initiative enhancing data analytics in financial markets.
- **Centre for Precision Medicine:** An €8.6 million project using data to improve clinical decision-making and patient safety.

CARL brings together these investments, totaling around £30 million, to create a consolidated research hub. This integration aims to foster international collaboration and achieve world-leading research outcomes in cognitive analytics.

1.3. Cognitive Analytics and Data Science at CARL

Cognitive analytics represents the next paradigm shift in data analytics, combining artificial intelligence (AI) and machine learning with advanced data analytics techniques. As data generation continues to accelerate, with 2.5 quintillion bytes created daily, cognitive analytics harnesses this vast data pool to deliver intelligent, human-like insights.

Cognitive analytics involves several intelligent technologies, including semantics, AI algorithms, deep learning, and machine learning. These technologies enable systems to learn and improve over time, enhancing their effectiveness and intelligence. This approach offers significant benefits, such as mining untapped data sources, providing highly personalized services, improving service consistency and quality, and enhancing knowledge sharing.

The application of cognitive analytics creates a competitive advantage for businesses by offering real-time answers, contextual understanding, and the ability to sift through massive amounts of information to find optimal solutions. This capability opens up new opportunities for businesses to leverage data for strategic gains.

Ulster University, with its rich history of research excellence in neuro-inspired cognitive analytics and a substantial track record in data analytics, is uniquely positioned to lead the way in cognitive analytics research. Through CARL, the university is set to make significant strides in this field, contributing to both academic advancements and practical applications that have a global impact.

MEG based classification of Mild Cognitive Impairment in a passive audiovisual task

ABSTRACT

This research project focuses on the implementation of machine learning based classification techniques on the Magnetoencephalography (MEG) signals for the detection of Mild Cognitive Impairment (MCI) by leveraging evoked potential p50 responses to paired auditory stimuli. MCI is a neurocognitive disorder which involves cognitive impairments beyond those expected based on an individual's age and education but which are not significant enough to interfere with most activities of daily living. It includes both memory and non-memory impairments.

MCI represents a critical area of investigation in cognitive research, particularly because it is a precursor to neurodegenerative conditions such as Alzheimer's disease and dementia. The International Working Group on MCI has highlighted a significant gap in our understanding of the specific functional changes associated with MCI, underscoring the need for further exploration in this field [1]. This project aims to address this gap by focusing on the intricate relationship between MCI and complex attentional deficits, particularly manifested as an inability to filter out redundant auditory signals.

Several studies have examined the nature of attentional impairments related to the capacity to divide and focus attention [3]. While these studies present reliable evidence for attentional deficits in early Alzheimer’s disease, controversy exists as to whether they necessarily co-occur with impairments of focused attention in MCI patients. In this work, we design a novel paradigm in which elderly healthy controls and people with MCI view a silent movie while experiencing occasional brief auditory clicks in pairs, acting as distractors. The participants undergo MEG scan while performing this task and also in resting state. By analysing the evoked potential P50 response to auditory stimuli and Event Related Potentials (ERPs), we found high classification accuracies between resting state and task state, as well as for anomaly detections of MCI, delineating neuromarkers specific to cognitive impairment. The proposed approach presents a novel avenue for early diagnosis and intervention strategies for MCI.

2. INTRODUCTION

2.1. Project Overview

In this study, we leverage a novel dataset comprising MEG signals of healthy individuals and MCI patients to employ time-frequency analysis and Event-Related Potentials and delineate markers specific to cognitive impairment in MCI. There are four subcategories of data for each subject, including interleaved eyes open and eyes closed signals, as well as signals corresponding to the 1st and 2nd auditory clicks. In terms of the final objective of the project, the development of binary classifiers and anomaly detectors enables the differentiation between resting state and task state data, as well as distinguishing between healthy individuals and MCI patients across various conditions.

2.2. Nature and Scope of Project

The practical implications of this study are multifaceted. Firstly, gaining a deeper understanding of the nature and extent of attentional impairments in individuals with MCI holds immense significance for early diagnosis and intervention strategies. Moreover, elucidating the specific functional changes associated with MCI can inform the development of targeted interventions tailored to address these deficits. Furthermore, the utilization of advanced neuroimaging techniques such as magnetoencephalography (MEG) offers a non-invasive means of assessing cognitive function, thereby enhancing our ability to detect and monitor cognitive decline over time. Therefore, this study has the potential to not only enhance our theoretical understanding of MCI but also translate this knowledge into practical applications that benefit individuals at risk of cognitive decline.

2.3. Objectives

The primary objective of this research project is to advance the understanding of Mild Cognitive Impairment (MCI) through detailed analysis of attentional deficits using MEG data. This goal is broken down into several specific objectives:

1. **Characterize Attentional Impairments in MCI:**

- **Investigate Attentional Deficits:** Utilize time-frequency analysis and Event-Related Potentials (ERPs) to examine attentional impairments in individuals with MCI, with a specific focus on the P50 evoked potential responses to paired auditory stimuli.
- **Compare with Healthy Individuals:** Differentiate the attentional profiles of MCI patients from those of healthy individuals by analyzing MEG data under varying conditions (eyes open, eyes closed, first and second auditory clicks).

2. **Data Preparation:**

- **Preprocess and Clean Data:** Implement robust preprocessing techniques, including temporal filtering, demeaning, and artifact correction using MATLAB's FieldTrip toolbox, to ensure high-quality data for analysis.

3. **Feature Extraction and Analysis:**

- **Derive Neural Signatures:** Extract meaningful features from Power Spectral Density (PSD) and Event-Related Potentials (ERPs) to identify neural markers associated with attentional deficits in MCI.
- **Develop suitable channel selection techniques:** Analyze features from different subsets of channels on the basis of their cerebral location or from specific auditory locations to determine the optimal channel subset for each category of data.

4. **Binary Classification:**

- **Feature Selection:** Employ LASSO with cross-validation (LASSOCV) and the SelectFromModel method to identify and retain the most informative features for model training.
- **Distinguish Resting and Task States:** Develop a binary classification model using a Random Forest Classifier to differentiate between resting state (eyes open and closed) and task state (paired auditory stimuli) data in both healthy individuals and MCI patients.

5. **Anomaly Detection:**

    - Implement a One-Class SVM model to detect anomalies in mixed shuffled data from healthy and MCI subjects after training the same on features of the channels selected

in objective 3. This is to be done for each of the four classes of MEG data, namely, eyes closed, eyes open, 1st auditory click response and 2nd auditory click response, thereby distinguishing healthy subjects from those with MCI.

6. **Research Contribution:**
    - To contribute to the field of MCI diagnostics by developing a focused attention based novel MEG pipeline. The findings and methodologies from this project are intended to be shared with the broader research community through publications and presentations.

By achieving these objectives, the project aims to bridge the existing knowledge gap in the functional changes associated with MCI, thereby contributing significantly to both cognitive research and clinical practice.

3. BACKGROUND AND RELEVANCE

Persons diagnosed with mild cognitive impairment (MCI) do not meet the criteria for Alzheimer's disease (AD) but are at elevated risk for its development. While functional impairments in dementia, AD, and schizophrenia have been extensively studied, limited research has focused on functional changes in MCI.

Presence of attention deficiency is a key component in the characterization of MCI and therefore, the identification of reliable neuromarkers indicating attention deficiency holds profound significance. These markers not only offer invaluable insights into the underlying neurobiological mechanisms but also harbor the potential to revolutionize early diagnosis and intervention strategies.

Sensory gating disturbances in MCI often manifest as an inability to filter redundant sensory stimuli, resulting in decreased inhibition of neuronal responses, particularly evident in the P50 wave [4]. In other words, these characterize a decreased ability of the brain to inhibit various responses to insignificant stimuli. Such deficits reflect various impairments in perceptual and attentional functions. Auditory sensory gating, extensively studied in schizophrenia [5], [6], [7],

[8], assesses cortical responses to recurring information and has demonstrated deficits in inhibitory mechanisms, suggesting its potential in identifying neuromarkers for MCI.

Additionally, the involvement of cholinergic pathways in modulating sensory gating mechanisms underscores its relevance in AD pathogenesis [4], suggesting a potential link between sensory gating deficits and cognitive impairment in MCI. The Posner model [2] provides a theoretical framework for understanding attentional networks involved in spatial attention, offering insights into deficits observed in Alzheimer's disease. Specifically, studies employing spatial cueing tasks reveal impaired disengagement of attention in Alzheimer's patients, indicating potential parallels with MCI-related attentional deficits.

Recent research [4] has highlighted the potential of utilizing evoked potential P50 responses to paired auditory stimuli as indicators of attention deficiency. These auditory stimuli are usually one of the three types of focused attention tasks [10], namely, simple reaction time tasks (SRTs), choice reaction time (CRTs) tasks or cued choice reaction time (CCRTs) tasks. In an SRT, subjects respond as rapidly as possible to a single stimulus whereas, in a CRT task, participants are required to carry out one of two response options based on the nature of the stimulus. A CCRT task involves exposure to a cue before stimulus presentation so as to assess a cueing effect. Attention deficits found in Schizophrenic subjects underscore slowed RTs [5], [6], [7], which provides evidence for the inability to benefit from a cue in cognitive impairment groups. Therefore, there is potential for utilizing attention deficiency to paired auditory stimuli in order to identify neuromarkers indicative of MCI.

Building upon established paradigms like sensory gating, which assess pre-attentive inhibition of redundant information and drawing parallels with findings in AD and Schizophrenia research, we hereby leverage a novel dataset comprising MEG signals recorded from both resting and task states. Our research endeavors to investigate differences in P50 responses to paired auditory clicks between healthy individuals and MCI patients. Drawing on methodologies from cognitive neuroscience and machine learning, our study seeks to classify resting state versus task state data for both healthy individuals and MCI patients, discerning patterns unique to cognitive impairment. Furthermore, we aim to explore additional channels indicative of auditory attention deficiency and develop binary classifiers and anomaly detectors to differentiate between healthy and MCI cohorts across various task conditions.

4. METHODOLOGY

This project aims to introduce an anomaly detection-based approach to identify neuro-markers of cognitive impairment or dysfunction, eventually laying the foundation for developing more efficient, robust early diagnostic strategies for MCI. We leverage the evoked p50 response to paired auditory click sounds in order to learn the distinction between healthy and MCI MEG data from a machine learning perspective. In addition, random-forest based binary classifiers are also designed to differentiate between resting state and task state ERPs for a given individual.

4.1. Dataset Description

The data utilized in this study were acquired using the MEGIN Triux Scanner, a state-of-the-art system renowned for its high-quality neuroimaging capabilities. The scanner records neural activity through 306 MEG channels, comprising 102 magnetometer and 204 gradiometer channels, ensuring comprehensive coverage of brain signals. Data were sampled at a frequency of 1000Hz, capturing rapid neural dynamics with precision.

The experimental design included interleaved conditions of eyes open and eyes closed, aimed at eliciting robust alpha rhythm activity. Participants received explicit auditory cues of "Open" and "Close" to indicate transitions between the two conditions. During eyes open epochs, subjects were instructed to maintain fixation on a central cross, minimizing eye movements and blinks to preserve data integrity.

Each condition was randomized in duration, varying between 12 and 18 seconds to prevent habituation effects. The total duration of the experiment spanned 8 minutes, comprising 32 trials in total, with a brief exclusion of the initial 2 seconds post-transition to mitigate potential artifacts associated with condition switching and blinking.

Furthermore, attentional processes were probed using an auditory sensory gating paradigm to assess inhibitory gating deficits, particularly relevant in conditions such as Alzheimer's disease. Paired clicks, characterized by a duration of 40 ms and an inter-stimulus interval of 500 ms, were presented at 60 dB above the individual's hearing threshold. Participants were engaged in a

secondary task, either watching a silent movie or reading, while instructed to ignore the auditory stimuli.

To ensure data validity, participants were advised to abstain from smoking and caffeine consumption at least 12 hours prior to the MEG session. The experimental setup allowed for 80 trials of paired clicks within an 8-minute duration, facilitating robust investigation of attentional processes.

Overall, the dataset comprises MEG signals recorded from 16 healthy subjects and 5 Mild Cognitive Impairment (MCI) subjects. There are four subcategories of MEG data for each subject, including interleaved eyes open and eyes closed signals, as well as signals corresponding to the 1st and 2nd auditory clicks. The comprehensive data acquisition parameters and experimental design employed in this study provide a rich dataset for investigating neural dynamics underlying resting-state activity and attentional processes, offering valuable insights into cognitive functioning and potential biomarkers of neurological disorders like Mild Cognitive Impairment.

4.2. Data Preprocessing

The dataset comprised MEG signals obtained from 16 healthy subjects and 5 subjects diagnosed with Mild Cognitive Impairment (MCI). Notably, one subset of the MCI dataset corresponding to eyes closed condition had 4 subjects. The preprocessing steps were performed in MATLAB using FieldTrip toolbox, where channels specified by the 'MEG' parameter were selectively processed and continuous data handling techniques are applied. Firstly, the raw MEG signals were loaded and subjected to temporal filtering, specifically a lowpass filter with a cutoff frequency of 40 Hz. This filtering helps remove high-frequency noise while retaining relevant neural signals, effectively isolating neural oscillations within the desired frequency band. Then, the data was demeaned to remove the mean from each channel, which helps in reducing the influence of DC offsets and ensuring that the data is centred around zero. Additionally, artifact correction was performed using a Z-score based automatic artifact rejection method implemented through the MATLAB Fieldtrip toolbox, ensuring the removal of noise and non-neural signals.

Through the implemented preprocessing pipeline, the initial dataset consisting of 306 MEG channels was streamlined into 102 channels of magnetometer readings and 204 channels of

gradiometer readings. Finally, the 204 planar gradiometer channels were selected and combined using the Pythagorean theorem, thus computing the magnitude of the magnetic field vector at the particular location on the scalp. This helps simplify data analysis and interpretation by reducing the dimensionality of the dataset to 102 gradiometer readings while preserving spatial information. This comprehensive preprocessing pipeline ensures that the MEG data is adequately filtered, normalized, and organized for subsequent analyses.

Before preprocessing, the trial duration for resting-state data was standardized to 10,000 ms. However, due to discernible noise patterns observed in the ERPs, the last 99 ms of each trial were excluded from analysis to ensure data integrity. Similarly, for task-state data, each trial initially spanned 400 ms, with the first 200 ms representing prestimuli duration. After preprocessing, which involved the exclusion of the initial 200 ms and the last 49 ms due to visible noise in the signal, the trial duration reduced to 9,901 ms for resting-state data and 151 ms for task-state data.

Table 1 presents a detailed summary of the dataset statistics, including the number of subjects, number of trials, trial durations before and after preprocessing, mean values across 102 channels, and standard deviations across 102 channels. These statistics were computed on the grand averaged MEG data using MNE-python. Subsequently, overall metrics were derived by averaging across all channels' means and standard deviations. The mean and standard deviation values provide valuable insights into the characteristics of neural activity within each subset, serving as essential metrics for understanding the neurophysiological processes underlying both healthy and MCI conditions.

Subset	Number of Subjects	Number of Trials	Trial Duration before preprocessing (ms)	Trial Duration after preprocessing (ms)	Mean (across 102 channels) (pT)	Standard Deviation (across 102 channels) (*0.1 pT)
Healthy Eyes Closed	16	256	10000	9901	4.57	7.36
Healthy Eyes Open	16	256	10000	9901	4.52	8.42

Healthy 1st Click	16	525	400	151	3.72	4.09
Healthy 2nd Click	16	548	400	151	3.98	3.39
MCI Eyes Closed	4	64	10000	9901	9.12	1.37
MCI Eyes Open	5	79	10000	9901	7.23	1.16
MCI 1st click	5	206	400	151	7.2	6.56
MCI 2nd Click	5	194	400	151	7.39	5.68

Table 1: Data statistics before and after preprocessing

4.3. Feature Extraction

For each subclass of the data, PSDs and ERPs were computed and utilized for feature extraction. The PSD of MEG data represents the distribution of power across different frequencies within the recorded neural signals. Extracting features from the PSD captures essential aspects of neural dynamics and can be crucial in distinguishing between different brain states or conditions. For example, features extracted from specific frequency bands, such as theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (>30 Hz), reflect distinct neural processes related to attention, memory, or motor function.

ERPs in MEG data refer to synchronized neural responses elicited by specific events or stimuli, such as sensory stimuli or cognitive tasks. ERPs are time-locked to the onset of the event, enabling the isolation and analysis of neural activity associated with particular cognitive or sensory events. In our study, these events consisted of paired auditory clicks presented while subjects viewed a silent movie. The first click served as a CRT task to assess focused attention, and the second click served as a CCRT task to evaluate the benefit of cue availability prior to stimulus presentation. Features such as peak amplitude, latency, duration, and spatial distribution of ERP components

encode essential information about cognitive processing, sensory perception, and neural dynamics. These features derived from the PSD and ERP provide valuable insights into the underlying neural mechanisms, aiding in the identification of biomarkers or neural signatures associated with specific cognitive tasks or neurological disorders.

In this study, the features were calculated from grand-averaged MEG data, averaged across trials for each subject, and subsequently across subjects. ERP features include peak amplitude, latency, area under the curve (AUC), slope, peak-to-peak amplitude, mean absolute amplitude, root mean square (RMS) amplitude, standard deviation, skewness, kurtosis, number of zero crossings, adaptive autoregressive coefficients (AAR), and zero-crossing rate over kurtosis (ZORK). Similarly, PSD features include power in the alpha band, power in the beta band, and spectral entropy in the alpha and beta bands. These features capture various aspects of MEG waveforms, providing insights into neural responses to specific stimuli or events.

By extracting these features for all data classes, we obtained a comprehensive feature set for each subject, where each of the 102 channels had 13 features extracted from ERPs and 4 features extracted from PSDs. These features form a robust corpus for exploring different channel selection, feature selection, and feature reduction techniques in the design of binary classifiers and anomaly detectors.

4.4. Training Pipeline for Binary Classification of Resting vs. Task State Data

The proposed training pipeline focuses on the binary classification of resting versus task state data for healthy and mild cognitive impairment (MCI) subjects. The following sections detail the preparation, feature selection, model training, and evaluation processes employed to develop robust classifiers for distinguishing between these two states.

- **Data Preparation and Labeling:** The initial step involves preparing the feature sets for both resting and task (movie) states by concatenating PSD and ERP features. Corresponding labels are assigned to these feature sets, with resting states labeled as 0 and task states labeled as 1. The resultant dataset, comprising both feature sets and their labels, has a dimensionality of (32, 1734) for healthy subjects and (9,1734) for MCI subjects.

- **Data Shuffling and Reshaping:** To ensure unbiased training and evaluation, the combined dataset is shuffled randomly. The shuffled feature set is then reshaped to consolidate the features of each sample into a single dimension, converting the dataset from a three-dimensional array (samples, channels, features) to a two-dimensional array (samples, consolidated features). This reshaped dataset, with dimensions (32, 1728) for healthy subjects and (9, 1728) for MCI subjects after removing any NaN values, forms the basis for subsequent training and evaluation steps.
- **Training and Testing Splits:** The training pipeline includes a repeated random splitting procedure to ensure robust evaluation. Specifically, the data is split into training and testing sets in 10 iterations, with each iteration using 80% of the data for training and the remaining 20% for testing. This procedure helps to mitigate the impact of data variability and ensures comprehensive model assessment. Consequently, the training set consists of 25 samples, and the testing set comprises 7 samples for resting state. The training set consists of 8 samples, and the testing set comprises 1 sample for task state.
- **Feature Selection Using LASSO:** Feature selection is performed using the LASSO (Least Absolute Shrinkage and Selection Operator) method with cross-validation (LassoCV). The LASSO method helps to identify and retain only the most relevant features for the binary classification task by imposing a penalty on the absolute size of the coefficients. The selected features from the training data are then used to transform both the training and testing sets, reducing the feature dimensionality while retaining the most informative features. This process ensures that the model is trained on a compact and relevant feature set.
- **Model Training and Cross-Validation:** A Random Forest classifier is employed for the binary classification task. To ensure the robustness and reliability of the classifier, a five-fold stratified cross-validation is performed during the training phase. This cross-validation approach helps to assess the model's performance across different subsets of the data, thereby providing a more reliable estimate of its generalizability. The classifier is then trained on the entire training dataset using the selected features.
- **Model Evaluation:** The trained model's performance is evaluated on the test set for each iteration. Classification metrics, including accuracy, precision, recall, and F1-

score, are computed for both classes (resting state and task state). The evaluation also includes macro-averaged and weighted-averaged metrics to provide a comprehensive assessment of the classifier's performance across different classes. The results from all iterations are averaged, and the standard deviations are computed to report the overall performance metrics.

4.5. Channel Selection for Anomaly Detection Tasks:

Due to the evident imbalance in the dataset, as shown in Table 1, accurately detecting MCI from MEG signals necessitates the design of anomaly detectors trained on data from healthy subjects. To achieve this, we focus on the healthy data subsets of each of the four experimental conditions: eyes closed, eyes open, 1st click, and 2nd click. Consequently, it is imperative to identify the optimal subset of channels and features from the healthy data that are most suitable for training these anomaly detectors. By selecting the best channels, we aim to enhance the performance and reliability of the anomaly detection models, ensuring robust and accurate detection of MCI in imbalanced datasets.

4.5.1 Resting state data:

Resting state data, encompassing both eyes closed and eyes open MEG signals, serves as a crucial source for understanding neural functioning, devoid of attention-related factors or evoked P50 auditory responses. Our methodology employs an iterative channel elimination technique, where we start with the initial set of 102 MEG channels and iteratively remove one channel at a time to form a temporary channel subset. For each temporary channel subset, we select the corresponding features from the healthy eyes closed and healthy eyes open feature corpora and compute the average classification accuracies obtained by training one-class SVM-based anomaly detectors for each condition. If the average performance improves, we proceed to the next iteration, keeping the eliminated channel excluded. Otherwise, we re-include the channel and continue with the next iteration. This iterative process results in the identification of a subset comprising 94 MEG channels, as illustrated in Figure 2. Given that all channels of the human brain are conductive of neural activity in the resting state, subsequent feature selection is deemed unnecessary for the feature corpus derived from the 94 selected channels.

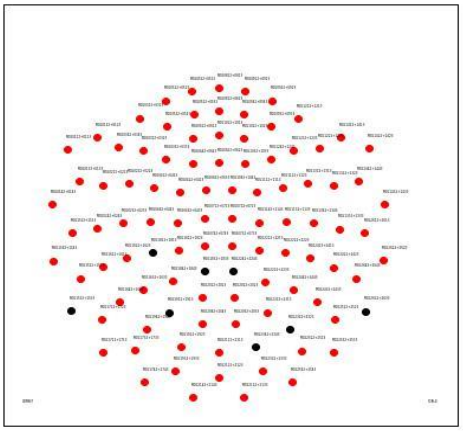


Fig 2: 94 channels selected after iterative channel elimination for resting state data

4.5.2 Task state data:

In the context of task state data encompassing paired auditory stimuli, a meticulous approach to channel selection, distinct from that employed for resting state data, is imperative. This two-phase channel selection strategy ensures the inclusion of MEG channels conducive to capturing both auditory gating deficits and other inhibitory mechanisms.

4.5.2.1 Phase One: Initial Channel Selection

The initial phase focuses on selecting the best channels from the left and right cerebral hemispheres that are most conducive to auditory processing. The methodology employed comprises the following steps:

1. **Pipeline Creation:** The pipeline integrates `SelectKBest`, a feature selection technique that identifies the best features based on statistical tests, and `OneClassSVM`, an algorithm suitable for identifying anomalies in the data.
2. **Parameter Grid Definition:** A parameter grid is established for the `SelectKBest` step, where ‘k’ represents the number of features to be selected. This grid includes a range of values for ‘k’, enabling systematic exploration of different numbers of selected features.
3. **Custom Scoring Function:** To evaluate model performance during the grid search, a custom scoring function based on the F1-score is defined. The F1-score, balancing precision and recall, provides a robust measure of the model's performance, particularly suitable for the anomaly detection task.

4. **Grid Search Implementation:** `GridSearchCV` is employed to conduct an exhaustive search over the specified parameter grid. This search leverages cross-validation to rigorously evaluate different configurations and identify the optimal value of ‘k’. Cross-validation ensures that the model's performance is assessed on multiple subsets of the data, enhancing the reliability of the selected features.
5. **Feature Selection:** The optimal value of ‘k’ obtained from the grid search is used to select the top ‘k’ features from the training data. This process ensures retention of only the most informative features, contributing to the robustness and accuracy of the anomaly detection model.

This pipeline is applied to 10 channels located on the left cerebral hemisphere in the auditory processing region and to 10 similar channels on the right cerebral hemisphere. The strategy results in the selection of features from two channels on the left side and a few features from a single channel on the right side.

4.5.2.2 Phase Two: Iterative Channel Selection

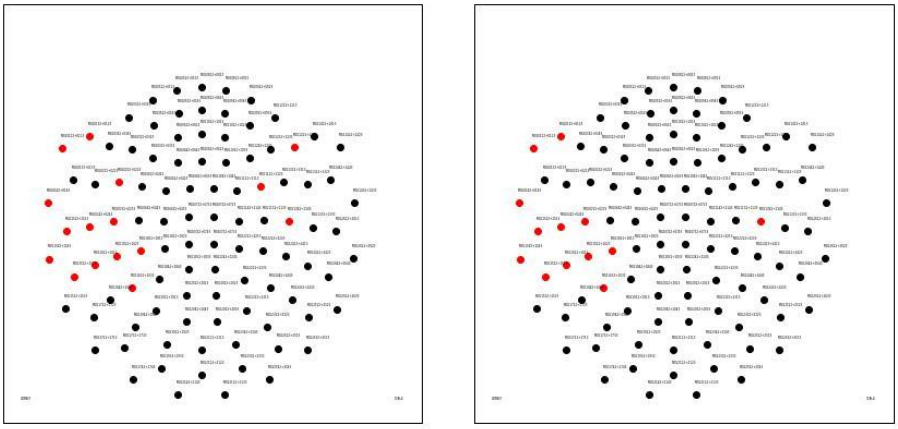
In the second phase, an iterative channel selection technique is employed. Starting with the data from 20 channels concerned with auditory processing—10 from each hemisphere—channels are iteratively added to the channel subset list. The inclusion of each remaining channel is tested to determine if it improves the average classification performance of a One-Class SVM-based anomaly detector. If the inclusion of a channel enhances performance, it is retained; otherwise, it is removed, and the next channel is tested. Additionally, an elimination strategy, analogous to the one used with resting state data, is applied to include only those channels that distinguish between healthy and MCI data patterns. This technique yields a subset of 15 channels deemed most useful.

4.5.2.3 Re-evaluation of 16 channel subset for 2nd click data:

The union of channels obtained from both phases results in an optimal subset of 16 MEG channels, as illustrated in Figure 3. This comprehensive selection strategy ensures the inclusion of channels that are most effective for capturing relevant auditory processing deficits and inhibitory mechanisms.

The final channel subset comprising 16 channels gives relatively poor results with 2nd click data. We further apply iterative channel elimination on these 16 channels, resulting in the exclusion of 3 channels.

Therefore, features from a subset of 16 channels are used for training a one-class SVM based anomaly detector for 1st click data and those from a refined 13 channel subset are used for training the anomaly detector for 2nd click data in the next phase of the project.



Optimal channel subset for 1st click data

Optimal channel subset for 2nd click data

Fig 3: Channels selected by the two-phase methodology for task state data

4.6. Training Pipeline for One-Class SVM-Based Anomaly Detection

In this section, we outline the training pipeline utilized for developing a one-class SVM-based anomaly detector for cognitive impairment detection. This method is consistently applied across four classes of training data, each representing different anomaly detectors but maintaining the same dimensionality. The training process involves several key steps, from data preparation to model evaluation, as described below.

4.6.1. Data Preparation

- **Data Structuring**:

Initially, the data is prepared by selecting features of the specific channels selected for that particular class of data in the Channel Selection process described in Section 4.5. Following are the changes in dimensions of data after this step:

Dataset (healthy & MCI)	Subjects	Initial Dimensions	After Reshaping
Resting State (for each eyes closed and eyes open)	21	(21,94,17)	(21,1598)
1st click	21	(21,16,17)	(21,272)
2nd click	21	(21,14,17)	(21,238)

Table 2: Dimensions of features selected for 4 classes of data before and after reshaping

- **Removal of Constant Features using Variance Filtering:**

  Features with constant values across all subjects are identified and removed. This step ensures that only informative features are retained for model training and evaluation, changing the dimensions of MEG data as follows:

Dataset (healthy & MCI)	Subjects	Initial Dimensions	After Variance Filtering
Resting State (for each eyes closed and eyes open)	21	(21,1598)	(21,1411)
1st click	21	(21,272)	(21,240)
2nd click	21	(21,238)	(21,182)

Table 3: Dimensions of features selected for 4 classes of data before and after variance filtering

- **Handling Missing Values using NaN Filtering:**

  Subsequently, any features containing NaN values are removed from the datasets. Only eyes open and eyes closed data subsets contained NaN valued features, which after removal, led to the following feature dimensions:

Dataset (healthy & MCI)	Subjects	Initial Dimensions	After NaN Filtering
Resting State (for each eyes closed and eyes open)	21	(21,1411)	(21,1405)
1st click	21	(21,240)	(21,240)
2nd click	21	(21,238)	(21,182)

Table 4: Dimensions of features selected for 4 classes of data before and after NaN filtering

- **Cross-Validation Setup: Permutation of Training and Testing Sets**

  To ensure robust model training, a cross-validation approach is employed. Initially, the dataset of healthy subjects is divided into two sets: Set A (first 11 subjects) and Set B (remaining 5 subjects). Each subject from Set A is iteratively replaced by each subject from Set B, creating a total of 55 unique permutations of training and testing sets. This procedure ensures comprehensive coverage and utilization of the available data.

- **Feature Selection Using Grid Search:**

  For each permutation, a GridSearchCV is employed to determine the optimal number of features to retain using `SelectKBest`. The grid search evaluates different values of `k` (number of features) and selects the value that maximizes the F1 score through cross-validation on the training data. The best set of features is then used to transform both the training and testing datasets, ensuring consistency and relevance in the selected features.

4.6.2. Anomaly Detection:

The one-class SVM model is trained on the processed training data. The testing set, comprising the remaining healthy subjects and all MCI subjects, is used to evaluate the model. The performance is assessed using several metrics, including accuracy, precision, recall, and F1 scores for both classes (healthy and MCI subjects). Additionally, macro and weighted averages of these metrics are calculated to provide a comprehensive evaluation of the model's performance.

We perform leave-one-out cross-validation on the training data, trains the one-class SVM, and evaluate it on the testing set. This returns detailed performance metrics for each iteration, which are aggregated to compute the mean and standard deviation of the performance scores across all permutations.

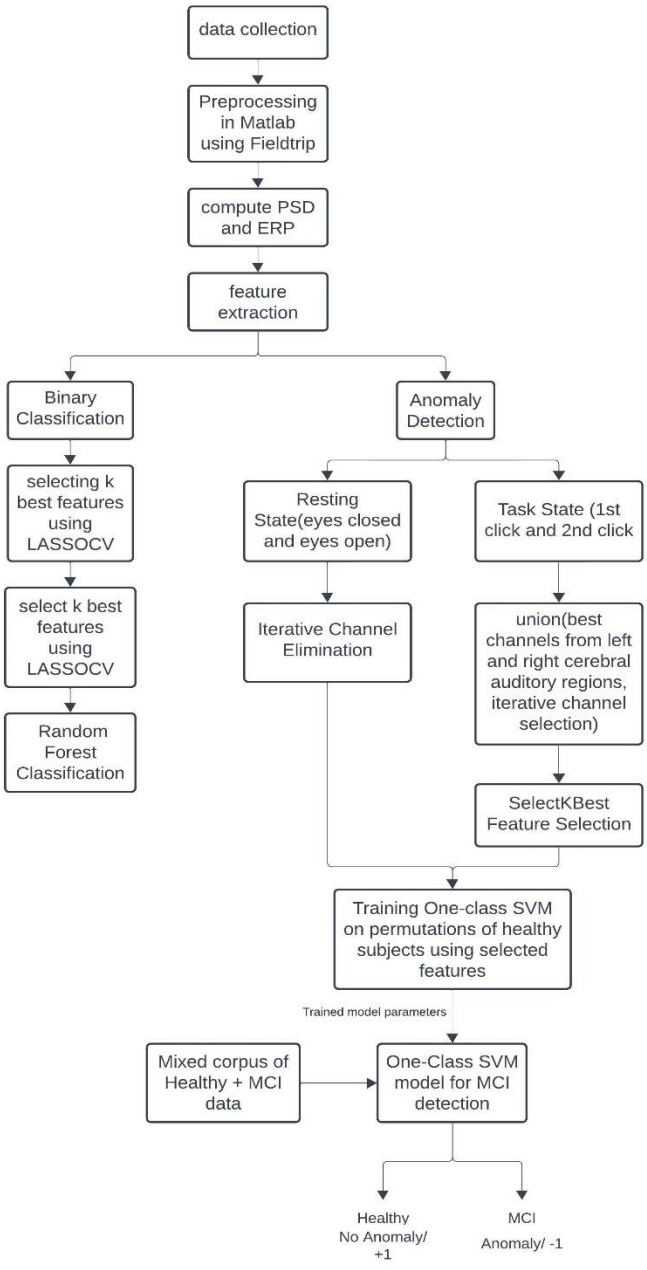


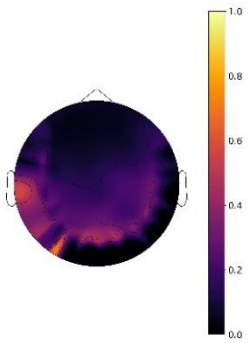
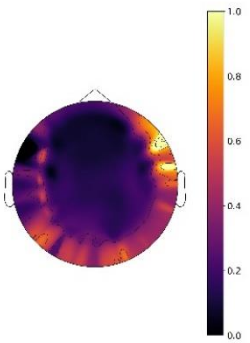
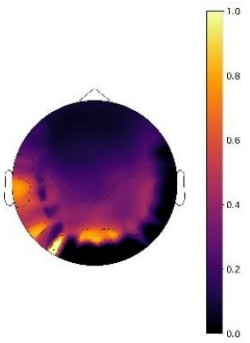
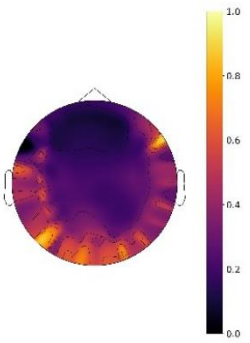
Fig 4: Workflow of the methodology adopted to machine learning based MCI detection from MEG data

5. OBSERVATIONS AND FINDINGS

5.1. Preliminary Data Exploration

In the preliminary phase of data exploration, we computed the band powers in the alpha and beta frequency bands for 10 categories of data, namely, (1) eyes closed healthy, (2) eyes closed MCI, (3) Eyes open healthy, (4) Eyes open MCI, (5) 1st click healthy, (6) 1st click MCI, (7) 2nd click healthy, (8) 2nd click healthy, (9) Movie state healthy, (10) Movie state MCI.

Figure 5 illustrates the marked differences in band powers across these categories. These figures reveal the potential of using ERP and PSD features for distinguishing between classes from a machine-learning perspective, thus guiding the methodology adopted in this research.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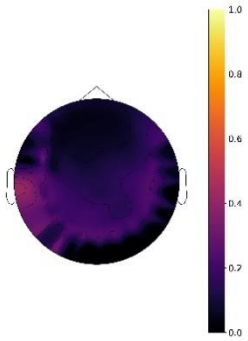
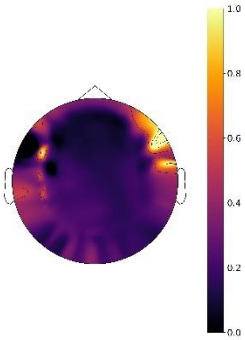
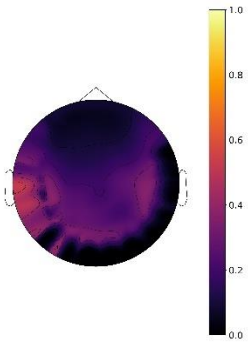
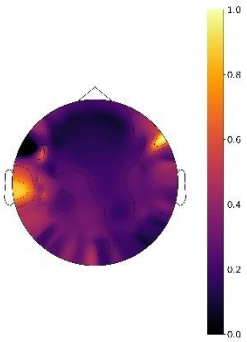
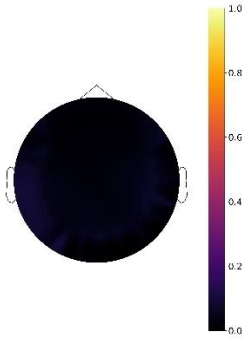
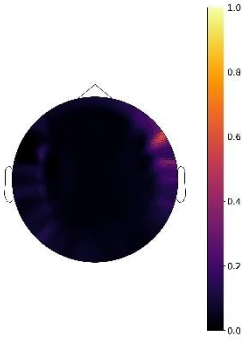
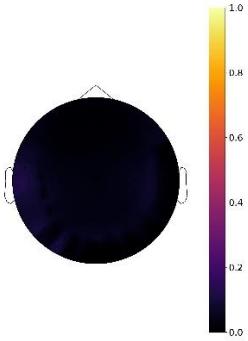
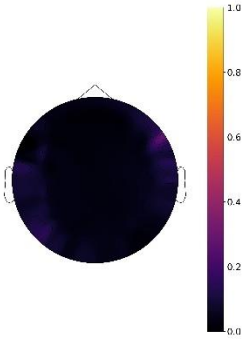
			
topoplot of eyes open data for healthy subjects in alpha frequency range	topoplot of eyes open data for MCI subjects in alpha frequency range	topoplot of eyes open data for healthy subjects in beta frequency range	topoplot of eyes open data for MCI subjects in beta frequency range
			
topoplot of movie state data for healthy subjects in alpha frequency range	topoplot of movie state data for MCI subjects in alpha frequency range	topoplot of movie state data for healthy subjects in beta frequency range	topoplot of movie state data for MCI subjects in beta frequency range

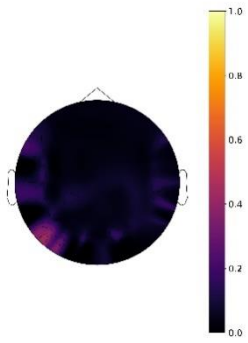
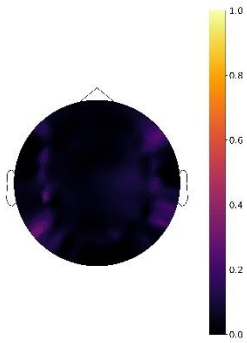
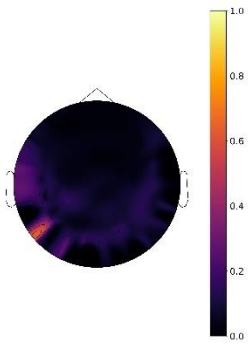
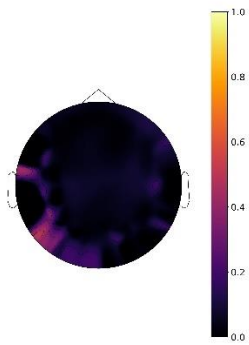
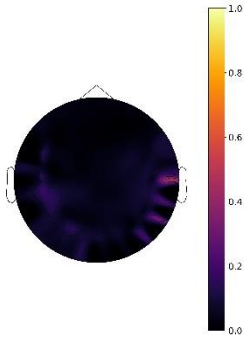
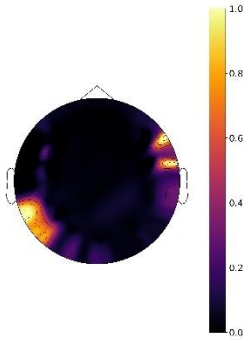
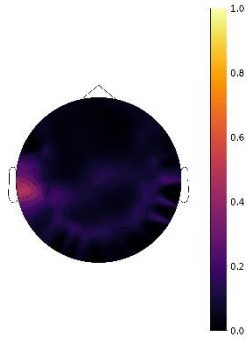
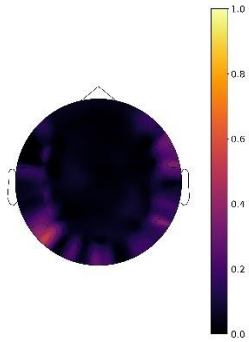
			
topoplot of 1st click data for healthy subjects in alpha frequency range	topoplot of 1st click data for MCI subjects in alpha frequency range	topoplot of 1st click data for healthy subjects in beta frequency range	topoplot of 1st click data for MCI subjects in beta frequency range
			
topoplot of 2nd click data for healthy subjects in alpha frequency range	topoplot of 2nd click data for MCI subjects in alpha frequency range	topoplot of 2nd click data for healthy subjects in beta frequency range	topoplot of 2nd click data for MCI subjects in beta frequency range

Fig 5: Band Powers of healthy and MCI subject data in Alpha and Beta frequency regions.

These preliminary results demonstrate significant variations in neural activity patterns between healthy and MCI subjects, as well as between different states (resting, task-related). These differences provide a foundational basis for the methodologies described in the previous sections and emphasize the feasibility of using machine learning techniques to differentiate between these conditions.

5.2. Binary Classification Results

1) Healthy Subjects: Resting vs. Task State

The binary classification results for healthy subjects, distinguishing between resting and task states, are as follows:

	Precision	Recall	F1 Score
Resting State	0.85 ± 0.30	0.88 ± 0.30	0.86 ± 0.29
Task State	0.97 ± 0.10	0.93 ± 0.11	0.94 ± 0.08
Macro Avg	0.91 ± 0.15	0.91 ± 0.17	0.90 ± 0.16
Weighted Avg	0.97 ± 0.05	0.94 ± 0.07	0.95 ± 0.06
Accuracy	0.94 ± 0.07		

Table 5: Performance metrics of random forest based classification on healthy subject data

These results indicate that the model can accurately distinguish between resting and task states in healthy subjects, with high precision, recall, and F1-scores.

2) MCI Subjects: Resting vs. Task State

The binary classification results for MCI subjects, distinguishing between resting and task states, are as follows:

	Precision	Recall	F1 Score
Resting State	0.69 ± 0.35	0.75 ± 0.35	0.67 ± 0.29
Task State	0.45 ± 0.47	0.50 ± 0.50	0.47 ± 0.48
Macro Avg	0.60 ± 0.34	0.65 ± 0.30	0.60 ± 0.33
Weighted Avg	0.70 ± 0.37	0.70 ± 0.24	0.67 ± 0.30

Accuracy	0.70 ± 0.24

Table 6: Performance metrics of random forest based classification on MCI subject data

While the model shows a reasonable performance in detecting resting states, its performance drops in identifying task states for MCI subjects, indicating the complexity of cognitive impairments affecting task-related neural activity.

5.3. Anomaly Detection Results

1) Resting State: Eyes Closed

	Precision	Recall	F1 Score
Healthy	0.56 ± 0.50	0.13 ± 0.12	0.21 ± 0.19
Mixed Population of Healthy and MCI data	0.48 ± 0.04	1.00 ± 0.00	0.65 ± 0.03
Macro Avg	0.52 ± 0.26	0.56 ± 0.06	0.43 ± 0.11
Weighted Avg	0.53 ± 0.29	0.52 ± 0.07	0.40 ± 0.12
Accuracy	0.52 ± 0.07		

Table 7: Performance metrics of one-class SVM based anomaly detection on eyes closed data

The results indicate that while the model can detect anomalies in mixed populations, its performance is limited when distinguishing healthy data.

2) Resting State: Eyes Open

	Precision	Recall	F1 Score
Healthy	0.95 ± 0.09	0.65 ± 0.16	0.76 ± 0.11

Mixed Population of Healthy and MCI data	0.75 ± 0.10	0.96 ± 0.08	0.83 ± 0.06
Macro Avg	0.85 ± 0.06	0.81 ± 0.08	0.80 ± 0.08
Weighted Avg	0.85 ± 0.06	0.81 ± 0.08	0.80 ± 0.08
Accuracy	0.81 ± 0.08		

Table 8: Performance metrics of one-class SVM based anomaly detection on eyes open data

The model performs significantly better in the eyes open condition, with high precision, recall, and F1-scores for detecting anomalies.

3) 1st Click

	Precision	Recall	F1 Score
Healthy	0.77 ± 0.10	0.71 ± 0.17	0.73 ± 0.12
Mixed Population of Healthy and MCI data	0.75 ± 0.12	0.79 ± 0.09	0.76 ± 0.06
Macro Avg	0.76 ± 0.09	0.75 ± 0.08	0.75 ± 0.09
Weighted Avg	0.76 ± 0.09	0.75 ± 0.08	0.75 ± 0.09
Accuracy	0.75 ± 0.08		

Table 9: Performance metrics of one-class SVM based anomaly detection on 1st click data

The model demonstrates robust performance in detecting anomalies during the 1st click condition, with balanced precision, recall, and F1-scores.

4) 2nd click

	Precision	Recall	F1 Score

Healthy	1.00 ± 0.00	0.63 ± 0.19	0.75 ± 0.15
Mixed Population of Healthy and MCI data	0.74 ± 0.11	1.00 ± 0.00	0.85 ± 0.07
Macro Avg	0.87 ± 0.05	0.81 ± 0.10	0.80 ± 0.11
Weighted Avg	0.87 ± 0.05	0.83 ± 0.08	0.80 ± 0.09
Accuracy	0.83 ± 0.08		

Table 10: Performance metrics of one-class SVM based anomaly detection on 2nd click data

The anomaly detection model for the 2nd click condition shows high precision and F1-scores, indicating strong performance in identifying cognitive impairment patterns.

6. CONCLUSIONS AND FUTURE WORK

6.1. Conclusions

The results from the binary classifications reveal that distinguishing between resting and task states is more accurate for healthy subjects compared to MCI subjects. This suggests that cognitive impairment introduces variability in neural responses, making it more challenging to classify states accurately.

Anomaly detection results show varying performance across different conditions, with notably better performance in eyes open resting state and auditory tasks compared to eyes closed resting state. These findings suggest that certain neural markers and conditions are more conducive to detecting anomalies associated with cognitive impairment. The results reveal that models perform better in task-related conditions (eyes open, 1st click, 2nd click) compared to resting states, suggesting that task-induced neural activity provides more discriminative features for detecting cognitive impairment.

Overall, the methodologies employed, including preprocessing, feature extraction, binary classification, and anomaly detection, provide a robust framework for identifying neuro-markers of cognitive impairment. The findings support the methodological approach of utilizing machine learning techniques on MEG data to identify neural markers of cognitive impairment, paving the way for developing early diagnostic strategies for Mild Cognitive Impairment.

Here are the key conclusions drawn from the results:

- **Effectiveness of Methodological Approaches:** The preprocessing pipeline implemented using MATLAB and FieldTrip toolbox effectively filtered and normalized MEG signals, enhancing the quality of data for subsequent analyses. This preprocessing was crucial for distinguishing neural oscillations and reducing noise, thereby preparing the data for accurate feature extraction.
- **Feature Extraction and Classification:** PSD and ERP features provided robust feature sets that captured essential aspects of neural dynamics. Binary classification results demonstrate that healthy subjects could be distinguished with high accuracy between resting and task states, whereas distinguishing these states in MCI subjects proved more challenging, indicating the variability introduced by cognitive impairment.
- **Anomaly Detection:** The application of One-Class SVM-based anomaly detectors showed promising results, particularly in task-related conditions such as eyes open and auditory stimuli tasks. This suggests that task-induced neural activity may serve as more discriminative for detecting cognitive impairment compared to resting-state conditions.
- **Implications for Early Diagnosis:** The methodologies explored lay a foundation for potential early diagnostic strategies for Mild Cognitive Impairment. By identifying neural markers associated with cognitive tasks and anomalies, this study contributes to ongoing efforts in understanding and diagnosing cognitive disorders at their early stages.

6.2. Learnings

This research project provided significant learnings that contributed to its successful completion:

- **Integration of Multimodal Data:** The integration of PSD and ERP features from MEG data highlighted the importance of multimodal approaches in capturing comprehensive

neural activity patterns. This approach allowed for a nuanced understanding of how cognitive tasks and resting states manifest in neurophysiological data.

- **Challenges in Cognitive Impairment Studies:** The complexities involved in distinguishing neural responses between healthy and cognitively impaired subjects underscored the need for refined methodologies and larger datasets. Future studies could benefit from addressing these challenges through more sophisticated feature selection and model optimization techniques.
- **Validation of Machine Learning Models:** The validation and evaluation of machine learning models across different conditions provided insights into their robustness and limitations. Understanding these aspects is crucial for translating research findings into clinical applications.

6.3. Future Work

Moving forward, several avenues for future research can build upon the findings of this study:

- **Longitudinal Studies:** Conducting longitudinal studies to track neural activity changes over time in individuals at risk of cognitive impairment could provide deeper insights into disease progression and the development of biomarkers.
- **Enhanced Feature Selection:** Exploring advanced feature selection techniques, including deep learning approaches, could improve the discriminative power of models in identifying subtle neural markers associated with cognitive states.
- **Clinical Translation:** Further validating the developed methodologies and models in larger clinical cohorts would be essential for their integration into clinical practice. This involves testing the models across diverse populations and demographic groups to ensure their robustness and generalizability.
- **Multimodal Integration:** Integrating MEG data with other neuroimaging modalities such as functional MRI (fMRI) or structural MRI could provide complementary insights into brain connectivity and structural changes associated with cognitive decline.

By pursuing these avenues, future research can advance our understanding of neural correlates of cognitive impairment and contribute to the development of effective diagnostic and therapeutic strategies.

BIBLIOGRAPHY

[1] Winblad, B et al. “Mild cognitive impairment--beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment.” *Journal of internal medicine* vol. 256,3 (2004): 240-6.

[2] Perry, R J, and J R Hodges. “Attention and executive deficits in Alzheimer's disease. A critical review.” *Brain: a journal of neurology* vol. 122 (Pt 3) (1999): 383-404.

[3] Baddeley, A D et al. “Attentional control in Alzheimer's disease.” *Brain: a journal of neurology* vol. 124, Pt 8 (2001): 1492-508.

[4] Thomas, Christine et al. “P50 gating deficit in Alzheimer dementia correlates to frontal neuropsychological function.” *Neurobiology of aging* vol. 31,3 (2010): 416-24.

[5] Adler, L E et al. “Schizophrenia, sensory gating, and nicotinic receptors.” *Schizophrenia bulletin* vol. 24,2 (1998): 189-202.

[6] Bramon, Elvira et al. “Meta-analysis of the P300 and P50 waveforms in schizophrenia.” *Schizophrenia research* vol. 70,2-3 (2004): 315-29.

[7] Vlcek, Premysl et al. “Sensory disturbances, inhibitory deficits, and the P50 wave in schizophrenia.” *Neuropsychiatric disease and treatment* vol. 10, 1309-15. 14 Jul. 2014

[8] Tregellas, J.R., Freedman, R. (2008), Nicotinic Cholinergic Cortical Dysfunction in Schizophrenia. In: O'Donnell, P. (eds) Cortical Deficits in Schizophrenia. Springer, Boston, MA.

[9] Vlcek, Premysl, and Petr Bob. “Schizophrenia, Bipolar Disorder and Pre-Attentional Inhibitory Deficits.” *Neuropsychiatric disease and treatment* vol. 18 821-827. 8 Apr. 2022

[10] Levinoff, Elise J et al. “Focused attention deficits in patients with Alzheimer's disease and mild cognitive impairment.” *Brain and cognition* vol. 57,2 (2005): 127-30.