Deep Learning Techniques for Brain Connectivity

Rabindra Khadka
Research Supervisor:
Prof. Anis Yazidi
Department of Computer Science,
Oslo Metropolitan University, Norway

June 15, 2021

1. **Introduction:**

   The increasing life expectancy and the rise in the proportion of elderly citizens in most developed countries have led to a critical question regarding sustainable healthcare assistance for elderly citizens in the context of increasing pressure over economic resources for the healthcare system. To put it in context, it is more expensive in terms of providing health care and social assistance for dementia patients than for cancer patients [3]. One of the conditions that are prevalent in the elderly population group is mild cognitive impairment (MCI), affecting more than 50 million people worldwide as mentioned in the report by AI-Mind [1]. MCI is the condition that reduces the ability of people to be self-caring and leads to social isolation, depression, and even mortality. MCI can further develop into dementia which is one of the biggest challenges that human society will face in the coming 30 years [2]. There are efforts to identify the early risks of cognitive impairment and to eliminate the time-consuming inefficient process for investigating the patient's conditions. This could help in taking timely steps to slow down the progress of the disease and map the prognosis which can also contribute to reducing the cost of dementia and MCI treatment. Intending to improve the early diagnosis of dementia, researchers are working on predicting the risk of dementia based on machine learning. [4, 5].

   Deep learning is one of the potential solutions for predicting the risk of MCI without the need for human interventions. Deep neural networks (DNN) have achieved state-of-art performance for classifying images or recognizing objects in images and videos [6] but the application of DNN has not been explored much in neuroimaging domain. Some of the caveats that exist while applying DNN in neuroimaging domain are; (i) Data Scarcity (ii) Data mismatch. Data Scarcity refers to the limited availability of neuroimaging datasets and can negatively affect the performance of deep learning models. Data mismatch refers to the failure of the model to generalize well in unseen test conditions or during deployment. It can be associated with inter-and intra- subject tests in the neuroimaging domain, plus the data acquisition shift while collecting the data. However, there are research works based on DNN using convnet, RNN, deep belief networks to extract features from Electroencephalogram (EEG) [7] with a moderate amount of dataset. EEG data signals are multi-channel recordings that explore the potential differences on the scalp induced due to cortical activity. EEG is widely used for biomarkers as it is obtained through the non-invasive procedure and is cost-effective too.

The state-of-art work for recognizing mental state from EEG signals applies manual feature selection and extraction procedures, which then adopts classical supervised learning to classify the features [8]. With the existing approaches, it is still possible to build good models by leveraging pre-processing techniques but that may not generalize well over the data signals received from multiple patients at different locations or even EEG signals from the same patient at different time intervals. Therefore, it is challenging to build a model that can generalize well not only to unseen EEG data coming from various brain activities but also with a limited amount of data. To handle these above-mentioned challenges, we propose to investigate some new methods based on deep learning with the aim of extracting robust biomarkers for predicting the risk of MCI and dementia. With the quest of developing robust deep learning methods that can generalize well during deployment, the proposed methods would also incorporate the explainability for the obtained predictions so that the important EEG features could be further curated in order to improve the model's performance. Explainability would also help in developing a trustworthy AI system that would allow encompassing the principle of fairness while serving the model.

2. Related Work

In some previous studies, features from EEG signals are extracted manually which is not so efficient as it is a time-consuming process and requires domain-specific trained personnel. For instance, the work done by [14] applies a manual feature selection process to select features from 1-d EEG time series data and then uses a supervised learning method to classify the states. The application of deep learning networks to medical imaging has shown some promising results and lately, it has been adopted to neuroimaging domain [9, 10, 11]. The work by Mirowski et al. [7] applies a convolutional neural network to discriminate features from EEG time series data. In the work by [4], the recurrent neural network is applied to learn representation from multiple channel EEG time series data by transforming the signal into a multi-dimensional tensor. Similarly, RNN architecture with gated recurrent units is used to learn a meaningful representation of brain activity from 1D time-series EEG data without manual interventions [12]. The obtained results demonstrate that deep learning models outperform the models trained with manually feature-engineered EEG data [4, 12, 13].

One of the above mentioned approaches [4] which requires 2D representation of EEG channels can cause information loss during flattening since mapping is done from 3D space to 2D. Furthermore, the above methods do not capture long range dependencies due to the limited memory capacity of RNN and CNN based models. Furthermore, all these above mentioned research work do not consider the model's performance under a limited dataset setting and also, the generalization capacity of the model is not tested with an inter-subject dataset or EEG dataset from different sources. In addition, these studies do not take into account the integration of the multi-modal data that can be recorded from an individual to predict the risk of MCI.

3. Research Questions

Extracting robust features from EEG signals without human intervention and training deep learning methods to predict the risk of MCI with good generalization capacity is challenging. During this research project, we seek answers to the following questions:

- How to extract robust features from EEG time series data with minimum or zero human interventions so that the topological structure of EEG channels is well explored to learn more discriminative EEG patterns?

- How can the challenge of data scarcity be handled in the neuroimaging domain while training deep learning models?
- Can we leverage the multi-modal data to better predict the risk of MCI or dementia?
- How to build a deep learning model with good generalization capacity that can handle EEG data shifts during deployment as EEG signals vary significantly across different subjects?
- How can the model's prediction be explained to clinicians/patients to design a trustworthy AI system?

4. Methods

A) Meta-Learning:

Meta-Learning is the notion of learning to learn by leveraging prior knowledge from various tasks [15]. The idea is to learn from different tasks with few examples and make predictions over a new task. The Model Agnostic Meta-Learning algorithm (MAML) [16] is one of the gradient-based meta-learning algorithms which demonstrates state-of-art result in image classification problem under the few-shot setting. Recent work by [18] is known as iMAML that overcomes some of the caveats related to computation and efficiency shown by MAML.

The concept of meta-learning is gaining popularity in the ML community recently as it allows one to learn from various tasks with only a few examples and then adapt to a new task quickly. The recent study by [17], works on the idea of a few shot learning which uses a meta-learning algorithm like MAML++ to decode brain activation maps and find useful biomarkers from EEG signal. However, there has not been much work with meta-learning in the field of neuroimaging. We aim to explore the efficacy of optimization-based meta-learning methods like MAML [16] and iMAML [18] with EEG time series data. The objective is to address the challenges posed by data scarcity and data shifts in neuroimaging domain while predicting the risk of MCI or dementia.

B) Graph based Recurrent Neural Network (GraphRNN):

The concept of GraphRNN [21] approach is to adopt the hierarchical recurrent neural network (RNN) to model the edge dependencies that incorporate the auto-regressive model in the graph-based deep learning network. Time varying signal can be viewed as a chain graph that can represent operations like temporal shifts using adjacency and Laplacian matrices. As the connection and sparseness of the adjacency matrix in RGNN closely relates to how the human brain is connected, this can be a suitable technique to capture robust patterns from EEG time series data. Graph based analysis of the human brain has been an ongoing study in the neuroscience field [20]. In a recent work by Zhong et al. [19], regularized graph neural network address the problem of data shifts due to noise or labeling discrepancy in the EEG data. They consider each channel as a node in the graph and applies simple graph convolution network method where they capture local and global inter-channel relationship.

During the project, we will seek answers to our questions by using Graph based RNN to extract robust biomarkers from EEG time series data as graph based neural networks preserve the local and global inter-channel relationship without human interventions. The GRNN model can be difficult to train and scale due to the need for back-propagation through many steps of RNN. One of the mitigation methods that can be explored would be using GNN to model the autoregressive generation process rather than RNN.

C) Deep Learning Architecture with Attention Mechanism:

The attention mechanism within a deep learning network is one of the most effective and influential ideas in the deep learning community [22]. It is relevant as it addresses the idea of identifying the most prominent and relevant information for the final prediction. The attention mechanism allows to explain the final prediction and increase the interpretability of the deep learning model. There has been some work in the neuroimaging domain like the work by Cisotto et. al [24] where they integrated attention mechanism with a recurrent neural network like LSTM to classify EEG signals. Another work by [25] proposed a multi-view attention network (MuVAN) that helps to learn fine-grained representation from multi-variate time series data.

We look to design deep learning architecture integrated with an attention module that can capture the importance of each electrode. Another possible solution would be enhancing the graph based neural network (GNN) with an attention mechanism to predict the risk of MCI and dementia from EEG signals. The goal would be to capture the relevant signals in both the spatial and time domains which would provide a reliable method to recognize robust features from EEG signals.

D) Multi-modal AI:

Previously, the diagnosis of dementia was done through clinical evaluation and cognitive tests which are part of neuropsychological tests. With the progress in the medical field, the diagnosis not only relies on clinical assessment but also on biomarkers from imaging like MRI, PET scans, EEG signals [26]. So, combining these tests and markers to make the early diagnosis is a challenge. Multi-modal intelligence is an emerging topic within the machine learning community. It allows to combine data in various forms and provides a more in-depth way to investigate a subject. Most of the studies related to MCI and dementia use single data modality to make predictions such as the risk of MCI or stages of MCI. Recently, there has been some research work on the application of multi-modal AI for the early diagnosis of dementia. The work by Leracitano et. al [27] applies multi-modal machine learning for the automatic classification of EEG recordings in dementia. Their results show that given the multi-modal input, the multi-layer perceptron outperforms other models like an autoencoder, logistic regression, and support vector machine. However, their study does not take into account the application of multi-modality with deep learning models.

We aim to seek to take a holistic approach to predict the risk of MCI and dementia by combining EEG data, MRI or PET scans, genomics data, and other clinical assessments. We look to co-align and co-fuse the extracted features i.e individual modality representations, to produce novel biomarkers useful for clinical practice with relation to early diagnosis of MCI and dementia. This would allow clinicians to understand how risk factors like family history of dementia and other genotype affect brain structure and functions across the lifespan of the individual subject in a holistic way.

5. **Ethics and Explainablity**

Experts in the field of artificial intelligence (AI) agree that for AI to be ethical, it needs to be explainable, transparent, and accountable. With the introduction of GDPR rules and the new AI regulation act by the EU commission [28], AI ethics have been the discussion topic in broader society. Now, AI engineers and scientists must focus on the explainability of their AI models as well.

When dealing with EEG signals and other forms of data from a variety of subjects, researchers should be aware of how the model makes decisions and also which part of the data or information is relevant for a particular output. Similarly, from the patients' perspective, they should be able to participate in the decision-making process with a consensual relationship with artificial intelligence. It is also important for the researchers to know if any kind of bias has been injected into the model through data so that the generalization capacity of the model can be improved.

During this project, we aim to recognize important features through explainable AI techniques and concurrently make deep learning models interpretable and reliable. Attention mechanism [22], gradients-based explanation techniques [29], SHAP [30], and LIME [31] methods can be adopted to explain the results from the deep learning networks.

6. **Progress Plan**

The following table depicts my progress plan. The Phd program is for 8 semesters (4 years) including the teaching/supervision task which is not shown in the table below. The plan includes literature review, preparing of research proposal, data collection and designing experiment set up, development of algorithm, deploying of the model, validation, external collaborations, thesis writing and submission. The table also includes the plan for summer work placement in relevant research department of an external university or a company. *External collaborations* refer to writing papers collaboratively, attending conferences and workshops, research collaborations with concerned actors, up-skilling, tutoring and other research related activities.

	Progress Plan for completing the Thesis											
	2021		2022				2023				2024	
	Aug-Oct	Nov-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun
Literature Review	■	■	■	■	■	■	■	■	■	■	■	■
Research Proposal	■	■	■									
External Collaborations	■	■	■	■	■	■	■	■	■	■		
Algorithm Development				■	■	■						
Experiments Setup						■	■					
Deployment and Validation							■	■	■	■		
Summer Placement					■				■			
Thesis write up		■		■		■	■	■		■	■	
Submission of thesis												■

Figure 1: Progress Plan for thesis completion

References

[1] Ira Haraldsen, Oslo University Hospital. In *https://cordis.europa.eu/article/id/429227-artificial-intelligence-for-dementia-prevention*

[2] Eibhlín Ní Ógáin, Katie Mountain. In *https://nestainvestments.org.uk/wp-content/uploads/2014/12/Remember-Me-v7.pdf , 2015*

[3] World Health Organisation. Dementia. In *www.who.int/en/news-room/fact-sheets/detail/dementia*

[4] Pouya Bashivan, Irina Rish, Mohammed Yeasin, Noel Codella. Learning Representations from EEG with Deep Recurrent-Convolutional Neural Networks. In *ICLR 2016*

[5] SK Walters, S Hardoon , I Petersen, S Iliffe, R Z Omar, I Nazareth, G Rait. Predicting dementia risk in primary care: development and validation of the Dementia Risk Score using routinely collected data . In *https://pubmed.ncbi.nlm.nih.gov/26797096/,2016*

[6] Karpathy, Andrej and Toderici, G. Large-scale video classification with convolutional neural networks. In *Computer Vision and Pattern Recognition (CVPR), pp. 1725–1732, 2014. doi: 10.1109/CVPR.2014.223.*

[7] Mirowski, Piotr, Madhavan, Deepak, LeCun, Yann, and Kuzniecky, Ruben. Classification of patterns of EEG synchronization for seizure prediction. In *Clinical Neurophysiology, 120(11):1927–1940, 2009. ISSN 13882457. doi: 10.1016/j.clinph.2009.09.002.*

[8] Subasi, Abdulhamit and Ismail Gursoy, M. EEG signal classification using PCA, ICA, LDA and support vector machines. In *Expert Systems with Applications, 37(12):8659–8666, dec 2010. ISSN 09574174. doi: 10.1016/j.eswa.2010.06.065.*

[9] Z Yang, S Zhong, A Carass, S H Ying, and J L Prince. In *Pro-ceedings of MICCAI 2014 Machine Learning in Medical Imag- ing (MLMI) workshop, chapter Deep Learning for Cerebellar Ataxia Classification and Functional Score Regression, pages 68–76. Springer International Publishing, Cham, 2014*

[10] S Liu, S Liu, W Cai, S Pujol, R Kikinis, and D Feng. Early Diagnosis OF Alzheimer's Disease With Deep Learning. In *IEEE ISBI, pages 677–680, Beijing, 2014. IEEE.*

[11] T Brosch and R Tam. Manifold learning of brain MRIs by deep learning. In MICCAI, volume 8150 LNCS, pages 633–640. Springer, 2013.

[12] Subhrajit Roy, Isabell Kiral-Kornek, and Stefan Harrer. ChronoNet: A Deep Recurrent Neural Network forAbnormal EEG Identification . In *Signal Processing (eess.SP),2018*

[13] Silvia López. Automated Interpretation of Abnormal Adult Electroencephalograms. In *https://www.isip.piconepress.com/ publications/* $ms_theses/2017/abnormal/$, 2017.

[14] Lotte, F and Congedo, M. A Review of Classification Algorithms for EEG-based Brain-Computer Interfaces. In *Journal of neural engineering, 4:1–24, 2007.*

[15] Thrun, S., Pratt, L.: Learning to learn (2012).

[16] Finn, C., Abbeel, P., Levine, S.: Model-agnostic meta-learning for fast adaptation of deep networks. In *International Conference on Machine Learning. pp. 1126–1135(2017)*

[17] Myriam Bontonou, Giulia Lioi, Nicolas Farrugia, Vincent Gripon. Few-shot Decoding of Brain Activation Maps. In *Machine Learning (cs.LG),2020*

[18] Rajeswaran, A., Finn, C., Kakade, S., Levine, S.: Meta-learning with implicit gradients. In: *33rd Conference on Neural Information Processing Systems (NeurIPS)* 2019) (2019)

[19] Peixiang Zhong, Di Wang, Chunyan Miao, EEG-Based Emotion Recognition Using Regularized Graph Neural Networks. In *https://arxiv.org/pdf/1907.07835.pdf, arXiv, 2020*

[20] E. Bullmore and O. Sporns, "Complex brain networks: graph theoretical analysis of structural and functional systems," In: *Nature Reviews Neuroscience, vol. 10, no. 3, p. 186, 2009.*

[21] J. You, R. Ying, X. Ren, W.L. Hamilton, and J. Leskovec. GraphRNN: Generating realistic graphs with deep auto-regressive models. In *ICML, 2018.*

[22] Alana de Santana Correia, Esther Luna Colombini. Attention, please! A survey of Neural Attention Models in Deep Learning. In *CoRR, 2021.*

[23] Ashish Vaswani, Noam Shazeer, Niki Parmar, Jakob Uszkoreit, Llion Jones, Aidan N. Gomez, Lukasz Kaiser, Illia Polosukhin . Attention Is All You Need. In *NIPS 2017.*

[24] Giulia Cisotto, Alessio Zanga , Joanna Chlebus , Italo Zoppis, Sara Manzoni,and Urszula Markowska-Kaczmar . Comparison of Attention-based Deep Learning Models for EEG Classification. In *BIOSIGNALS. 2020, pp. 214–219.*

[25] Y. Yuan, G. Xun, F. Ma, Y. Wang, N. Du, K. Jia et al., "Muvan:A multi-view attention network for multivariate temporal data," In *IEEE International Conference on Data Mining, ICDM, ser. 2018 IEEE International Conference on Data Mining, ICDM 2018. United States: Institute of Electrical and Electronics Engineers Inc., 2018, pp. 717–726.*

[26] Xin Y. Zhang, Zhen L. Yang, Guang M. Lu, Gui F. Yang,* and Long J. Zhang . PET/MR Imaging: New Frontier in Alzheimer's Disease and Other Dementias. In *Front Mol Neurosci. 2017; 10: 343.*

[27] Cosimo Ieracitano, Nadia Mammone, Amir Hussain, Francesco C. Morabito. A novel multimodal machine learning based approach for automatic classification of EEG recordings in dementia. In *IRCCS Centro Neurolesi ,176-190 ,2020*

[28] https://digital-strategy.ec.europa.eu/en/library/proposal-regulation-laying-down-harmonised-rules-artificial-intelligence

[29] Simonyan, K.; Vedaldi, A.; Zisserman, A. Deep inside convolutional networks: Visualising image classification models and saliency maps.In *arXiv 2014, arXiv:1312.6034.*

[30] Lundberg, S.M.; Lee, S.I. A unified approach to interpreting model predictions. In *Proceedings of the Advances in Neural Information Processing Systems, Long Beach, CA, USA, 4–9 December 2017; pp. 4765–4774*

[31] Garreau, D.; von Luxburg, U. Explaining the Explainer: A First Theoretical Analysis of LIME. In *Proceedings of the 23rd International Conference on Artificial Intelligence and Statistics, AISTATS 2020, Palermo, Sicily, Italy, 26–28 August 2020; Volume 108, pp. 1287–1296*