FUNCTIONAL NETWORK CONNECTIVITY BASED MENTAL HEALTH CATEGORY PREDICTION FROM REST-FMRI DATA

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ABSTRACT

One of the most significant health issues the world is now experiencing is mental health. Since it is challenging to measure, it fails to motivate behavioral change or other interventions targeted at improving it. The lack of such measurements discourages learning and behavior modification, which are critical for enhancing healthy habits. Neuroimaging promises to provide a window into mental health. The use of resting fMRI (rs-fMRI) models capable of categorizing mental health at the individual level has the potential to provide insights into how it impacts the brain. Here, we applied a deep learning approach to classify a mental health score using static functional network connectivity (FNC) derived from rs-fMRI data. Comparisons were made against traditional machine learning approaches to evaluate the model's performance. The discriminative features present in each mental health category were analyzed for interpreting the deep learning model. The experiments resulted in a classification accuracy of 91%, 91%, 100%, and 100% for excellent, good, fair, and poor mental health classes. Results also highlighted the most salient brain network in the sFNC matrix for each mental health score classification.

***Index Terms*—** Mental health, rs-fMRI, static functional network connectivity, deep learning

1. INTRODUCTION

Mental health disorders are characterized by a clinically significant impairment in a person's intellect, emotional control, or behavioral conduct. On the other hand, a mental health condition is a term that encompasses mental diseases, psychosocial impairments, and mental states linked to considerable distress, functional impairment, or risk of self-harm. According to the World Health Organization, the COVID-19 pandemic caused an increase in the number of people affected by anxiety and depression disorders in 2020 [1, 2]. Initial projections indicate a 26% and 28% increase in anxiety and severe depressive disorders, respectively, in just one year. Therefore, it is crucial to monitor mental health to identify and address any underlying mental illnesses. In recent years many scientists sought to identify mental disorders using MRI-based data. Many studies focus on categorizing each MRI scan as coming from a patient, or a healthy control, and diagnosing the condition [3]. In the case of schizophrenia, a summary of the classification performance showed a high prediction performance with sMRI and fMRI followed by diffusion-weight MRI. Moreover, some studies also used various clinical measures such as Depression, Inventory-II (BDI-II) [4] and Positive and Negative Affect Schedule (PANAS) [5] for assessing the symptoms related to depression and mood.

With the increasing application of machine learning models in fMRI data, several studies have used static functional network connectivities (sFNC) for classification tasks [6, 7]. In this work, we use sFNC matrices and the self-reported measures of mental health collected from the UK Biobank database to predict the mental health score category for each subject. The subjects are classified into four categories es corresponding to excellent, good, fair, and poor mental health. The sFNC matrices are passed into a 1-dimensional convolutional neural network (1D-CNN) to extract the relevant connectivity measures for distinguishing the mental health classes. The main contributions of this work are (1) the use of neuroimaging data to predict mental health (2) the proposed novel approach to flexible prediction allowing any combination of scores to contribute to a given question (3) the use of deep learning to predict health category from neuroimaging data (4) visualization of both brain function relevant to each category, and relevant questions for each category.

2. METHODS

2.1. Data Acquisition and Preprocessing

The neuroimaging dataset used in this study is the UK Biobank (UKB) [8]. After a quality check on the subject fMRI scans, 1000 people were initially selected for the study, with participants ages ranging from 52 to 85. The sex distribution of the subjects in the dataset was also evenly distributed. On the 4D preprocessed UKB rs-fMRI data, a fully automated spatially constrained ICA was applied using the NeuroMark technique [9]. Later, after spatially matching correlated group-level independent components (ICs) between two healthy control fMRI datasets, a template of replicable independent components (ICs) was generated using the Neuromark method. The identified highly replicated intrinsic connection networks (ICNs) were used as the network templates which acted as a prior for spatially constrained ICA algorithm that was applied independently to each UKB subject. This analysis found 53 functionally relevant resting-state networks (RSNs) and corresponding time courses (TC). Further, these RSNs are categorized as subcortical (SC), auditory (AUD), sensorimotor (SM), visual (VS), cognitive control (CC), default mode (DM), and cerebellar (CB) domains. The Pearsons correlations between the TCs of ICNs were also computed to derive the sFNC. The degree of interconnectivity between the various ICNs was described by using the sFNC.

The mental health measures used in this study consist of a set of self-report questions related to mental health included in the UKB. Table 1 summarizes different mental health questions used in the experiments. The first 12 questions were used to calculate the Eysenck Neuroticism score. Neuroticism is characterized by high adverse effects, such as depression and anxiety. The summed-up neuroticism scores helped classify the subjects with bipolar disorder and severe depression [10]. The four self-report questions from 14-17 measured the state-level depression on the day of scanning. They indicated four different depressive domains that measured depressed mood, disinterest, restlessness, and tiredness. Similar measures were considered in the commonly used Hamilton Depression Rating Scale (HAM-D) [11] and the Montgomery–Asberg Depression Scale (MADRS) [12]. These questions were asked the day of the imaging scan, and hence it provides a timely assessment of a subject's mental state, compared to other questions, which were assessed at a different time point from the imaging scan. The rest of the questions helped evaluate the probable depression status. Hence combining these questions enabled the calculation of a mental health score for each subject. Therefore, the summed score across these questionnaires ranged between 0-20. These scores were further divided into four categories for the classification task as shown in Table 2. The proposed deep learning model classified each subject into its corresponding mental health category.

Table 1. Mental health questions used for calculating the mental health score.

No.	Mental health questions
1.	Mood swings
2.	Miserableness
3.	Irritability
4.	Sensitivity/hurt feeling
5.	Fed-up feeling
6.	Nervous feeling
7.	Worrier/anxious feeling
8.	Tense/highly strung
9.	Worry to long after embarrassment
10.	Suffer from nerves
11.	Loneliness/isolation
12.	Guilty feelings
13.	Risk taking
14.	Frequency of depressed mood in last two weeks
15.	Frequency of unenthusiasm/disinterest in last two weeks
16.	Frequency of tenseness/restlessness in last two weeks
17.	Frequency of tiredness/lethargy in last two weeks
18.	Seen doctor gp for nerves, anxiety, tension or depression
19.	Seen a psychiatrist for nerves, anxiety, tension or depression
20.	Illness, injury, bereavement, stress in last two years

Table 2. Mental health questionnaire classification

Mental health score	Level of mental health
0-5	Excellent
5-10	Good
10-15	Fair
15-20	Poor

2.2. Deep Learning Model

Fig 1 shows the 1D-CNN architecture used for the proposed mental health score estimation. The network uses three convolutional layers of kernel size 3 with 16, 32, and 64 filters for each layer. All convolutional layers and two fully connected layers are followed by the rectified linear unit (ReLU) activation layer. Max-pooling layers are added to the model to reduce feature maps' dimensionality and avoid overfitting. Another regularization technique used in this model is a batch normalization layer, which helps to normalize the previous layer's output. Hence it accelerates and stabilizes the training of the overall model. Additionally, a dropout layer is also used to prevent overfitting. It works by randomly disabling specific neurons with a probability p. This prevents the network from relying too much on the dropped-out neurons and forces the rest to learn more robust features. Thus, the model uses 3 Max-pooling layers of kernel size 2, three batch-normalization layers, and a dropout layer with a probability of 0.5. The feature maps from the dropout layer are flattened and then fed into the following fully connected layers. The first two fully connected layers have 64 and 16 neurons. In contrast, the final fully connected layer has four neurons with a Softmax activation layer that outputs the probabilities associated with each class. We use TensorFlow and Keras to implement the 1D-CNN architecture in this paper.

2.3. Training Criterion

The proposed CNN is trained for 100 epochs using the Adam optimizer with a learning rate set to 0.001. The learning rate has a decay factor of 0.95 and the training is done using a batch size of 8. The dataset is split at subject level and in the experiments, 70% of the data is used for training, 10% for

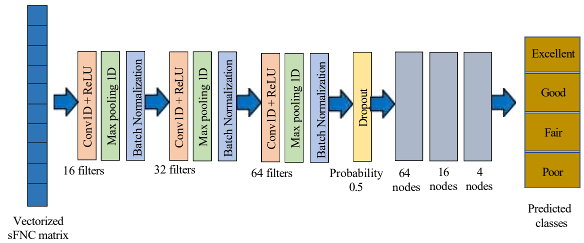


Fig. 1. Architecture of the proposed 1D-CNN. This model comprises convolutional layers, max-pooling layers, batch normalization layers, dropout, and fully connected layers.

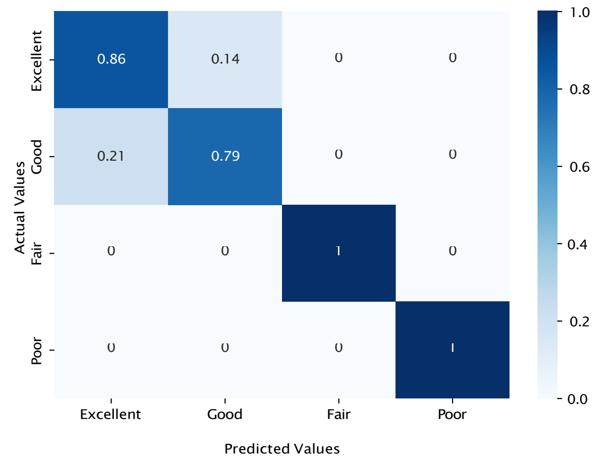


Fig. 2. Confusion matrix of multiclass classification of mental health category using 1D-CNN.

validation and the rest are used for testing. Since the data was imbalanced for the four different classes, Synthetic Minority Over-sampling Technique (SMOTE) [13] was used to create a balanced dataset. It is an approach in which the minority class is over-sampled by creating synthetic examples rather than by over-sampling with duplicated real data entries. Depending upon the amount of over-sampling required, neighbors from the k nearest neighbors of a sample from the minority class are randomly chosen. This resulted in about 1710 samples in training, 190 in validation and 476 in testing.

3. RESULTS AND DISCUSSION

The proposed 1D-CNN was trained and tested for mental health classification tasks on the UKB dataset. The network uses k-fold cross-validation with k=5 to evaluate the robustness and generalization of our proposed network. Fig 2 shows the final confusion matrix for the four mental health categories. From the confusion matrix, all poor and fair mental health cases are classified correctly with no misclassification. On the other hand, in excellent and good mental health cases, few of the subjects were misclassified.

In order to visualize the separability between the classes, t-Distributed Stochastic Neighbor Embedding (t-SNE) [14] was used in the 1D-CNN. It is an unsupervised method for visualizing the arrangement of data in high-dimensional space. This method helped to project the 16-dimensional representations of subjects extracted from the last hidden layer of the trained 1D-CNN model to a 2D plane. Fig 3 shows the internal representation of the four categories in the samples used for testing. The tSNE result denotes that the proposed model could filter features successfully and separate the different categories.

The multiclass receiver operating characteristic (ROC) curve for 1D-CNN for the four mental health classes is shown in Fig 4. When the curves are closer to the top-left corner, it denotes better performance. In this multiclass model, we

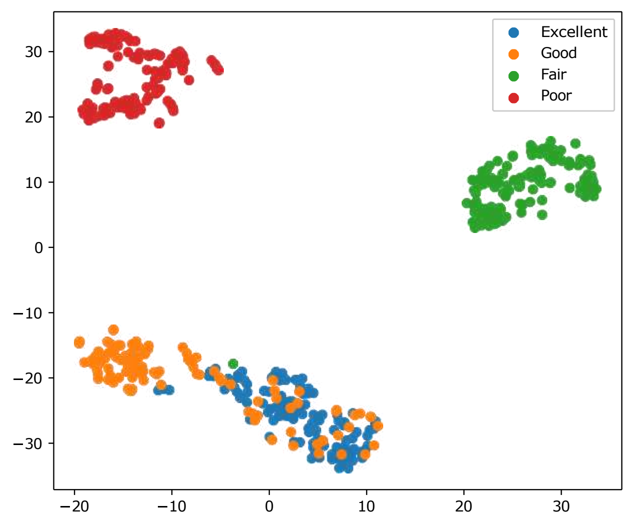


Fig. 3. t-SNE visualization of the last hidden layer representation in the proposed 1D-CNN

plot the 4 ROC curves using the one vs. all methodology associated with the mental health categories. The area under the ROC curve (AUC) tells us how much the model can distinguish between classes. In this case, the 1D-CNN achieves a significantly high AUC of 0.96, 0.96, 1, and 1 for excellent, good, fair, and poor mental health classes.

We compared the proposed 1D-CNN with three traditional machine learning classifiers such as Support Vector Machine (SVM), Random Forest (RF), Naive Bayes, and Deep Neural Network (DNN), as shown in Table 3. The input for training all the models is the sFNC matrix. The table illustrates that all the models achieve competitive sensitivity, specificity, accuracy, and AUC for the fair and poor mental

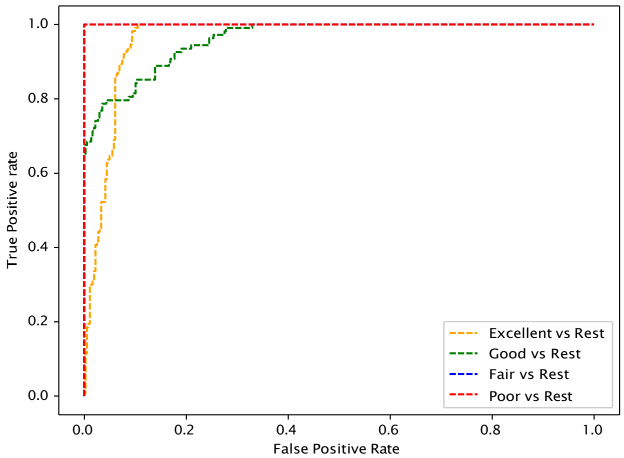


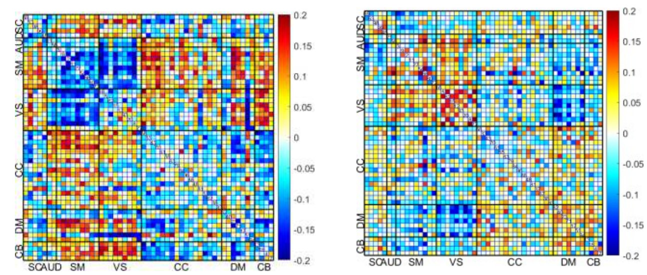
Fig. 4. Multi-class ROC curves using the proposed 1D-CNN.

health categories. It also shows that the worst-performing mental health categories are excellent and good. In the case of the excellent mental health category, the 1D-CNN achieves the best performance with sensitivity 85%, specificity 93%, accuracy 91%, and AUC 0.96 due to CNN's ability to learn higher-level structural and spatial features present in the connectivity measures. The improvements demonstrate that CNN can effectively capture discriminative information that could reveal significant relationships between mental health and rs-fMRI.

Table 3. Mental health classification performance and comparison of the proposed method with various state-of-the-art machine learning models.

Models	Classes	Sensitivity	Specificity	Accuracy	AUC
SVM	Excellent	63%	86%	80%	0.89
	Good	67%	88%	83%	0.90
	Fair	90%	98%	96%	0.99
	Poor	100%	100%	100%	1
Random Forest	Excellent	67%	90%	84%	0.92
	Good	73%	88%	85%	0.92
	Fair	96%	100%	99%	0.99
	Poor	100%	100%	100%	1%
DNN	Excellent	57%	91%	69%	0.79
	Good	73%	89%	68%	0.89
	Fair	99%	96%	90%	0.99
	Poor	100%	100%	100%	1
Naive Bayes	Excellent	57%	86%	58%	0.85
	Good	36%	86%	46%	0.73
	Fair	80%	92%	60%	0.86
	Poor	85%	100%	100%	0.98
Proposed 1D-CNN	Excellent	**85%**	**93%**	**91%**	**0.96**
	Good	**78%**	**95%**	**91%**	**0.96**
	Fair	**100%**	**100%**	**100%**	**1**
	Poor	**100%**	**100%**	**100%**	**1**

The histogram analysis of the responses to each question determined the top contributing questions in each category. Table 2 shows that excellent mental health corresponds to a low score ranging from 0-5. The contributing questions in this category were sensitivity/hurt feelings, worrier/anxious feelings, worry too long after embarrassment, risk-taking, and the frequency of tiredness/lethargy in the last two weeks. Secondly, in the case of the good mental health category, mood swings, miserableness, sensitivity/hurt feelings, fed-up feelings, worrier/anxious feelings, worry too long after embarrassment were the most important questions. There is a significant overlap between these two categories. Thirdly, the fair mental health category had all the questions mentioned in the good category along with irritability, nervous feeling, tense/highly strung, suffer from nerves, guilty feeling, and seen doctor gp for nerves, anxiety, tension, or depression. Finally, in the case of poor mental health, the scores range between 15-20; hence, almost all the questions were significantly important to this class. Fig 5 illustrates the mean sFNC on test subjects corresponding to excellent and poor categories of mental health.



(a) Excellent category (c) Poor category

Fig. 5. Mean sFNC for two categories of mental health. The excellent category showed strong positive connectivity between the CC-SM, DM-SM, and CB-VS domains whereas the poor category demonstrates positive connectivity in the VS and SM domains.

4. CONCLUSION

In this study, we proposed a 1D-CNN-based deep learning architecture for classifying mental health scores into different categories. It was observed that this model outperformed the traditional machine learning methods for this classification task using a smaller-sized dataset. The higher dimensional visualization of the features showed a well-defined separation between the classes. This study suggests that rs-fMRI-based data has great potential as a reliable imaging marker to discriminate individuals based on their mental health. The future work will incorporate the TCs and the RSNs by extending the proposed deep-learning model. Additionally, we will also explore more meaningful and interpretable ways of finding biological markers for the various mental health categories.

5. COMPLIANCE WITH ETHICAL STANDARDS

This research study was conducted retrospectively using human subject data made available in open access by UK Biobank. Ethical approval was not required as confirmed by the license attached with the open access data.

6. ACKNOWLEDGMENTS

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