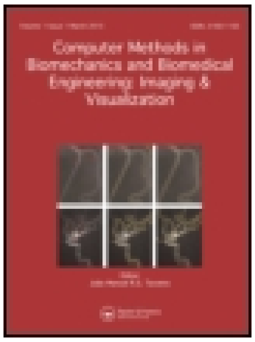

Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/tciv20

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To cite this article: Samira Jafari, Afshin Almasi, Hamid Sharini, Sajad Heydari & Nader Salari (2022): Diagnosis of borderline personality disorder based on Cyberball social exclusion task and resting-state fMRI: using machine learning approach as an auxiliary tool, Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization, DOI: 10.1080/21681163.2022.2161415

To link to this article: https://doi.org/10.1080/21681163.2022.2161415

Published online: 25 Dec 2022.

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Diagnosis of borderline personality disorder based on Cyberball social exclusion task and resting-state fMRI: using machine learning approach as an auxiliary tool

Samira Jafari[a], Afshin Almasi[b], Hamid Sharini[c], Sajad Heydari[d] and Nader Salari[e,f]

[a]Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran; [b]Clinical Research Development Center, Imam Khomeini and Mohammad Kermanshahi and Farabi Hospitals, Kermanshah University of Medical Sciences, Kermanshah, Iran; [c]Department of Biomedical Engineering, Faculty of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran; [d]Industrial and systems engineering faculty, Tarbiat Modares University, Tehran, Iran; [e]Department of Biostatistics, School of Health, Kermanshah University of Medical Sciences, Kermanshah, Iran; [f]Sleep Disorders Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

ABSTRACT

To diagnose patients with borderline personality disorder (BPD) based on Cyberball social exclusion task and resting-state functional magnetic resonance imaging (fMRI) using machine learning approach. In the current study, the researchers used fMRI images to examine social brain function and learning in BPD. Thirty-six participants completed the 'Cyberball' task. Data questionnaire and features extracted from fMRI data were used to diagnose BPD. In this study, three statistical models were used to diagnosing BPD, and the best model was introduced based on appropriate criteria. Also, important features are identified by the models. Totally, 20 people had BPD and 16 were healthy. 83.3% were women and 16.7% men. Logistic Lasso Regression (LLR) was the best model for the diagnosis of patients with BPD. Physical abuse, sexual abuse and the use of antidepressants and antipsychotic drugs were selected as important features by the models. Due to the structure of the machine learning models used in the study, there is no need to feature selection stage and important features can be identified in the models. Also, the diagnosis of BPD has been done with high accuracy, so that clinical physicians can diagnose BPD with all available information, including questionnaire information and fMRI data.

ARTICLE HISTORY
Received 6 August 2022
Accepted 18 December 2022

KEYWORDS
Borderline personality disorder; diagnosis; Cyberball task; functional magnetic resonance imaging; machine learning

Introduction

Borderline personality disorder (BPD), which is known as the most common personality disorder among the clinical population, is characterised by instability, identity disorder, interpersonal difficulties and harmful behaviours that must be deemed stable and have a significant impact on daily functioning (Porter et al. 2020). Because this disorder is associated with emotional instability and impulsiveness, people with BPD have many problems in many cases, including the development of interpersonal relationships (Martino et al. 2020). This disorder, which requires high personal and socio-economic costs, is associated with very high levels of self-harm and suicide (Luyten et al. 2020). Also, self-conscious emotions, shame and guilt have a central clinical relevance to BPD in this disorder (Göttlich et al. 2020). Many researchers have identified borderline personality traits such as problems in social interactions (Kaurin et al. 2020), fears of abandonment (Wiesenfeller et al. 2020), social exclusion (Seidl et al. 2020) and emotional instability (Martino et al. 2020). The prevalence of this disease in the United States is between 0.5% and 1.4%. It is also a cautious assumption that, in general, the prevalence of BPD in the population is about 1% (ten Have M et al. 2016).

BPD is diagnosed by questionnaires such as Diagnostic and Statistical Manual of Mental Disorders (Clifton and Pilkonis 2007). DSM, a questionnaire with 12 questions, is a standard language used by physicians, researchers and public health officials in the United States to communicate about mental disorders (Regier et al. 2013).

To assess BPD, studies on brain mapping methods such as Electroencephalography (EEG) (Flasbeck et al. 2017), functional Near Infrared Spectroscopy (fNIRS) (Husain et al. 2020), etc., have been performed and in recent years, neuroscientists have used functional Magnetic Resonance Imaging (fMRI) as a non-invasive method to measure neural activity in the brain of people with BPD (Irani et al. 2007). 'fMRI uses advantage of the coupling between neuronal activity and haemodynamics (the local control of blood flow and oxygenation) in the brain to enable non-invasive localisation and measurement of brain activity' (Heeger and Ress 2002). The basic signal of fMRI is dependent on blood oxygen (BOLD), which is produced by hydrogen atoms (Heeger and Ress 2002). Information obtained from fMRI is very valuable in assessing brain activity and function and provides unique results (Bennett and Miller 2010). In a study conducted by Henk Cremers et al. in 2020, the aim was to borderline personality disorder classification based on brain network. In this study, in which individuals performed an fMRI emotion regulation task, different properties of brain connectivity properties were systematically tested and predictive power was used to diagnose borderline personality disorder. The statistical model used to classify this disease is the linear support vector machine method, which has an accuracy of 55% in classifying sick versus healthy people (Cremers et al. 2021).

CONTACT Afshin Almasi afalmasa@gmail.com Clinical Research Development Center, Imam Khomeini and Mohammad Kermanshahi and Farabi Hospitals, Kermanshah University of Medical Sciences, Kermanshah, Iran

In a meta-analysis study conducted by Porter C et al., the objective was to better understand the magnitude and consistency of the association between childhood adversity and borderline personality disorder (BPD) between case studies, epidemiology and prospective cohorts. In this study, published in 2020, 97 studies were reviewed which used logistic regression. This meta-analysis confirms the theoretical proposals that exposure to adverse life experiences is associated with BPD. This highlights the importance of paying attention to childhood adversity when treating people diagnosed with BPD (Porter et al. 2020).

Today, machine learning (ML) has advanced a lot, which reduced human labour (Charbuty and Abdulazeez 2021). ML techniques can be classified into four types, which include supervised ML techniques, unsupervised ML techniques, semi-supervised ML techniques and reinforcement ML techniques (Jain et al. 1999). Supervised ML techniques utilise knowledge from the previous and present data using labels to forecast events. This technique is initiated from the training process of dataset and developed an inferred function to foresee the output values (Onan 2022). The least absolute shrinkage and selection operator (Lasso) is a variable selection technique that has been recently applied to corporate bankruptcy forecasts (Tian et al. 2015). This method deals well with multicollinearity and minimises the numerical instability that may occur due to overfitting (Pereira et al. 2016). Logistic regression analysis is focused on predicting whether or not an event occurred such as failure or success, diseased or healthy, yes or no (Araveeporn 2021). Recently, logistic elastic net regression, an elastic net penalty, which combines the desirable properties of its special cases ridge and lasso regression, was developed to solve dimension reduction and feature selection problem by Zou et al. (Münch et al. 2021). Also, Zou proposed a model, which uses adaptive weights for penalising different coefficients in the lasso penalty. The adaptive lasso leads to an optimal estimator on the generalised linear model and contains the oracle properties by utilising the adaptive weights (Araveeporn 2021).

In the mentioned studies, the models had low accuracy and all the available information was not used. While in the present study, the researchers used the data which has been obtained from both questionnaire and fMRI methods and collected the features of these methods to use all available information to achieve an optimal classification. However, not all features of BPD data will lead to a good classification result, because there are always some unrelated and redundant features. To solve this problem, the researchers used three machine learning models, Logistic Lasso Regression (LLR), Adaptive Lasso Logistic Regression (ALLR) and Logistic Elastic Net Regression (LENR) models for diagnosis of patients with BPD and compared these models with each other using appropriate criteria. These methods can be used as auxiliary tools to diagnose BPD. In addition to interviews and questionnaires, psychologists and psychiatrists can use machine learning methods to more reliably and accurately diagnose people with borderline personality disorder and also determine important and influential features.

Methods and materials

For a better understanding, the research steps are shown graphically in Figure 1.

Participants

fMRI images and questioner data were obtained from https://openneuro.org/and people with BPD were recruited from outpatient and support services from around Edinburgh, Scotland. In summary, fMRI data was acquired at 3T, with TR 1560 ms, 347 volumes, resolution $3.4 \times 3.4 \times 5$ mm. A T1 structural image was acquired with resolution 1 mm isotropic. According to previous studies, the sample size was 40 people in the age group (20–52) and 4 people were excluded from the study due to technical issues during scanning. Structured clinical interview for DSM-IV was used for the diagnosis of BPD (SCID-II; http://www.scid4.org/). Zanarini Rating Scale for Borderline Personality Disorder and Childhood Trauma Questionnaire were used to assess current symptoms and adverse childhood events, respectively. Exclusion criteria included pregnancy, MRI contraindications, diagnosis of a psychotic disorder, previous head injury or current illicit substance dependence. Ethical approval was obtained from the Lothian National Health Services Research Ethics Committee (09/S1101/49). All participants provided written consent before participation in it.

Experimental task

Participants performed Cyberball social exclusion task during fMRI. The task involves playing 'catch' with two computer-controlled players, during which the participant can be systematically included (inclusion) or removed from the game (exclusion). This task activates a range of social brain regions. This task consisted of four steps: 0%, 33%, 66% and 100% that was into blocks of nine throws, respectively, involving zero, one, two or three throws to the participant. These percentages indicate the degree to which people are involved in computer games, for example, 100% inclusion means that the participant received three throws per nine-throw block, like the other players. Mean block duration was 24 s. Figure 2 shows Cyberball social exclusion task during fMRI.

Preprocessing

Preprocessing includes Slice timing, Realignment, Coregistration, Segmentation, Normalisation and Smoothing. These steps were performed using the spm12 toolbox in Matlab software. To achieve the magnetic balance of the device, usually the first few frames of data are removed (Chao-Gan and Yu-Feng 2010). According to past studies and data evaluation, the first eight frames are removed to eliminate the effects of the instability of the scanner magnetic pins. The first step of preprocessing[1] will be correcting the difference between the times that slice images received. In the next step, the correction of the head movement[2] is done by matching different scans on each other. In this step, the mean of all slices are used as a reference and the corrections are made based on the reference (if the patient's head movement was

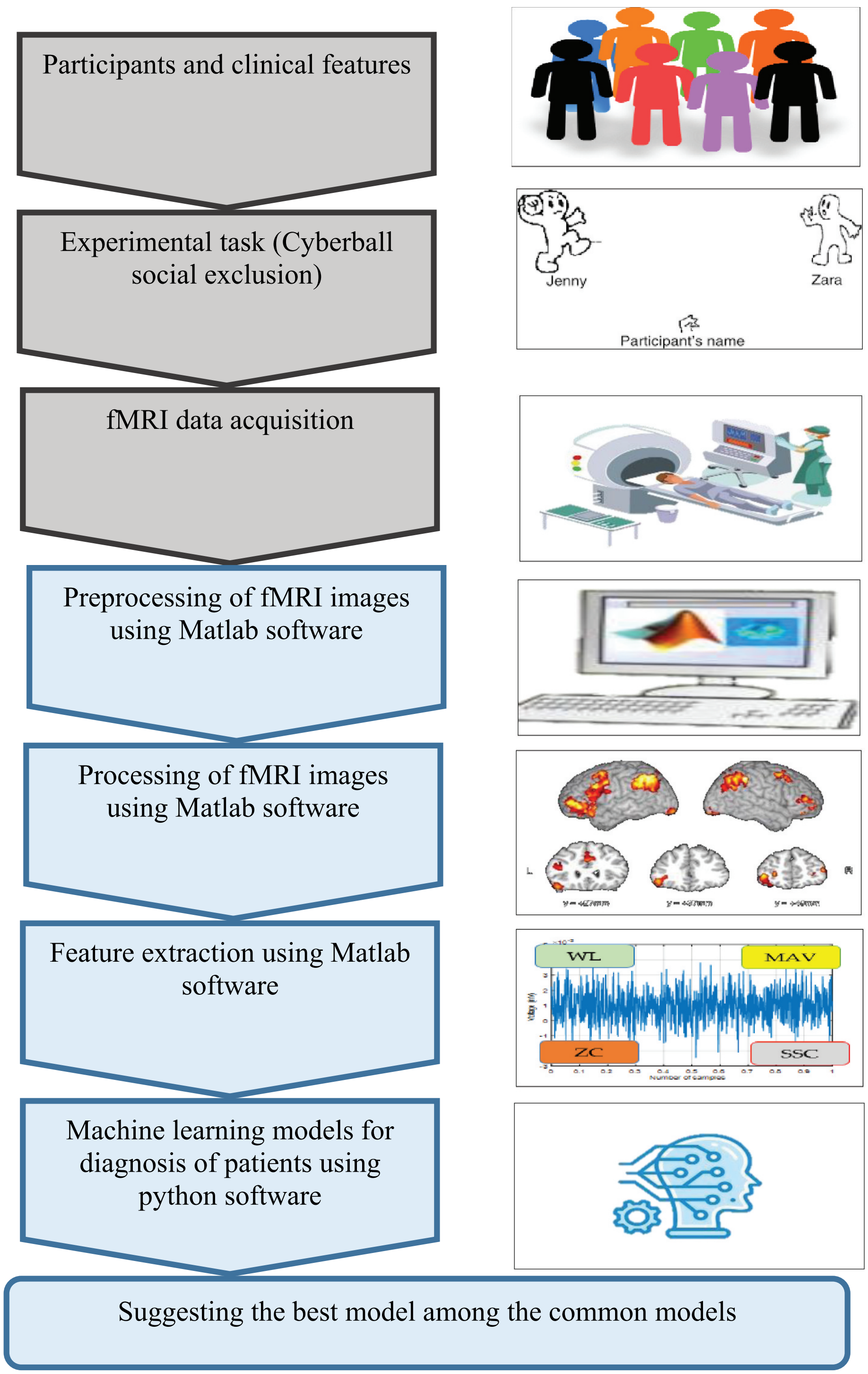

Figure 1. Graphical abstract (Gray shapes represent the steps performed by physicians and the rest of the steps performed by the researchers in the present study).

more than 3 mm, the data will be excluded from the study). Segmentation is performed to remove the unwanted effects of the tissues and for measuring and visualising the brain's anatomical structures. The anatomical image is adapted to the functional images, and also the images are normalised (transfer of data to a standard space). In the last step, as the changes in the blood in the brain are slow, a low-pass filter to remove high-frequency noise will be applied to the functional images using a 6-mm-wide Gaussian filter (Sladky et al. 2011).

Processing

Processing includes two stages: individual and group analysis. In individual analysis, the activity of individual brain regions is calculated individually. Quantitative parameters resulting from this activity are extracted. In group analysis, the activities of all individuals are compared, and the common active regions of the brain are identified. Analysis of brain activity is performed by the Generalized Linear Model (GLM). GLM method is a

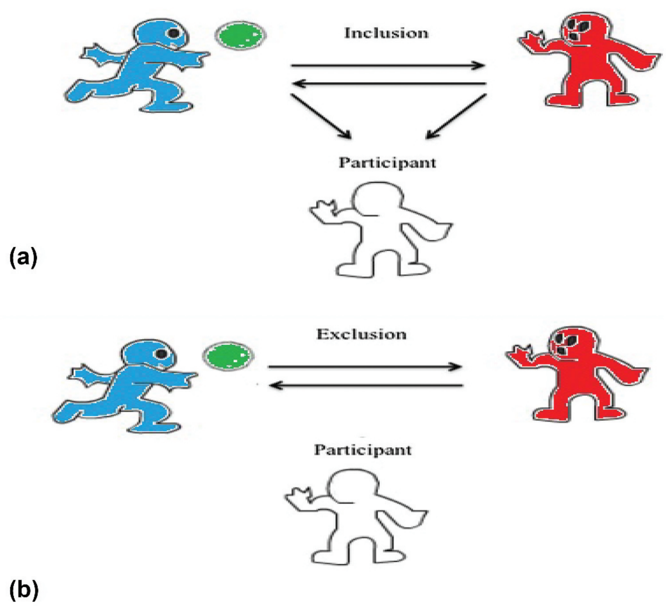

Figure 2. Cyberball social exclusion task during fMRI that the participant either receives the ball (inclusion) or does not receive it (exclusion).

powerful tool for analysing fMRI data, which is mathematically equivalent to multiple regression. This method has the ability to integrate several independent qualitative and quantitative variables. The GLM method can be expressed using a matrix form that includes a predictor, voxel time course, beta values and residues. Positive and negative stimulation and resting state are modelled as predictors in the fMRI design matrix. The three beta weights B1, B2 and B3 are interpreted as the decreasing and increasing activity relative to the baseline modelled signal level using a fixed term (CT) regardless of resting state. In the present study, both conditions (inclusion and exclusion) were used to identify the active regions of the brain and reaction times were analysed within a repeated measures ANOVA. Twenty-two active and common regions of the brain were identified by physicians and neurologists, which are shown in Figure 3. Also, Table 1 represents the coordinates and the names of these regions.

Feature extraction

To increase the accuracy of the models, a combination of clinical features and imaging biomarkers have been used. In this study, 20 clinical features were considered which were valuable from the point of view of the clinical expert. One feature is related to the total score of the Hamilton Depression Questionnaire (HAM-D), one feature is related to the total score of Young Mania Rating (YMRS) questionnaire, nine features are related to Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD), and five features are related to the scores of Childhood Trauma Questionnaire (CTQ) including physical abuse, emotional abuse, sexual abuse, physical neglect and emotional neglect. Two features are related to the use of antidepressant and antipsychotic drugs. Sex and age are reported too.

Also, for imaging, since we were looking for automatic methods, we turned to time series, which is easily extracted from imaging and requires less processing. In time series data, we were looking for parameters that express time series changes between healthy people and people with BPD. We selected all the features that were extracted from the images, which included Absolute Value of Summation of exp root, Absolute Value of Summation of Square Root, Average

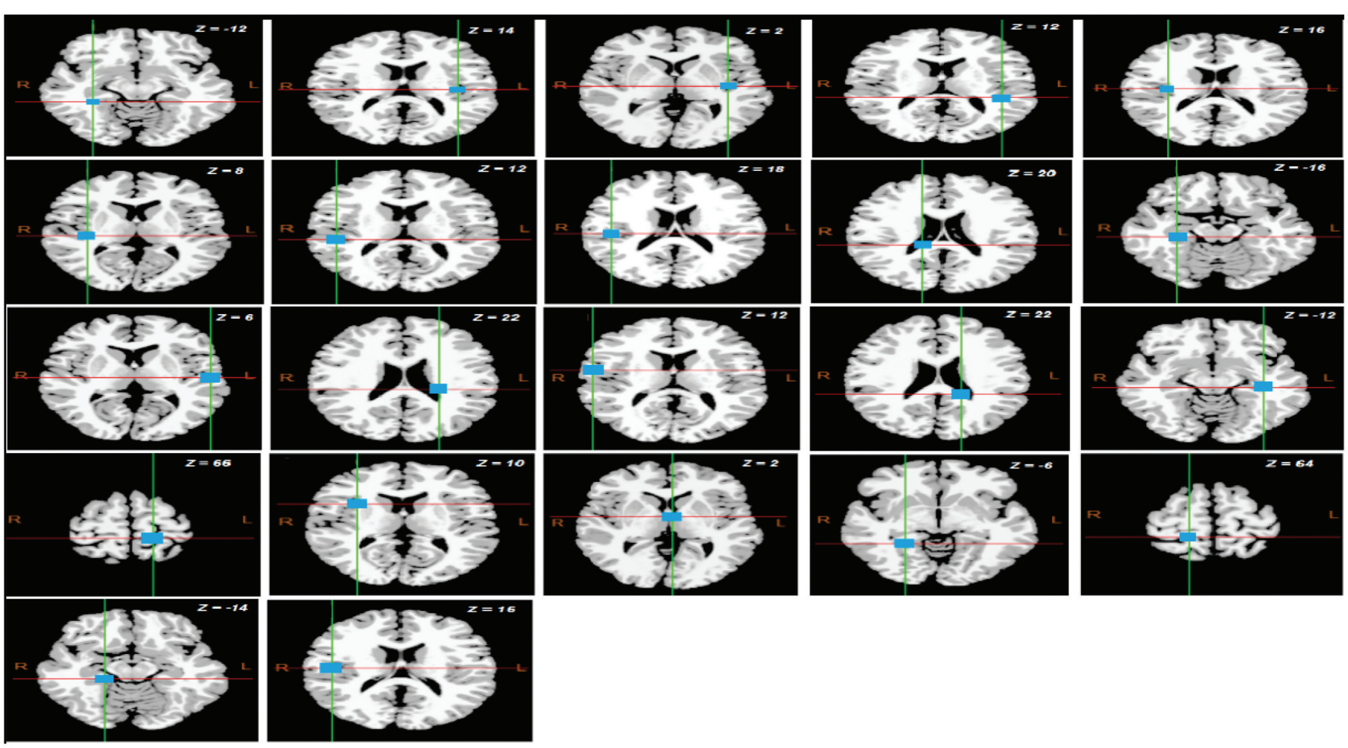

Figure 3. fMRI images that blue points represent the location of active regions of the brain.

Table 1. Coordinates and the name of active and common regions.

Active region	X	Y	Z
Right Parahippocampal Gyrus	34	−38	−12
Left Insula	−38	−18	14
Left Insula	−38	−14	2
Left Primary Auditory	−42	−34	12
Right Insula	36	−14	16
Right Primary Auditory	38	−22	8
Right Primary Auditory	50	−28	12
Right Supramarginal Gyrus	48	−22	18
Outside defined BAs	16	−32	20
Right Parahippocampal Gyrus	32	−26	−16
Left Primary Auditory	−56	−16	6
Outside defined BAs	−24	−28	22
Right Primary Motor	60	−2	12
Outside defined BAs	−16	−38	22
Left Hippocampus	−36	−26	−12
Left Primary Sensory	−16	−38	66
Right Broca Opercularis	34	12	10
Left Thalamus	−2	−4	2
Right Visual Association	26	−46	−6
Right Sensory Association	18	−42	64
Right Parahippocampal Gyrus	22	−30	−14
Right Primary Sensory	50	−14	16

Table 3. The results of comparing LLR, ALLR and LENR.

Models	ACC	PRE	REC	SE	SP
LLR	0.91	1	0.8	0.86	1
ALLR	0.82	1	0.6	0.75	1
LENR	0.73	0.75	0.6	0.71	0.75

Amplitude Change, Average Energy, Cardinality, Coefficient of Variation, Difference Absolute Mean Value, Difference Absolute Standard Deviation Value, Difference Variance Value, Enhanced Mean absolute value, Enhanced Wavelength, Integrated EMG, Interquartile Range, Kurtosis, Log Detector, Log Difference Absolute Mean Value, Log Difference Absolute Standard Deviation, Log Tiger Kaiser Energy Operator, Maximum Fractal Length, Mean Absolute Deviation, Mean Absolute Value, Modified Mean Absolute Value, Modified Mean Absolute Value 2, Mypulse Percentage Rate, New Zero Crossing, Root Mean Square, Simple Square Integral, Skewness, Slope Sign Change, Standard Deviation, Temporal Moment, Variance, V-Order, Waveform Length, Willison Amplitude and Zero Crossing.

Finally, all these features were given to the machine learning models as input features and some of the features were selected as important and effective features by the models. The results are reported in Table 4.

Table 4. Important features selected by statistical models.

LLR		ALLR	
features	Scores	features	Scores
New Zero Crossing	−0.516	Kurtosis	0.044
Skewness	0.339	New Zero Crossing	−0.080
Temporal Moment	0.099	Skewness	0.023
HAM-D	1.110	Physical abuse in childhood	0.040
Zanarini-2	0.329	Sexual abuse in childhood	−0.116
Physical abuse in childhood	0.153	Drugs	0.396
Sexual abuse in childhood	−0.229	-	-
Drugs	0.046	-	-

LLR method

In machine learning, LASSO is a popular method for model selection and shrinkage estimation. It was originally introduced in geophysics and later by Robert Tibshirani. This method is a penalised regression approach that estimates the regression coefficients by maximising the log-likelihood function (or the sum of squared residuals) with the constraint that the sum of the absolute values of the regression coefficients is less than or equal to a positive constant. In the LLR model, the logistic regression model uses a lasso penalty for a better fit. The maximum likelihood function is constructed according to this penalty and is used to estimate the model parameters. By using Lasso method, it is possible to provide a suitable method for modelling the response variable based on the least and most appropriate number of independent variables. Since the word 'Lasso' means rope and lassoing, this method also tries to separate the most suitable variables from the rest of the variables by using lassoing and provides a simpler model.

ALLR method

Adaptive Lasso Logistic Regression that is an evolution of the Lasso was proposed initially by Zou (2006), and the idea behind it is pretty straightforward: assigning a higher weight to the small coefficients and lower weight to the large coefficients and as a regularisation method, avoids overfitting penalising large coefficients. Besides, it has the same advantage that Lasso: it can shrink some of the coefficients to exactly zero, performing thus a selection of attributes with the regularisation. This procedure reduces the selection bias.

LENR method

Logistic Elastic Net Regression, a type of machine learning, performs variable selection and regularisation simultaneously using penalties from both the lasso and ridge techniques to regularise regression models (L1 and L2 penalties, respectively). This method improves the regularisation of statistical models by combining both the lasso and ridge regression methods. The use of this new combination penalty in the logistics model is the LENR model. In this method, a hyperparameter (alpha) is provided to assign how much weight is given to each of the L1 and L2 penalties. Alpha is a value between 0 and 1 and is used to weight the contribution of the L1 penalty and one minus the alpha value is used to weight the L2 penalty.

In this study, classifying the training data was done with three classification methods in Python software. Python is an open-source programming language that provides very powerful and professional methods to work with different languages and tools as easily as possible. These three methods were used to diagnose patients with BPD, and the best models are introduced based on classification criteria including accuracy (ACC), precision (PRE), recall (REC), sensitivity (SE) and specificity (SP). Also, receiver operating characteristic curve (ROC curve) is plotted to compare the three machine learning methods.

ACC is a classification criteria that is calculated by the number of correct predictions divided by the total number of predictions (Othman et al. 2018). PRE is defined as a ratio between the number of positive samples correctly classified to the total number of samples classified as positive. REC is the ratio between the number of positive samples correctly classified as positive to the total number of positive samples (Yacouby and Axman 2020). SE is defined as the probability that a test result will be positive when the disease exists. SP or true negative rate is the probability that a test result will be negative when the disease is not present (Böger et al. 2021). ROC curve is a graphical plot that illustrates the performance of a classification model at all classification thresholds. The larger area under this curve represents that the model is better (Vuk and Curk 2006). For comparing methods by these criteria, a model which achieves the highest values of the criteria is the best model. Totally, 57 features were used in this study. LLR and ALLR models, based on their structure, score features and select features with higher scores as the important features.

Also, in the present study, the heatmap graph is shown. A heatmap is a two-dimensional graphical representation of data where each value of a matrix is represented as a colour. The colours indicate the intensity of the relationship between variables (Saunders et al. 2014).

Result

Table 2 describes the demographic characteristics of all the participants based on BPD. Totally, 20 people had BPD and 16 were healthy. Also, 30 (83.3%) of them were women and 6 (16.7%) men and 17 (47.2%) of them were receiving antidepressant drug and 12 (33.3%) antipsychotic drug. The mean (±SD) age was 34.94 years. It showed that people who suffered from BPD were young. Patients' scores of Childhood Trauma Questionnaire were higher than those of healthy individuals that means patients have suffered from these abuses in childhood. The results of the table show that people with BPD were more depressed and more manic than healthy people. Also, the use of Antidepressant and Antipsychotic drugs in healthy people was zero, which indicates that people with BPD used these drugs more.

Figure 4 illustrates the heatmap that compares relationships between clinical and extracted features of fMRI data. Note that, in this figure, binary features are not considered. According to the figure guide, the stronger the relationship between the features, the brighter the colour of the cells. In contrast, the weaker ones coloured darker. According to this graph, for instance, all the experimentation features have a stronger relationship with each other totally. Moreover, this is vital to mention that Coefficient of Variation (COV) has the most powerless relationship with physical neglect in childhood and Zanarini-1 scale features. It means that the extracted features like COV can be used instead of the clinical features like physical neglect in childhood and Zanarini-1. Also, relationships between skewness and clinical features like YMRS and HAM-D questioners are very strong. The rest of the features can also be checked according to the graph guide and colour intensity.

Table 3 shows the results of comparing five criteria (ACC, PRE, REC, SE and SP) between three classification methods. As explained in the method section, for best classification, the criteria values must be high. So, in general, LLR model is the best model for classifying BPD patients with the highest values of criteria (ACC = 0.91, PRE = 1, REC = 0.8, SE = 0.86 and SP = 1). After that, ALLR model is a suitable model for this data.

The ROC curves of the models are shown in Figure 5. According to the figure, LLR model was the best model for classifying BPD patients with area under the curve of 0.91. Also, for models ALLR and LENR, the area under the curves were 0.82 and 0.73, respectively.

As mentioned, LLR and ALLR models also have the ability to select the most important features. Table 4 shows the important features selected by these two models and their scores. According to this table, LLR and ALLR models have selected eight and six features as important features, respectively. New Zero Crossing, skewness, physical and sexual abuse in childhood and the use of antidepressants and antipsychotic drugs are important features that have been selected by both models. This indicates that these features affect BPD disease more than other features.

Discussion

The aim of the current study was to diagnose patients with BPD by machine learning approach based on Cyberball social exclusion task and resting-state fMRI using machine learning approach. In this study, all features (57 features) including questionnaires and fMRI data were used for optimal classification. Features were extracted from fMRI data after pre-processing and processing using Matlab software. According to the heatmap graph, Coefficient of Variation (COV) has the most powerless relationship with physical neglect in childhood and Zanarini-1 scale features. It means that the extracted features like COV can be used instead of the clinical features like physical neglect in childhood and Zanarini-1. Also, relationships

Table 2. Subject characteristics based on BPD.

Row	variables	Total, n (%) or mean ± SD	With BPD, n (%) or mean ± SD	Without BPD, n (%) or mean ± SD
1	Age	34.94 ± 8.38	35.75 ± 8.61	33.94 ± 8.24
2	HAM-D	8.58 ± 10.02	15.45 ± 8.56	0
3	YMRS	1.28 ± 2.51	2.30 ± 3.03	0
4	CTQ-PhysAbuse	1.786 ± 1.38	2.505 ± 1.45	0.888 ± 0.49
5	CTQ-EmotAbuse	2.556 ± 1.67	3.790 ± 1.10	1.013 ± 0.62
6	CTQ-SexAbuse	2.206 ± 1.76	3.140 ± 1.74	1.038 ± 0.87
7	CTQ-PhysNeglect	1.650 ± 1.06	2.140 ± 1.10	1.038 ± 0.59
8	CTQ-EmotNeglect	1.77 ± 1.64	2.18 ± 1.96	1.25 ± 0.92
9	Zanarini-1	0.56 ± 0.94	1.00 ± 1.08	0
10	Zanarini-2	1.28 ± 1.45	2.30 ± 1.17	0
11	Zanarini-3	1.06 ± 1.45	1.90 ± 1.48	0
12	Zanarini-4	0.86 ± 1.15	1.55 ± 1.15	0
13	Zanarini-5	1.19 ± 1.39	2.15 ± 1.18	0
14	Zanarini-6	0.50 ± 0.94	0.90 ± 1.12	0
15	Zanarini-7	0.89 ± 1.28	1.60 ± 1.35	0
16	Zanarini-8	0.58 ± 0.87	1.05 ± 0.94	0
17	Zanarini-9	0.69 ± 1.06	1.25 ± 1.16	0
18	Mean	−0.0000007 ± 0.98	−0.0000007 ± 1	−0.0000008 ± 1
19	Absolute Value of Summation of exp root	−0.0000004 ± 0.98	0.0000000 ± 1	−0.0000008 ± 1
20	Absolute Value of Summation of Square Root	0.0000007 ± 0.98	0.0000007 ± 1	0.0000008 ± 1
21	Average Amplitude Change	−0.0000004 ± 0.98	0.0000000 ± 1	−0.0000008 ± 1
22	Average Energy	0.0000004 ± 0.98	0.0000000 ± 1	0.0000008 ± 1
23	Cardinality	0.0000000 ± 0.98	0.0000007 ± 1	−0.0000008 ± 1
24	Coefficient of Variation	0.0000004 ± 0.98	0.0000007 ± 1	0.0000000 ± 1
25	Difference Absolute Mean Value	0.0000000 ± 0.98	−0.0000007 ± 1	0.0000008 ± 1
26	Difference Absolute Standard Deviation Value	−0.0000004 ± 0.98	0.0000000 ± 1	−0.0000008 ± 1
27	Difference Variance Value	−0.0000015 ± 0.98	−0.0000021 ± 1	−0.0000008 ± 1
28	Enhanced Mean absolute value	0.0000000 ± 0.98	0.0000000 ± 1	0.0000000 ± 1
29	Enhanced Wavelength	0.0000015 ± 0.98	0.0000021 ± 1	0.0000008 ± 1
30	Integrated EMG	0.0000000 ± 0.98	−0.0000007 ± 1	0.0000008 ± 1
31	Interquartile Range	−0.0000004 ± 0.98	−0.0000007 ± 1	0.0000000 ± 1
32	Kurtosis	0.0000000 ± 0.98	0.0000007 ± 1	−0.0000008 ± 1
33	Log Detector	0.0000004 ± 0.98	0.0000000 ± 1	0.0000008 ± 1
34	Log Difference Absolute Mean Value	−0.0000007 ± 0.98	0.0000000 ± 1	−0.0000015 ± 1
35	Log Difference Absolute Standard Deviation	0.0000000 ± 0.98	−0.0000007 ± 1	0.0000008 ± 1
36	Log Tiger Kaiser Energy Operator	0.0000000 ± 0.98	0.0000000 ± 1	0.0000000 ± 1
37	Maximum Fractal Length	−0.0000011 ± 0.98	−0.0000014 ± 1	−0.0000008 ± 1
38	Mean Absolute Deviation	−0.0000004 ± 0.98	−0.0000007 ± 1	0.0000000 ± 1
39	Mean Absolute Value	0.0000004 ± 0.98	0.0000000 ± 1	0.0000008 ± 1
40	Modified Mean Absolute Value	0.0000000 ± 0.98	0.0000000 ± 1	0.0000000 ± 1
41	Modified Mean Absolute Value 2	−0.0000004 ± 0.98	−0.0000007 ± 1	0.0000000 ± 1
42	Mypulse Percentage Rate	0.0000000 ± 0.98	−0.0000007 ± 1	0.0000008 ± 1
43	New Zero Crossing	0.0000004 ± 0.98	0.0000000 ± 1	0.0000008 ± 1
44	Root Mean Square	0.0000004 ± 0.98	0.0000000 ± 1	0.0000008 ± 1
45	Simple Square Integral	0.0000007 ± 0.98	0.0000007 ± 1	0.0000008 ± 1
46	Skewness	0.0000004 ± 0.98	−0.0000007 ± 1	0.0000015 ± 1
47	Slope Sign Change	0.0000004 ± 0.98	0.0000007 ± 1	0.0000000 ± 1
48	Standard Deviation	0.0000000 ± 0.98	−0.0000007 ± 1	0.0000008 ± 1
49	Temporal Moment	−0.0000004 ± 0.98	−0.0000014 ± 1	0.0000008 ± 1
50	Variance	0.0000000 ± 0.98	0.0000000 ± 1	0.0000000 ± 1
51	V-Order	0.0000004 ± 0.98	0.0000000 ± 1	0.0000008 ± 1
52	Waveform Length	−0.0000007 ± 0.98	−0.0000007 ± 1	−0.0000008 ± 1
53	Willison Amplitude	0.0000007 ± 0.98	0.0000007 ± 1	0.0000008 ± 1
54	Zero Crossing	0.0000004 ± 0.98	0.0000014 ± 1	−0.0000008 ± 1
55	Sex, n (%)			
	Male	6 (16.7)	3 (15.0)	3 (18.8)
	Female	30 (83.3)	17 (85.0)	13 (81.3)
56	Antidepressant drugs, n (%)			
	Yes	17 (47.2)	17 (85.0)	0 (0.0)
	No	19 (52.8)	3 (15.0)	16 (100)
57	Antipsychotic drugs, n (%)			
	Yes	12 (33.3)	12 (60.0)	0 (0.0)
	No	24 (66.7)	8 (40.0)	16 (100)

between skewness and clinical features like YMRS and HAM-D questioners are very strong. Due to the small sample size and large number of features, three methods, LLR, ALLR and LENR were used. LLR model was introduced as the best model using appropriate criteria including ACC, PRE, REC, SE, SP and ROC curves. New Zero Crossing, skewness, physical and sexual abuse in childhood and the use of antidepressants and antipsychotic drugs are important features that have been selected by LLR and ALLR models.

A study conducted by Bo Wang et al. in 2021 aimed to detect Bipolar Disorder (BD) and BPD with language and speech in non-clinical interviews. In this work, among the 139 participants, 53 had BD diagnosis, 33 were diagnosed with BPD, and 53 were healthy volunteers (H). These diseases were

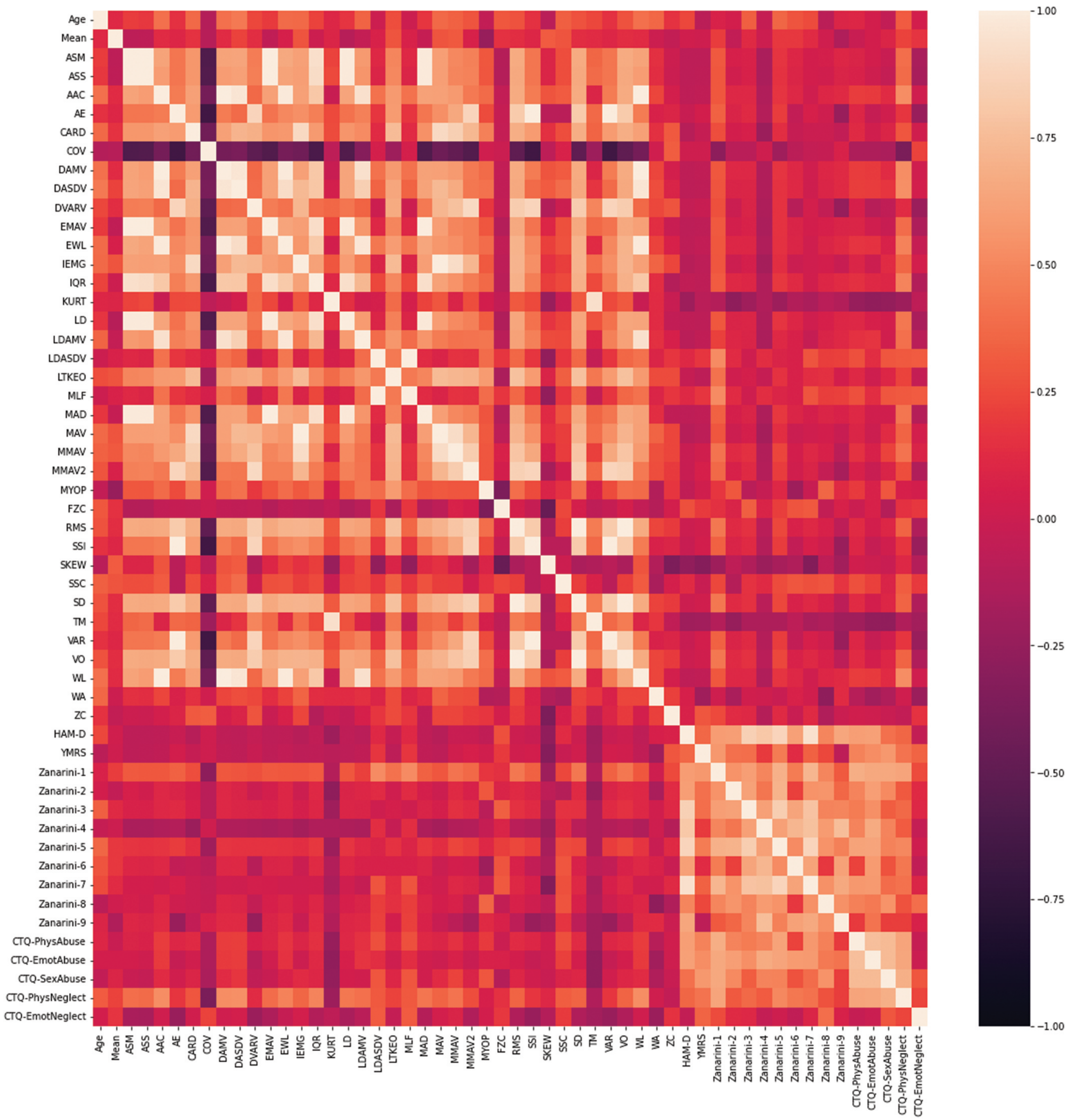

Figure 4. The heatmap that illustrates correlations of features.

diagnosed using the structured clinical interview for DSM-IV and the International Personality Disorder Examination. In this study, features from different aspects were considered: lexical diversity and density, syntax, semantic content and dialogue structure. The extracted features included linguistic complexity features, semantic content features and dialogue features. Logistic regression (LR) as the classification model was used to classify individuals after feature extraction. The area under curve (AUC) is calculated for all features, 0.810, 0.733 and 0.817 for H vs BD, H vs BPD and BD vs BPD, respectively (Wang et al. 2020). In this study, the selection of features is done in a separate step, while in the present study, the selection of appropriate features is done by the models. Also, only interview-related features were used, while in our study, fMRI data were also considered in addition to interview data.

In 2021, Mohamed Khazbak et al. conducted a study on the detection of BPD using a deep learning approach. In this study, a system called the MindTime system (a mobile app) is introduced, which aims to detect the symptoms of borderline personality disorder and the signs of self-harm. The users make

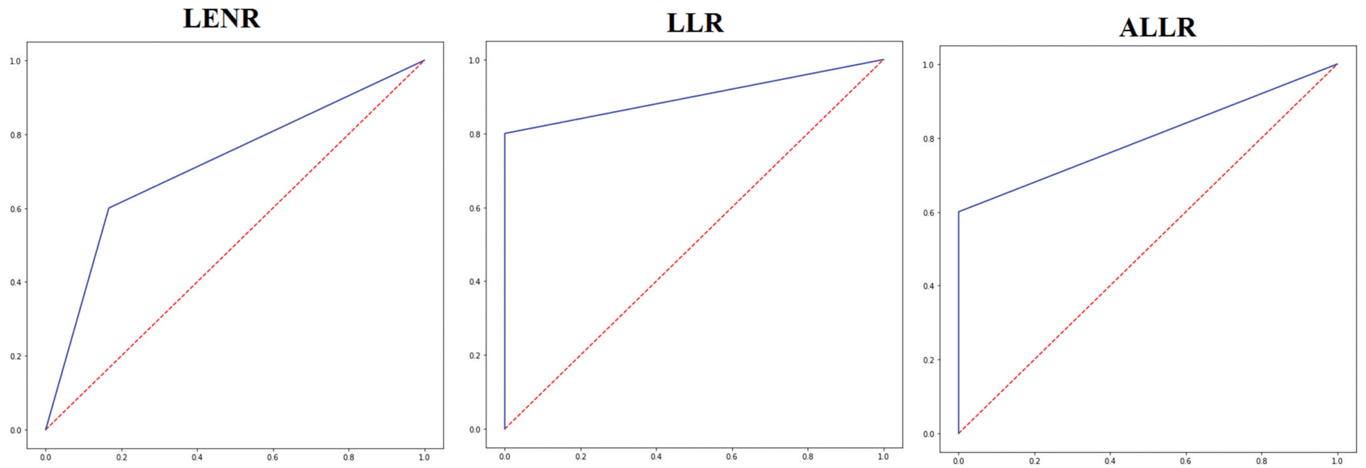

Figure 5. Roc curves of the machine learning methods (LENR, LLR and ALLR). The larger the area under the curve represents the suitable model.

notes of daily events, experiences, thoughts and feelings by this app. In the system, extracted features included password protection, mood tracking, text journals, voice recording and video recording. The classifiers were Naive Bayes (NB), Support Vector Machine (SVM), K-Nearest Neighbors (KNN), Convolutional Neural Network (CNN) and Long Short-Term Memory (LSTM), and the result showed that SVM and LSTM had the best accuracy. The used models' accuracy was 0.71, 0.90, 0.56, 0.65 and 0.91, respectively (Khazbak et al. 2021). The features and models used in this study are different from those used in the present study. Also, in the current study, different criteria were used for the comparison of the machine learning models, while in this study only the accuracy was used.

Objective of a study conducted by Henk Cremers et al. was to classify patients with BPD based on brain network measures during emotion regulation. This study, which was conducted in 2020, included 51 BPD patients, 26 cluster C personality disorder and 44 control and participants performed an fMRI emotion regulation task. In this study, the task during fMRI imaging included performing an emotion regulation paradigm, which involved the presentation of pictures that were preceded by a safe (emotion regulation) or look instruction. In this task that was one of the main therapies for BPD, participants were asked to imagine themselves as being in a safe situation. The sample consisted of women aged 18 to 65 years, and systematically, various brain connectivity properties were tested and predictive power was evaluated to diagnose BPD. The statistical model used to classify this disease was linear support vector machine method, which achieved an accuracy of 55% in classifying patients with BPD versus healthy people (Cremers et al. 2021). Low accuracy indicates that the support vector machine (SVM) model is not suitable for these data, while in the present study, the values of the criteria are appropriate and high. Also, in the study, the sample included only women and the results can be generalised to the women's community, but our study consists of both gender (women and men). Also, in the present study, important features have been identified using models, while the SVM model does not have the ability to select important features.

In a study conducted by Adam Bayes et al. in (2021), the objective was to make differentiation of BP versus BPD using machine learning approach. Among 134 participants, 82 met DSM criteria for BP and 52 for BPD. They were compared on measures examining cognitive and behavioural BPD constructs, emotion regulation strategies and parental behaviours during childhood. The used machine learning approach was random forest algorithm used to diagnose these two disorders. Accuracy of classification was 84.1%–87.8% for BP, 50% –57.7% for BPD, with overall accuracy of 73.1%–73.9%. Items like identity difficulties, relationship problems, female gender, feeling suicidal after a relationship breakdown and age, differed between the analyses with the overall most important items (Bayes et al. 2021).

Although in general, due to the difficult conditions of fMRI imaging, the number of people referring to this imaging is small, a multicenter study can be used to have a larger sample size and better generalisation to the community. In the multicenter study, fMRI data are collected from several centres and the researchers will have a higher sample size.

Conclusion

Since this disease is a dangerous mental illness and its diagnosis is of special importance, for better diagnosis, both data from various questionnaires and fMRI data were used to be able to use all the available information. In this study, to handle these relatively complex data, the machine learning approach was used to diagnose BPD and the three models were chosen based on the conditions of the present sample (low sample size and large number of independent variables). Due to the structure of the machine learning models used in the current study, there is no need for feature selection stage, and important features can be identified in the models. Also, using this approach can be useful in the fields of cognitive sciences, psychology, psychiatry and neuroscience and will help specialists of these fields in the diagnosis of BPD.

In the present study, Cyberball social exclusion task was used during fMRI. For future studies, it is suggested to use other tasks such as social judgement, chatroom, viewing paintings which are suitable for social exclusion and compare the results with the results of the present study. In another research, other parameters such as stress and anxiety can also be considered and people who have other disorders such as stress and anxiety in addition to BPD can be examined. It is suggested to use other models such as artificial neural networks, deep learning or genetic algorithm to diagnose BPD and compare with the results of the present model. It is also suggested to use EEG and fMRI imaging methods simultaneously in a study and compare the results of these two imaging methods.

Notes

1. Slice timing.
2. Realignment.

Acknowledgements

By Deputy for Research and Technology, Kermanshah University of Medical Sciences.

Author contributions

Samira Jafari and Afshin Almasi designed the study. Samira Jafari and Hamid Sharini extracted the data and features, and the data analysis was performed by Samira Jafari and Sajad Heydari. The final report was written by Samira Jafari, Afshin Almasi and Nader Salari. Finally, all the mentioned authors read the completed article.

Disclosure statement

No potential conflict of interest was reported by the authors.

Availability of data and material

Details of excluded papers are available from the Corresponding author on request.

Financial declaration

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Ethics approval

This research has been approved with the Ethics approval (IR.KUMS.REC.1401.022) in the committee of deputy of research and technology, Kermanshah University of Medical Sciences.

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