

Research Paper: Classification of schizophrenia from feature-model analysis of bilaterally correlated diagnosis, symptoms, and imaging findings pyramid



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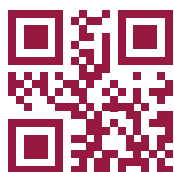
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ABSTRACT

Schizophrenia (SZ) is a mental illness that impairs a person's mental capacity, emotional dispositions, and personal and social quality of life. Manual SZ patient screening is time-consuming, expensive, and prone to human mistakes. As a result, a autonomous, relatively accurate, and reasonably economical system for diagnosing schizophrenia patients is required. Machine learning methods are capable of learning subtle hidden patterns from high dimensional imaging data and achieve significant correlations for the classification of Schizophrenia. In this study, the diverse types of symptoms of the affected person are selected which have the weights assigned by cross-correlations and the model classifies the probability of schizophrenia in the person based on the highest weighted symptoms present in the report of the patient using machine learning classifiers. The classification is made by various classifiers in which the Support Vector Machine (SVM) gives the best result. In the neuroscience domain, it has been one of the most popular machine-learning tools. SVM with Radial Basis Function kernel helps to distinguish between patients and healthy controls with significant accuracy of 76% without normalization and Principal Component Analysis (PCA). The K nearest neighbor's algorithm also with no normalization and PCA showed an accuracy of 73% in predicting SZ which is remarkably close to the SVM given the small size dataset.

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1. Background

Schizophrenia (SZ) is a neuropsychiatric condition that affects the brain. It is frequently linked to sadness, anxiety, and socio-psychological issues (1). Individuals who suffer from this significant mental illness frequently exhibit three distinct traits. Cognitive deficiency symptoms, positive and negative emotional responses, and delusions are among these features. Schizophrenic attacks are divided into two stages. The patient goes through numerous stages of cognitive impairment and depression in the first phase. They show signs of psychosis in the second phase (2). Seeing and hearing are responsible for most the brain's environmental perceptions (3). In patients with SZ, this issue is overshadowed. Furthermore, SZ has a significant detrimental impact on many parts of a person's life, including reasoning, memory, reading, speech, marriage, lifestyle, and behavioural characteristics. According to the World Health Organization (WHO), SZ affects around twenty million individuals globally (4). This serious brain condition usually manifests itself at an early age. If the patients are not treated, the brain damage will worsen over time (5).

Experts have yet to discover a well-known clinical test that may provide an accurate and reliable diagnosis of SZ. Because there are no recognized and accurate biological markers for SZ, diagnosis is subjective and relies on recorded symptoms (such as hallucinations, disorganized speech, etc.), their length, or apathy at work and/or social activities (6). Traditional clinical procedures are not trustworthy and accurate since SZ shares many clinical symptoms with other mental diseases (7). SZ is sometimes confused with mental illnesses such as bipolar disorder or severe depressive disorder. As a result, developing automated tools to assist clinicians in disease diagnosis is a challenging task.

A. Types of Schizophrenia

There are distinct types of SZ: all of which are determined by the symptoms shown by the patient. Firstly, Paranoid SZ is the most common type and typically reveals itself during a person's teenage or a young adult year, which is like Psychosis. Secondly, Schizoaffective in which a person suffers from SZ as well as depression or bipolar disorder. Symptoms include increased heart rate, lack of facial expressions, and sadness. Thirdly, Catatonic SZ is a rare form in which a person's physical actions are recognizable than their thoughts. Patients are often thought to be under

the influence of drugs or alcohol. Symptoms includes strange posture and resembles stupor. Fourthly, Disorganization SZ also called hebephrenia in which individual displays disorganized speech, thinking, and behavior. Young teens and adults are often seen suffering from hebephrenia. In this type, they have difficulty with cognitive skills such as memory, attention span, and intelligence (5). Fifthly, Residual SZ is the mildest form of SZ. An individual with residual SZ could be transitioning from an acute phase of SZ to remission or vice versa. It is not cyclic and can disappear or reappear at any time.

B. Challenges in SZ classification

The use of functional Magnetic Resonance Imaging (fMRI) to define and diagnose brain diseases such as SZ is a relatively novel approach. It has the potential to play a key role in the development of diagnostic tools, but it also poses several challenges in terms of analysis and interpretation. SZ disorder is so complicated that different combinations of symptoms may appear in different patients or even in the same patient at various times. For example, a patient may present with psychotic and disorganized symptoms, whereas another may present with primarily negative symptoms.

While the transit towards using machine learning in everyday clinical practice will involve an exceptional amount of knowledge to appropriately train and test generalizable models, which properly parse through phenotypic heterogeneity. To date, there are not any clear rules and guidelines concerning the way to generate new models. Importantly, there is still much to try to do for understanding the way to leverage these sophisticated methods to robustly investigate pathophysiological processes or use them to reinforce practices associated with precision or personalized medicine (21). Like many new machine learning and deep learning technologies, investigators are excited about the promise of these techniques, but it is unclear how they can be implemented in heterogeneous disorders to provide forecasts at the single-subject/patient level or as a factor of illustrating complex genotype-phenotype relationships.

The current challenges that face machine learning application for delivery of service and understanding phenotypic variation across behavioural, neural, and clinic indices remain unaddressed. In a review examining machine learning techniques for case diagnosis that was conducted recently, Kambeitz and colleagues (21) demonstrate that there are major inconsistencies to

testing and training methodologies. They further report that most of the traditional machine learning methods achieve specificities and sensitivities on the order of ~80%. It is unclear that what would be the acceptable performance standards before integrating the methods into single subject-level predictions, clinical trials, or treatment planning.

One of the most serious issues is data availability. If we take an example of Alzheimer's disease, the availability of clinical and large-scale neuroimaging databases allows individuals to show the feasibility of using large and well-structured datasets of neural phenotypes along clinical stages. However, there is a lack of availability of such kind of data to boost SZ research. Although many large-scale initiatives have been established recently, it may be a challenging task to integrate all these databases to implement methodologies for prognosis.

The problem of differential diagnosis in cases where individuals share clinical features is an interesting problem for machine learning addressed here.

However, some significant quandaries are still left to be addressed which include: ethical issues concerning data access and privacy, clinical responsibility, how to best deal with potential differences, and site-specific differences in clinical assessment criteria. Most effective methods for adopting machine learning models in clinical settings and to test and validate those models, and the integration of machine learning methods into clinical training are also facing some quandaries. Beyond the obvious technological obstacles, incorporating machine learning into clinical practice will necessitate accepting the challenges that access to technology presents.

The following paper is organized as a brief survey on SZ classification methods (Section II), analysis of the widely used dataset, an overview of our dataset and the general approach to classify SZ (Section III), experiments and results (Section IV), and conclusion (Section V).

2. Literature Review on SZ classification

In this section, the survey of SZ classification using various approaches is presented. Table I summarizes the various approaches used in the literature.

Zożycki et al. (16) have used regional volumetric, and the latest machine learning methods. They showed that overall brain abnormalities are well known in SZ. Individual classification of a patient shows that the main correlation with clinical measures is negative, not positive symptoms. Their results highlight the potential of neuroimaging data to dispense robust

and reproducible imaging to recognize SZ. Lei et al. (17) have included the wide connectivity and graph-based metrics in the group of SZ patients and Healthy Controls (HC). They have used three machine learning approaches i.e., logistic regression, Support Vector Machine (SVM), and deep learning technology. The resulting pattern of these approaches is the 'dysconnectivity hypothesis' of SZ. It is a neural-based disorder that understood the connectivity of functional alternations. The single-subject classification is with the highest accuracy (average 81%).

Gore et al. (18) have used the neural networks which they trained by backpropagation and error signals propagated backward through the network. They have pre-processed the data by using Statistical Parametric Mapping (SPM) and applied Independent Component Analysis (ICA) method to fMRI data for grouping data into independent components. The ICA method achieved an accuracy of 98.33%. Gheiratmand et al. (19) have used sparse multivariate regression to connect brain functional features. The Whole-brain link-weight features have achieved the highest accuracy of 74%. Several negative and positive symptom scores, such as inattentiveness and strange activity, were predicted by link-weight features. Overall, the suggested multi-step process may aid in the identification of more reliable multivariate patterns, allowing for more accurate prediction of SZ and its severity.

Suri et al. (20) have described the overview of machine learning approaches for detecting SZ. Out of all, they reviewed that SVM, deep neural network, and random forest achieved an accuracy between 70%-90%. SVM (nonlinear) achieved the highest accuracy of 91.8%. Salvador et al (21) have used the MRI images which generate the gray matter Voxel-based morphometry (VBM), 1back, and 2back levels of activation from fMRI-based datasets. They have used four unimodal classifiers like ridge, lasso, random forest, and gradient boosting among which lasso has achieved the highest accuracy of 84%.

Yang et al. (22) have used fMRI dataset for the classification of SZ. They have taken three steps to improve the result of fMRI-based data. i) Multiple visual features are extracted from the perspectives of linear sparse representation, nonlinear multiple kernel representation, and function linkage of brain areas, ii) to classify these visual features, they are fed into three separate capsule networks, and iii) using an ensemble technique, merging the outputs of these three deep capsule networks to produce their final findings. Guo et al. (23) have differentiated amygdaloid and hippocampal

Table 1. A survey on SZ classification methods

Researcher	Dataset	Samples	Methodology	Accuracy (in %)
Rozycki et. al. (2019) (16)	Created own dataset from 5 MRI Studies	941 samples, including, 440 patients with SZ and 501 HC patients	Multivariate classification using pooled data Leave-site-out validation	76 77
Lei et. al. (2019) (17)	Created own dataset by merging five different datasets	747 samples, including, 295 patients with SZ and 452 healthy HC patients	Logistic Regression SVM Deep Learning	Whole-brain images 52.74 Functional Connectivity 80.97 Graph based metrics 68.25 Whole-brain images 54.90 Functional Connectivity 81.74 Graph based metrics 72.0 Whole-brain images 51.99 Functional Connectivity 81.03 Graph based metrics 68.61
Gore et. al. (2013) (18)	Created own dataset by taking samples of SZ patients having age in between 18 and 70	450 samples, including twenty-four subjects	Neural Network	98.33
Gheiratmand et. al. (2017) (19)	FBIRN phase II fMRI dataset	380 Samples 95 subjects (46 patients, forty-nine controls) from a total of 164 subjects in the FBIRN phase II dataset	Sparse multivariate regression	74.0
Suri et. al. (2020) (20)	MRI data	Researchers used structural MRI and resting-state functional MRI data from 295 patients with SZ and 45 HC samples from five research centers.	SVM (nonlinear)	91.80
Salvador et al. (2019) (21)	Brain magnetic resonance imaging (MRI) datasets.	211 Samples including, 96 patients with SZ and 115 HC	Ridge classifier 2Back map 1Back map Lasso classifier ALFF GBC maps	87 80 65 84 71 60
Yang et. al. (2019) (22)	COBRE, UCLA and WUSTL	385 samples, including 152 patients with SZ and 232 HC	Multiple feature image capsule network ensemble	81.82

Researcher	Dataset	Samples	Methodology	Accuracy (in %)
Guo et. al. (2020) (23)	sMRI data from the Center for Biomedical Research Excellence database	147 samples, including seventy-two patients with SZ and 75 HC	Sequential backward elimination for feature selection with SVM classifier	81.75
Zeng et. al. (2018) (25)	Combined data from: Xijing Hospital, First Affiliated Hospital of Anhui Medical University, Second Xiangya Hospital in China, Center for Biomedical Research Excellence, University of California, Los Angeles, Conte Center for the Neuroscience of Mental Disorders at Washington University School of Medicine in St. Louis	1081 samples, including 474 SZ patients and 607 HC.	Multi-site pooling classification Leave-site out transfer classification	85.0 81.0
Xiao et. al. (2019) (26)	Created own dataset	326 samples, including 163 SZ patients and 163 HC	SVM model	Surface area 85% Cortical Thickness 81.1%
Oh et. al. (2020) (27)	Five public MRI data sets (BrainGluSchi, COBRE, MCICShare, NMorphCH, and NUSDAST)	873 samples, including 449 SZ, 424 of normal subjects	A three-dimensional convolutional neural network (3DCNN) & Deep learning algorithm	97
Qureshi et. al. (2017) (28)	COBRE	Seventy-two subjects from Each subgroup of the COBRE dataset.	Hybrid weight feature concatenation with Ensemble Learning Machine classifier	99.29
Mikolas et. al. (2018) (29)	Created own dataset	154 samples, including 77 HC & 77 SZ Patients)	Linear SVM	62.34
Cao et. al. (2014) (30)	Two types of data: SNP and fMRI	208 samples, including 96 SZ patients and 112 HC	Sparse representation-based variable selection	89.7

sub-regions in SZ. The accuracy of the Sequential Backward Elimination (SBE) SVM model is 81.75%. They proposed that machine learning techniques may use morphological features from the amygdaloid and hippocampal sub regions to classify SZ.

Filippis et. al. (24) have done a review of all methods using structural and functional neuroimaging. Zeng et al. (25) have collected a large multi-site functional MRI sample of a total of 734 patients including 357 with SZ. They used Multi-site pooling classification and Leave-site out transfer classification Methods. They achieved an accuracy of 85.0% and 81.0% respectively. Xioa et al. (26) have mentioned that several deficits which are complex and subtle are revealed by MRI which could be used as

objective biomarkers to discriminate SZ patients from HC. They involved a total of 326 participants and acquired high-resolution anatomic data via FreeSurfer software to obtain cortical thickness and surface area measurements. To explore the potential utility for both cortical thickness and surface area measurements in differentiating SZ patients and HC, they have used an SVM classifier.

Oh et al. (27) noted that distinctive structural abnormalities occur in patients suffering from SZ. A convolutional neural network was trained using 873 structural MRI datasets. With consistent performance, a deep learning algorithm trained on structural MR images recognized SZ in randomly selected images. When a new dataset containing younger patients and

a shorter length of sickness was supplied, the deep learning algorithm's classification ability deteriorated to an AUC of 0.71.

Qureshi et al. (28) have used multimodal features of structural and functional MRI of the brain which had assisted in the diagnosis of SZ patients. The classification was performed by machine learning and its efficiency was compared to linear and non-linear SVM and random forest bagged tree algorithms. 10-by-10 fold nested cross-validation was done for statistical significance and the conclusion was that this feature concatenation approach may assist the clinicians in SZ diagnosis.

Using diffusion tensor imaging, Mikolas et al. (29) employed a machine learning classifier to distinguish patients with SZ from HC. Methods applied by them for analyses of brain functional data are SVM and traditional tract-based spatial statistics from 154 participants. Accuracy of 62.34% was determined to distinguish both. The conclusion was that the white matter regions contribute to the correct identification of participants with SZ patients. Coa et al.(30) have faced a data integration problem which was addressed by developing a Generalized Sparse Model (GSM). So, they used weighting constituents to integrate multi-modality data for biomarker selection and developed a novel Sparse Representation-based Variable Selection (SRVS) algorithm. The results explained that the SRVS method helps identify the novel biomarkers that show stronger capability in differentiating SZ subjects from HC.

3. Analyses and Findings

Analysis of Dataset

From the above survey of all papers, we have analyzed the widely used dataset mentioned in Table II. SchizConnect (13) is an online database that connects data from the databases like fBIRN, COINS, XNAT Central, NUNDA, and NU REDCap. It has 1392 subjects in total. It allows all to access the data from several sites, dimensions, and modalities all in one place. Raw anatomical and functional MRI data from 72 SZ patients and 75 HC were provided by the Center for Biomedical Research Excellence (COBRE) (14) (ages ranging from 18 to 65 in each group). Northwestern University Schizophrenia Data and Software Tool (NUSDAST) (15) aim was to make structural MRI, genotyping, and neurocognitive data as well as an analysis tools for the SZ research community. This dataset can be accessed through SchizConnect. Functional Imaging Biomedical Informatics Research Network (fBIRN) (10) has three phases included

in which second and third are related to SZ. MIND Clinical Imaging Consortium (MCIC) (11) dataset can be downloaded through COINS.

Overview of Dataset

From the above analysis of all datasets available for SZ classification, we have chosen the MLSP 2014 SZ Classification Challenge dataset from Kaggle. In this dataset two modalities are used i.e., fMRI and sMRI recorded from 75 HC and 69 SZ patients. In this dataset two features are used namely Functional Network Connectivity (FNC) and Source-Based Morphometry (SBM).

1) FNC Features: FNC is a kind of correlation value that does the summarization of overall connection between independent brain maps over time. Therefore, the FNC feature gives a picture of connectivity patterns between independent networks (or brain maps) over time. The given FNC information is gained from fMRI from a set of HC at rest and SZ patients, using Group Independent Component Analysis (GICA). A set of brain maps and corresponding time courses was obtained in the results of the GICA decomposition of fMRI data. These time courses stated the activity of the corresponding brain map at each point in time. The FNC feature is correlated between these time courses. So, in a way, FNC indicates a subject's overall level of 'synchronicity' between the areas of the brain. FNCs are considered a functional modality feature (i.e., they describe patterns of the brain function) because this information is derived from functional MRI scans.

2) SBM Features: SBM loadings correspond to the weights of brain maps that are obtained by applying ICA of gray-matter concentration maps of all subjects. Gray-matter corresponds to the outer-sheet of the brain; it is the brain region where much of the brain signal processing occurs. In some ways, the amount of grey matter in each region of the brain suggests the amount of "computational power" available. Processing gray-matter concentration maps with the ICA yields independent brain maps whose expression levels (i.e., loadings) vary across subjects. Simply put, a near to zero loading for a given ICA-derived brain map indicates that brain regions that are outlined in that map are present in the subject lowly (i.e., the gray-matter concentration) in those regions are very low in that SBM loadings are considered a structural modality feature (i.e., they describe patterns of the brain structure) because this information is derived from structural MRI scans.

3) Feature Selection: We did feature selection to reduce the number of features.

Table 2. Widely used datasets

Dataset	Year	Modalities	Classes
FBIRN Phase II	2009	fMRI	Both have 87 SZ and 85 HC.
FBIRN Phase III (10)			
COBRE (14)	2012	rs-fMRI, Anatomical MRI	72 SZ and 75 HC
MCIC (11)	2012	sMRI, fMRI, DWI	162 SZ and 169 HC
SchizConnect (13)	2013	sMRI, fMRI	632 have no known disorder, 215 broad SZ, 384 strict SZ, 41 Schizoaffective, 10 bipolar, 44 sibling of SZ strict, 66 sibling of No known disorder
NUSDAST (15)	2013	sMRI	171 SZ, 170 Healthy, 44 Non-Psychotic Siblings, 66 Healthy Siblings
MLSP 2014 (9)	2014	fMRI, sMRI	69 SZ and 75 HC
UCLA (8)	2016	fMRI, sMRI, DWI	50 SZ, 49 Bipolar Disorder, 43 ADHD, 130 HC

However, this is only an optional step and should be evaluated whether it improves the performance of the classifiers. Another desirable choice is the Random Forest classifier, which exists in the scikitlearn library. We can also implement simple classifiers together with feature selection.

General Approach for SZ Classification

Figure 1 explains the entire approach of finding SZ behavior in subjects. All the three nodes of the triangle are bilaterally connected (diagnosis <--> imaging findings <--> symptoms) to each other (Two-way correlation of three sides of a triangle). The model has a diagnosis X on the top of a pyramid. We have considered the (n) numbers of imaging findings and (m) numbers of symptoms connected on different weights. We have to cross-correlate m kinds of symptoms and n kinds of imaging findings to get SZ classification. Different weights have been assigned to each of them. As an example, suppose that we have two symptoms of delusion & mutism and the weight that delusion has is more compared to the weight that selected mutism is having. So, that is how delusion is more correlated to

SZ. This model is called feature-model analysis & that is why we are using the SVM model. By the SVM, we have n! and m! of states or different conditions that the diagnosis X is being connected to symptoms or imaging. So, with the knowledge of all the combinations that are correlated to the diagnosis X, when any patient comes to the physician, he could easily classify SZ. With the given model, the physician has assisted support of machine that gives the probability. In that sense the model can predict at what level of probability the patient’s features comply with SZ and not depression. Our focus in this paper has not been the symptomology, but the imaging data.

We have applied various Machine Learning classifiers to classify the specific SZ symptoms. Some of these studies achieved higher accuracy. Figure 2 shows classifiers vs. accuracy data for various algorithms like Random Forest, SVM, Decision Tree, K nearest neighbors, and Gaussian Bayes. The SVM with RBF kernel provides the highest classification accuracy of equivalent to 76% without normalization and PCA. SVM maps feature in high dimension space, which uses linear and non-linear functions called kernels. The K nearest neighbors’ algorithm with no normalization

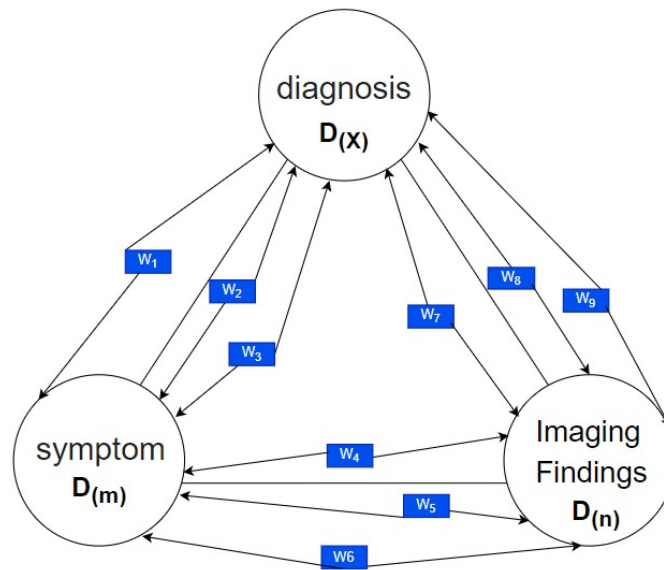


Figure 1. General approach to the study of SZ

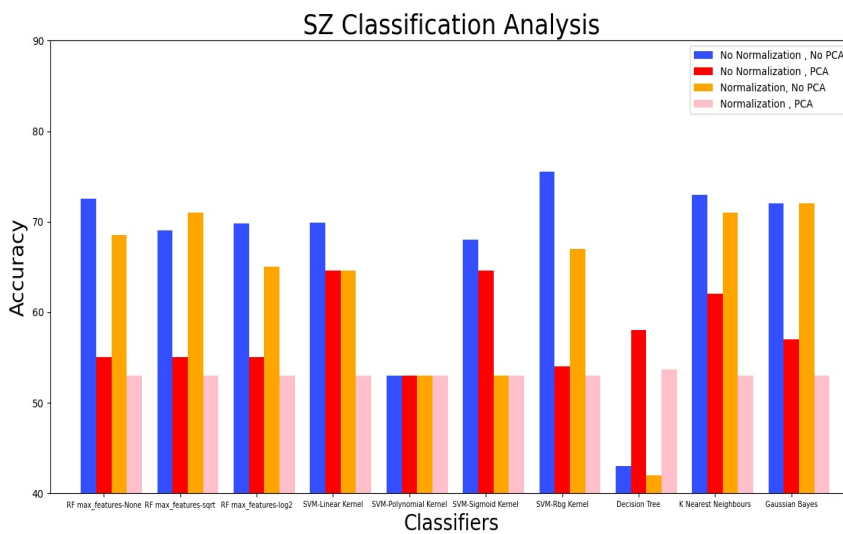


Figure 2. Accuracy of machine learning techniques

and no PCA also shows an accuracy of 73%, which is close to the SVM. We can see that the accuracy for SVM with Polynomial kernel is somehow similar for both - with and without normalization and PCA, which is 53%. The SVM classifier combined with the weighted symptoms is effective for the classification of schizophrenic diseases.

4. Conclusion

The proposed method of classifying SZ is simple, straightforward and provides favorable results. We

got higher accuracies even though we did not use normalization and PCA in SVM. We have also tried to implement ICA, but that did not give expected accuracy. With no normalization and no PCA, we are getting ~76% of accuracy in SVM and ~73% accuracy with KNN. We can conclude, as we are using smaller size of dataset this ~3% of difference in SVM and KNN classifier is not that significant. If we were using huge dataset of SZ cases, then the ~3% may be considered significant and will make clear difference in classification of SZ.

From the analysis and our findings, we can conclude

that this tool can provide promising assistance to the physicians in the diagnosis of SZ.

References

- [1] J.N. Samsom, A.H. Wong, Schizophrenia and depression co-morbidity: what we have learned from animal models, *Front. Psychiatry* 6 (2015) 13
- [2] P.T. Krishnan, et al., Schizophrenia DSchizophrenia detection using multivariate empirical mode decomposition and entropy measures from multichannel EEG Sentropy measures from multichannel EEG signal, *Biocyber. Biomed. Eng.* 40 (3) (2020) 1124–1139
- [3] H. Abouzid, et al., Signal speech reconstruction and noise removal using convolutional denoising audioencoders with neural deep learning, *Analog Integr. Circ. Sig. Process* 100 (3) (2019) 501–512.
- [4] WHO. Schizophrenia. 2019; Available from: <https://www.who.int/news-room/fact-sheets/detail/schizophrenia>.
- [5] Z. Aslan, M. Akin, Automatic detection of schizophrenia by applying deep learning over spectrogram images of EEG signals, *Traitement du Signal* 37 (2) (2020) 235–244.
- [6] Segal, D. L. (2010). Diagnostic and statistical manual of mental disorders (DSM-IV-TR). Corsini Encycl. Psychol. 1–3. doi: 10.1002/9780470479216.corpsy0271
- [7] S. Siuly, et al., A computerized method for automatic detection of schizophrenia using EEG signals, *IEEE Trans. Neural Syst. Rehabil. Eng.* 28 (11) (2020) 2390–2400.
- [8] R. A. Poldrack, E. Congdon, W. Triplett, K. Gorgolewski, K. Karlsgodt, J. Mumford, F. Sabb, N. Freimer, E. London, T. Cannon, et al., A phenome-wide examination of neural and cognitive function, *Scientific data* 3 (1) (2016) 1–12.
- [9] <https://www.kaggle.com/c/mlsp-2014-mri>.
- [10] S. Potkin, J. Turner, G. Brown, G. McCarthy, D. Greve, G. Glover, D. Manoach, A. Belger, M. Diaz, C. Wible, et al., Working memory and dlpc inefficiency in schizophrenia: the fbirn study, *Schizophrenia bulletin* 35 (1) (2009) 19–31
- [11] G. Repovs, D. M. Barch, Working memory related brain network connectivity in individuals with schizophrenia and their siblings, *Frontiers in human neuroscience* 6 (2012)
- [12] Oguz, Clark, et al., “A Review of Challenges in the Use of fMRI for Disease Classification / Characterization and A Projection Pursuit Application from A Multi-site fMRI Schizophrenia Study.” *Brain Imaging and Behavior* Springer (2008).
- [13] <http://www.schizconnect.org/>
- [14] G. Sidhu, Locally linear embedding and fmri feature selection in psychiatric classification, *IEEE journal of translational engineering in health and medicine* 7 (2019)
- [15] L.Wang, A. Kogan, D. Cobia, K. Alpert, A. Kolasny, M. I. Miller, D. Marcus, Northwestern university schizophrenia data and software tool (nusdast), *Frontiers in neuroinformatics* 7 (2013) 25
- [16] Rozycki, M.; Satterthwaite, T.D.; Koutsouleris, N.; Erus, G.; Doshi, J.; Wolf, D.H.; Fan, Y.; Gur, R.E.; Gur, R.C.; Meisenzahl, E.M. et al. Multisite machine learning analysis provides a robust structural imaging signature of schizophrenia detectable across diverse patient populations and within individuals. *Schizophr. Bull.* 2018, 44, 1035–1044.
- [17] Du Lei, Walter Pinaya, Therese van Amelsvoort, Machteld Marcelis, Gary Donohoe, David Mothersill, Aiden Corvin, Michael Gill, Sandra Vieira, Xiaqi Huang, Su Lui, Cristina Scarpazza, Jonathan Young, Celso Arango, Edward Bullmore, Gong Qiyong, Philip McGuire, and Andrea Mechelli. Detecting schizophrenia at the level of the individual: relative diagnostic value of whole-brain images, connectome-wide functional connectivity and graph-based metrics. *Psychological Medicine*, 2019.
- [18] Gore, Ranjana & Waman,. (2013). Automated Classification of Schizophrenia With Neural Networks. www.ijest.com.
- [19] Gheiratmand M, Rish I, Cecchi GA, Brown MRG, Greiner R, Polosecki PI, Bashivan P, Greenshaw AJ, Ramasubbu R, Dursun SM. Learning stable and predictive network-based patterns of schizophrenia and its clinical symptoms. *NPJ Schizophr.* 2017 May 16;3:22. doi: 10.1038/s41537-017-0022-8. PMID: 28560268; PMCID: PMC5441570.
- [20] G. S. Suri, G. Kaur and S. Moein, “Machine learning in detecting schizophrenia: an overview,” *Intelligent Automation & Soft Computing*, vol. 27, no.3, pp. 723–735, 2021.
- [21] Salvador, Raymond & Canales-Rodríguez, Erick & Guerrero-Pedraza, Amalia & Sarró, Salvador & Tordesillas-Gutiérrez, Diana & Maristany, Teresa & Crespo-Facorro, Benedicto & McKenna, Peter & Pomarol-Clotet, Edith. (2019). Multimodal Integration of Brain Images for MRI-Based Diagnosis in Schizophrenia. *Frontiers in Neuroscience*. 13. 1203. 10.3389/fnins.2019.01203.
- [22] Yang, Bo & Chen, Yuan & Shao, Quan-Ming & Yu, Rui & Li, Wen-Bin & Guo, Guan-Qi & Jiang, Jun-Qiang & Pan, Li. (2019). Schizophrenia Classification

- Using fMRI Data Based on a Multiple Feature Image Capsule Network Ensemble. *IEEE Access*. PP. 1-1. 10.1109/ACCESS.2019.2933550.
- [23] Guo, Y., Qiu, J., & Lu, W. (2020). Support Vector Machine-Based Schizophrenia Classification Using Morphological Information from Amygdaloid and Hippocampal Subregions. *Brain sciences*, 10(8), 562. <https://doi.org/10.3390/brainsci10080562>
- [24] de Filippis, R., Carbone, E. A., Gaetano, R., Bruni, A., Pugliese, V., Segura-Garcia, C., & De Fazio, P. (2019). Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: a systematic review. *Neuropsychiatric disease and treatment*, 15, 1605–1627. <https://doi.org/10.2147/NDT.S202418>
- [25] Zeng, Ling-Li & Huaning, Wang & Hu, Panpan & Yang, Bo & Pu, Weidan & Shen, Hui & Chen, Xingui & Liu, Zhening & Yin, Hong & Tan, Qingrong & Wang, Kai & Hu, Dewen. (2018). Multi-Site Diagnostic Classification of Schizophrenia Using Discriminant Deep Learning with Functional Connectivity MRI. *EBioMedicine*. 30. 10.1016/j.ebiom.2018.03.017.
- [26] Xiao Y, Yan Z, Zhao Y, Tao B, Sun H, Li F, Yao L, Zhang W, Chandan S, Liu J, Gong Q, Sweeney JA, Lui S. Support vector machine-based classification of first episode drug-naïve schizophrenia patients and healthy controls using structural MRI. *Schizophr Res*. 2019 Dec;214:11-17. doi: 10.1016/j.schres.2017.11.037. Epub 2017 Dec 6. PMID: 29208422.
- [27] Oh, J., Oh, B. L., Lee, K. U., Chae, J. H., & Yun, K. (2020). Identifying Schizophrenia Using Structural MRI With a Deep Learning Algorithm. *Frontiers in psychiatry*, 11, 16. <https://doi.org/10.3389/fpsyt.2020.00016>
- [28] Qureshi MNI, Oh J, Cho D, Jo HJ, Lee B. Multimodal Discrimination of Schizophrenia Using Hybrid Weighted Feature Concatenation of Brain Functional Connectivity and Anatomical Features with an Extreme Learning Machine. *Front Neuroinform*. 2017 Sep 8;11:59. doi: 10.3389/fninf.2017.00059. PMID: 28943848; PMCID: PMC5596100.
- [29] Mikolas, Pavol & Hlinka, Jaroslav & Skoch, Antonin & Pitra, Zbynek & Frodl, Thomas & Spaniel, Filip & Hajek, Tomas. (2018). Machine learning classification of first-episode schizophrenia spectrum disorders and controls using whole brain white matter fractional anisotropy. *BMC Psychiatry*. 18. 10.1186/s12888-018-1678-y.
- [30] Cao H, Duan J, Lin D, Shugart YY, Calhoun V, Wang YP. Sparse representation based biomarker selection for schizophrenia with integrated analysis of fMRI and SNPs. *Neuroimage*. 2014 Nov 15;102 Pt 1:220-8. doi: 10.1016/j.neuroimage.2014.01.021. Epub 2014 Feb 12. PMID: 24530838; PMCID: PMC4130811.