Combination of Machine Learning and Functional Networks Concept for Diagnosis of Autism Spectrum Disorder

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***Abstract*—The subjective assessment of experts and cost of evaluation make it much harder to diagnose an early stage autism. This could lead to other complications in later life. In this study, we approach the problem of autism identification based on functional connectivity via selecting and interpreting input features. We access the difference in alpha band connectivity in autistic and neuro-typical individuals and demonstrate how this difference can be used to identify individuals with autism. Our study highlights the importance of alpha band connectivity coupled with supervised machine learning in the diagnosis of autism spectrum disorder.**

***Index Terms*—Autism Spectrum Disorder, Electroencephalogram, Functional connectivity, Coherence, Machine learning, k-fold cross validation.**

I. Introduction

A wide range of early-appearing social communication difficulties and repetitive sensory-motor behaviors, caused by a significant genetic component as well as several other reasons, are together referred to as autism spectrum disorder (ASD). According to World Health Organization (WHO), 1 out of 100 children is suffering from autism [1]. Despite having standardized diagnostics procedures for autism, its detection and classification, to this day, is still a challenging task since the symptoms vary unimaginably from children to teenagers and no reliable biomarker is yet available.

The capability of machine learning algorithms to find pattern in large, complex and structurally unorganized raw data [2], [3] has attracted a huge attention in healthcare domain. Wide-scale use of machine learning in medical imaging [4]–[6], drugs discoveries and development [7], diseases identification and diagnosis [8], [9], and neurological disabilities identification [10] demonstrate its efficiency.

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In this work, we investigated the feasibility of using Support Vector Machine (SVM) trained on electroencephalogram (EEG) as a detection tool for ASD from age 2 to age 16. Because of the consequences of false negatives in healthcare domain, we specifically aimed to design a classifier with optimal recall and precision along with high accuracy. We also investigated the preposition of alpha band connectivity's alterations being a neural biomarker of autism by evaluating the performance of our classifier via feature selection and feature engineering. To generalize our model, we performed training and validation using an extensive dataset of 280 subjects.

The rest of the paper is organized as follows: after the presentation of some related work in Section II, Section III describes the implementation of the proposed methodology. Section IV presents the results and the discussion, and the paper is concluded in Section V.

II. Related Works

Advancements in machine/deep learning led researchers from all around the world to use it in the healthcare domain. The same trend can be seen in ASD detection and classification. Methods used to detect autism can be generally categorized into machine learning and deep learning methods.

In machine learning techniques, features are extracted manually and a classifier is then trained using these hand-crafted features. A combination of linear and non-linear features was employed in previous studies, particularly, modified MultiScale Entropy (mMSE) [11], texture parameters of higher order spectra of EEG bi-spectrum [12], Power Spectrum, Wavelet Transform, Fast Fourier Transform (FFT), Fractal Dimension, Correlation Dimension, Lyapunov Exponent, Entropy, Detrended Fluctuation Analysis and Synchronization Likelihood [13], Minimum-Redundancy-Maximum-Relevance (MRMR) [14], and physiological and

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behavioral features [15]. All these studies used raw EEG data with the exception of [14] and [15] which used eye-tracking data along with EEG. The mostly used classifier was SVM, giving a classification accuracy of above 70% with k-fold cross validation scheme [11], [13], [14].

In deep learning, the designed model extracts the features as a part of the training process. This technique though provides high accuracy, is dependent on an extensive amount of data, and the resulting models are often black boxes in nature. Grossi et al. proposed a novel approach of using a Multi-Scale Ranked Organizing Map coupled with Implicit Function as Squashing Time algorithm (MS-ROM/I-FAST) for classification [16]. MS-ROM/I-FAST is a complex Artificial Neural Network (ANNs) capable to extract features in EEG through the analysis of a few minutes of EEG without any preliminary pre-processing. An interesting advancement was done by Grossi et al. in [17] where EEG from only two sensors was used to check if the ASD signature is already present at birth using Genetic doping algorithm and a neural network. [18] and [19] used 2D representation of EEG signals to train deep neural networks.

III. Materials and Methods

A. Data acquisition

During the EEG recording experiment, the subjects had to sit with their eyes open and try not to make any visible movements. The EEG data were 19-channel recordings with an average duration of about several minutes at a sampling rate of 250 Hz, and the duration of the EEG recording for each individual subject was determined by his ability to perform the task as long as possible. The electrodes were placed according to a 10-20 arrangement. The EEG signals were preliminarily cleaned of artifacts using frequency filters and the ICA method.

After pre-processing, we defined four age groups. Table I shows the distribution.

TABLE I
Participants Distribution: Participants divided into 4 groups based on their age.

Group	Age	Total subjects	
		ASD	Control
A	$2 \leq age \leq 4$	46	37
B	$5 \leq age \leq 6$	37	46
C	$7 \leq age \leq 9$	46	52
D	$age \geq 10$	20	42

B. Connectivity analysis

To investigate the difference in functional connectivity of subjects with autism and typically developing individuals, we used the measure of coherence [20], [21]. Coherence between two neural rhythms $x(t)$ and $y(t)$ is defined as:

$$COH_{xy}(f) = \frac{|P_{xy}(f)|^2}{P_{xx}(f)P_{yy}(f)}$$

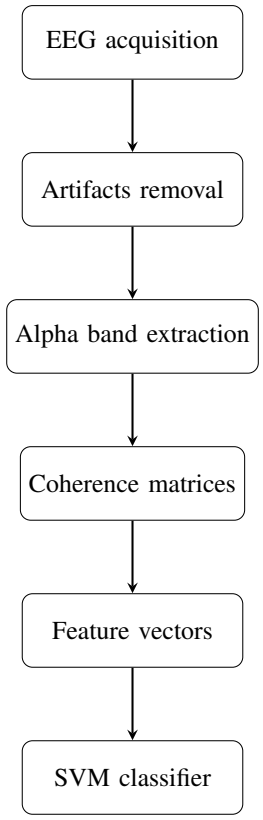

Fig. 1. **Flow chart of applied methodology:** Coherence functional connectivity was extracted from alpha band of cleaned EEG signals and fed to nonlinear kernalized SVM classifier.

Here, frequency f was defined in the range 8-12 Hz (Alpha band). Several previous studies have shown that a difference in alpha connectivity exists between these classes [22]–[27]. This makes alpha connectivity a useful neuromarker for the autism diagnosis. P_{xx} and P_{yy} are the power spectral densities estimates of x and y, respectively and P_{xy} is the cross-spectral density estimate of x and y. Coherence lies between 0 and 1, where 0 implies no coherence and 1 implies perfect coherence between x and y. We used Scipy module available in Python programming language to extract coherence matrices from EEG.

Coherence matrices were of size 19×19. Because of their symmetrical nature, we constructed coherence vectors from matrices by taking the upper triangular matrix. The resulting coherence vectors were of size $19 \times (19-1)/2$.

C. Machine learning

We used machine learning to classify subjects in their respective classes, i.e., autistic or typically developed. After computing connectivity features, we ranked them in decreasing order of their relevance in discrimination between subjects with and without autism. Taking top n features as input n = 1 .... N, where N is a maximum number of features,

we tested the performance of the nonlinear classifier. This allowed us to evaluate the performance of our classifier against the number of features used to train. We then choose an optimal number of input features that provided optimal accuracy with sufficient recall and precision. This chosen set of features provided a connectivity structure that was most informative for discrimination among subjects with and without autism.

1) Feature engineering: The performance of the machine learning model largely depends upon the features, we use for training. Generally, feeding all features for training negatively impacts the model's performance since most of them are irrelevant or less relevant to the response. Using all features also increases the computational cost of training. To avoid this, feature engineering is used. Feature engineering is a core concept of machine learning where we employ domain knowledge to use specific features in order to enhance the model's performance and decrease computational cost. Till now, we have $19 * (19-1)/2 = 171$ functional connections between sensors. In order to select key features out of these 171 features, we employed a filter-type feature selection algorithm [28]. In filter-type feature selection algorithm, the importance of a feature is calculated based on its characteristics such as feature variance and its relevance to the response. We used ANOVA f-test [29] as a feature selection criterion. Greater the test value, more helpful the feature for discrimination and vice versa.

2) Classifier: Proposing a complex neural network model in order to apprehend an already complex network, i.e., the brain, is not such a good option. That's why we employed a nonlinear support vector machine (SVM) classifier with radial basis function (RBF) as a kernel. Subjects with autism were assigned a numerical label of 1, whereas typically developing subjects were assigned a numerical label of 0. We used an equal number of subjects from all groups to prevent our classifier from bias. We used a k-fold cross-validation scheme to train and test our classifier. Since the number of subjects in groups is small, this validation scheme is suitable [30]. For each group, the k was chosen such that k = (number of subjects)/10. This made sure that for each iteration, we would have 10 subjects. During each iteration, the model was trained on $k^{th} - 1$ folds and validated on the remaining k^{th} fold. In order to further prevent our model to inherit bias, we repeated the training for 50 iterations (the data was randomly shuffled ones, in each iteration) and took the mean. For the performance measurement of our trained classifier, we used accuracy, precision, and recall. These performance metrics can be defined as:

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN}$$

$$Recall = \frac{TP}{TP + FN}$$

$$Precision = \frac{TP}{TP + FP}$$

Here, TP is a true positive, which means that a subject with autism is correctly classified; TN is a true negative, which means that a subject without autism is incorrectly classified as one with autism; FP is a false positive, which means that a subject without autism is correctly classified; FN is a false negative, which means that a subject with autism is incorrectly classified as one without autism.

IV. Results and Discussion

Figure 2 shows the top five connections/features that contributed most to classification. It is interesting to note that for *group A*, connectivity in the left temporal, frontal, and occipital lobes is prominent ($\alpha = 0.05, t_{49} = 156.4948, p \leq 0.001, \sigma = 0.0338$). For *group B*, connectivity between the right and left temporal lobe ($\alpha = 0.05, t_{49} = 271.0675, p \leq 0.001, \sigma = 0.0206$), for *group C*, connectivity in the frontal lobe ($\alpha = 0.05, t_{49} = 218.0905, p \leq 0.001, \sigma = 0.0245$), and for *group D*, in right temporal, frontal, and occipital lobes are prominent ($\alpha = 0.05, t_{49} = 127.9471, p \leq 0.001, \sigma = 0.0435$). Studies done by Muries et al. [22] and Just et al. [31] supported these findings indicating a weak coherence pattern that exists between the frontal lobe and the rest of the cortex in individuals with autism. Cognitive, sensory, and motor functions are largely dependent on the frontal lobe, and therefore it's somewhat unsurprising that a reduction is observed in frontal-posterior functional connectivity.

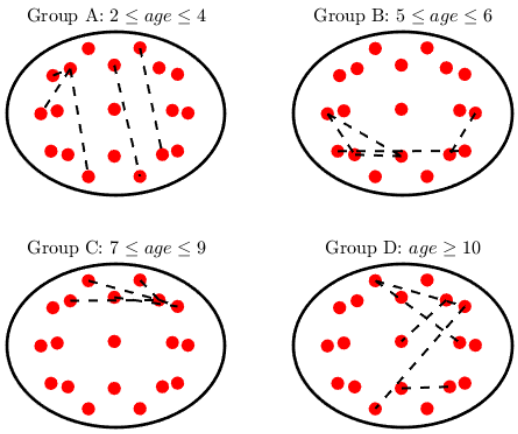

Fig. 2. **Functional connectivity structures:** Top five functional connection that contributed most in ASD identification, computed via ANOVA f-test. For groups A, C, and D, connectivity between frontal lobe and rest of cortex is prominent.

It is also interesting to note that for different groups, an optimal balance of accuracy, recall, and precision is achieved at a different number of features. Only 10, 38, 28, and 10 connections are most informative out of 171 connections for groups A, B, C, and D, respectively. This engineering of

input features is recently proven to be quite successful in classifying cognitive brain states [32]. Figure 3 presents the optimal accuracy, precision, and recall scores.

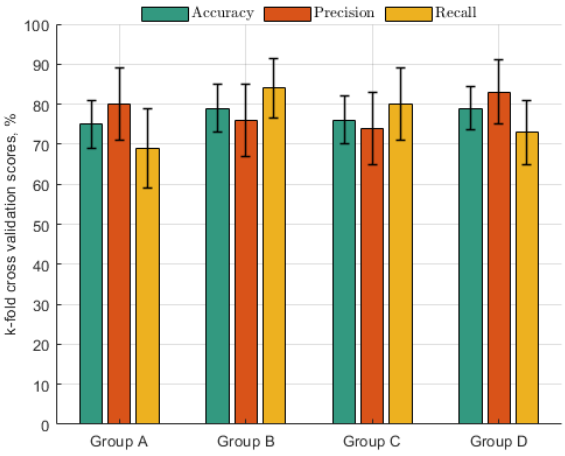

Fig. 3. **Performance metrics:** k-fold cross validation scores for each group. Bars represent mean and whiskers represent standard deviation over the folds and fifty simulations.

V. Conclusion

Autism spectrum disorder is a concerning neural disorder worldwide. In this work, we evaluated the performance of supervised machine learning in the identification of autism via capturing and analyzing EEG. The proposed methodology not only provided an optimal balance between accuracy, recall, and precision, but also emphasized the importance of the applicability of alpha band connectivity as a neural biomarker for autism detection in addition to finding the most informative connections in the alpha band and rejecting several irrelevant ones. We expect that our findings could effectively contribute to ongoing research in autism spectrum disorder and the development of effective AI diagnostic tools.

References

[1] "Autism," (accessed Jul. 25, 2022). [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/autism-spectrum-disorders

[2] S. Kurkin, E. Pitsik, and N. Frolov, "Artificial intelligence systems for classifying eeg responses to imaginary and real movements of operators," in *Saratov Fall Meeting 2018: Computations and Data Analysis: from Nanoscale Tools to Brain Functions*, vol. 11067. SPIE, 2019, pp. 42–47.

[3] A. Kuc, S. Korchagin, V. A. Maksimenko, N. Shusharina, and A. E. Hramov, "Combining statistical analysis and machine learning for eeg scalp topograms classification," *Frontiers in Systems Neuroscience*, vol. 15, 2021.

[4] B. J. Erickson, P. Korfiatis, Z. Akkus, and T. L. Kline, "Machine learning for medical imaging," *Radiographics*, vol. 37, no. 2, p. 505–515, Mar 2017. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5375621/

[5] P. Chholak, G. Niso, V. A. Maksimenko, S. A. Kurkin, N. S. Frolov, E. N. Pitsik, A. E. Hramov, and A. N. Pisarchik, "Visual and kinesthetic modes affect motor imagery classification in untrained subjects," *Scientific reports*, vol. 9, no. 1, pp. 1–12, 2019.

[6] P. Chholak, S. A. Kurkin, A. E. Hramov, and A. N. Pisarchik, "Event-related coherence in visual cortex and brain noise: An meg study," *Applied Sciences*, vol. 11, no. 1, p. 375, 2021.

[7] J. Vamathevan, D. Clark, P. Czodrowski, I. Dunham, E. Ferran, G. Lee, B. Li, A. Madabhushi, P. Shah, M. Spitzer, and S. Zhao, "Applications of machine learning in drug discovery and development," *Nature Reviews Drug Discovery*, vol. 18, no. 66, p. 463–477, Jun 2019. [Online]. Available: https://www.nature.com/articles/s41573-019-0024-5

[8] M. Fatima and M. Pasha, "Survey of machine learning algorithms for disease diagnostic," *Journal of Intelligent Learning Systems and Applications*, vol. 09, no. 0101, p. 1, 2017.

[9] O. E. Karpov, V. V. Grubov, V. A. Maksimenko, S. A. Kurkin, N. M. Smirnov, N. P. Utyashev, D. A. Andrikov, N. N. Shusharina, and A. E. Hramov, "Extreme value theory inspires explainable machine learning approach for seizure detection," *Scientific Reports*, vol. 12, no. 1, pp. 1–14, 2022.

[10] M. A. Myszczynska, P. N. Ojamies, A. M. B. Lacoste, D. Neil, A. Saffari, R. Mead, G. M. Hautbergue, J. D. Holbrook, and L. Ferraiuolo, "Applications of machine learning to diagnosis and treatment of neurodegenerative diseases," *Nature Reviews Neurology*, vol. 16, no. 88, p. 440–456, Aug 2020. [Online]. Available: https://www.nature.com/articles/s41582-020-0377-8

[11] W. Bosl, A. Tierney, H. Tager-Flusberg, and C. Nelson, "Eeg complexity as a biomarker for autism spectrum disorder risk," *BMC Medicine*, vol. 9, no. 1, p. 18, Feb 2011. [Online]. Available: https://doi.org/10.1186/1741-7015-9-18

[12] T.-H. Pham, J. Vicnesh, J. K. E. Wei, S. L. Oh, N. Arunkumar, E. W. Abdulhay, E. J. Ciaccio, and U. R. Acharya, "Autism spectrum disorder diagnostic system using hos bispectrum with eeg signals," *International Journal of Environmental Research and Public Health*, vol. 17, no. 33, p. 971, Jan 2020. [Online]. Available: https://www.mdpi.com/1660-4601/17/3/971

[13] D. Abdolzadegan, M. H. Moattar, and M. Ghoshuni, "A robust method for early diagnosis of autism spectrum disorder from eeg signals based on feature selection and dbscan method," *Biocybernetics and Biomedical Engineering*, vol. 40, no. 1, p. 482–493, Jan 2020. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0208521620300139

[14] J. Kang, X. Han, J. Song, Z. Niu, and X. Li, "The identification of children with autism spectrum disorder by svm approach on eeg and eye-tracking data," *Computers in Biology and Medicine*, vol. 120, p. 103722, May 2020. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0010482520301074

[15] M. Liao, H. Duan, and G. Wang, "Application of machine learning techniques to detect the children with autism spectrum disorder," *Journal of Healthcare Engineering*, vol. 2022, p. e9340027, Mar 2022. [Online]. Available: https://www.hindawi.com/journals/jhe/2022/9340027/

[16] E. Grossi, C. Olivieri, and M. Buscema, "Diagnosis of autism through eeg processed by advanced computational algorithms: A pilot study," *Computer Methods and Programs in Biomedicine*, vol. 142, p. 73–79, Apr 2017. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0169260716312081

[17] E. Grossi, G. Valbusa, and M. Buscema, "Detection of an autism eeg signature from only two eeg channels through features extraction and advanced machine learning analysis," *Clinical EEG and Neuroscience*, vol. 52, no. 5, p. 330–337, Jul 2021. [Online]. Available: https://doi.org/10.1177/1550059420982424

[18] M. N. A. Tawhid, S. Siuly, H. Wang, F. Whittaker, K. Wang, and Y. Zhang, "A spectrogram image based intelligent technique for automatic detection of autism spectrum disorder from eeg," *PLOS ONE*, vol. 16, no. 6, p. e0253094, Jun 2021. [Online]. Available: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0253094

[19] M. Baygin, S. Dogan, T. Tuncer, P. Datta Barua, O. Faust, N. Arunkumar, E. W. Abdulhay, E. Emma Palmer, and U. Rajendra Acharya, "Automated asd detection using hybrid deep lightweight features extracted from eeg signals," *Computers in Biology and Medicine*, vol. 134, p. 104548, Jul 2021. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0010482521003425

[20] A. M. Bastos and J.-M. Schoffelen, "A tutorial review of functional connectivity analysis methods and their interpretational pitfalls," *Frontiers in Systems Neuroscience*, vol. 9, Jan 2016. [Online]. Available: http://journal.frontiersin.org/Article/10.3389/fnsys.2015.00175/abstract

[21] A. E. Hramov, N. S. Frolov, V. A. Maksimenko, S. A. Kurkin, V. B. Kazantsev, and A. N. Pisarchik, "Functional networks of the brain: from connectivity restoration to dynamic integration," *Physics-*

Uspekhi, vol. 64, no. 6, p. 584–616, Sep 2021. [Online]. Available: https://iopscience.iop.org/article/10.3367/UFNe.2020.06.038807

[22] M. Murias, S. J. Webb, J. Greenson, and G. Dawson, "Resting state cortical connectivity reflected in eeg coherence in individuals with autism," *Biological psychiatry*, vol. 62, no. 3, p. 270–273, Aug 2007. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001237/

[23] J. Wang, J. Barstein, L. E. Ethridge, M. W. Mosconi, Y. Takarae, and J. A. Sweeney, "Resting state eeg abnormalities in autism spectrum disorders," *Journal of Neurodevelopmental Disorders*, vol. 5, no. 1, p. 24, 2013. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3847481/

[24] E. V. Orekhova, M. Elsabbagh, E. J. Jones, G. Dawson, T. Charman, and M. H. Johnson, "Eeg hyper-connectivity in high-risk infants is associated with later autism," *Journal of Neurodevelopmental Disorders*, vol. 6, no. 1, p. 40, 2014. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4232695/

[25] A. Dickinson, C. DiStefano, Y.-Y. Lin, A. W. Scheffler, D. Senturk, and S. S. Jeste, "Interhemispheric alpha-band hypoconnectivity in children with autism spectrum disorder," *Behavioural brain research*, vol. 348, p. 227–234, Aug 2018. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5993636/

[26] A. Dickinson, C. DiStefano, D. Senturk, and S. S. Jeste, "Peak alpha frequency is a neural marker of cognitive function across the autism spectrum," *The European journal of neuroscience*, vol. 47, no. 6, p. 643–651, Mar 2018. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5766439/

[27] J. C. Edgar, "Identifying electrophysiological markers of autism spectrum disorder and schizophrenia against a backdrop of normal brain development," *Psychiatry and Clinical Neurosciences*, vol. 74, no. 1, p. 1–11, 2020. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/pcn.12927

[28] W. Duch, *Filter Methods*, ser. Studies in Fuzziness and Soft Computing. Berlin, Heidelberg: Springer, 2006, p. 89–117. [Online]. Available: https://doi.org/10.1007/978-3-540-35488-8_4

[29] L. Stahle and S. Wold, "Analysis of variance (anova)," *Chemometrics and Intelligent Laboratory Systems*, vol. 6, no. 4, p. 259–272, Nov 1989. [Online]. Available: https://www.sciencedirect.com/science/article/pii/0169743989800954

[30] T. Fushiki, "Estimation of prediction error by using k-fold cross-validation," *Statistics and Computing*, vol. 21, no. 2, p. 137–146, Apr 2011. [Online]. Available: https://doi.org/10.1007/s11222-009-9153-8

[31] M. A. Just, T. A. Keller, V. L. Malave, R. K. Kana, and S. Varma, "Autism as a neural systems disorder: A theory of frontal-posterior underconnectivity," *Neuroscience and Biobehavioral Reviews*, vol. 36, no. 4, p. 1292–1313, Apr 2012. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3341852/

[32] N. Frolov, M. S. Kabir, V. Maksimenko, and A. Hramov, "Machine learning evaluates changes in functional connectivity under a prolonged cognitive load," *Chaos: An Interdisciplinary Journal of Nonlinear Science*, vol. 31, no. 10, p. 101106, 2021.