Computational Model of Functional Connectivity Distance Predicts Neural Alterations

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***Abstract*—Modelling brain signals play a crucial role in analysing the brain's architecture, functions and associated disorders. This paper aims to model the brain topology by exploring the relationship between complex neural correlates and functional connectivity-based distances. A computational model inspired by multivariate visibility graphs (VG) algorithm and Euclidean distance is proposed to analyse quantitatively the brain network data. When applied to resting-state EEG signals from three groups (typically developing (TD), autism spectrum disorder (ASD), and epilepsy (E)), the network topological properties (e.g., global efficiency, modularity, small-worldness, and betweenness centrality) demonstrate variations in connectivity distance probabilities among brain regions (e.g., frontal, temporal, parietal, and occipital) via the model's delay and connection distance parameters. The results showed a higher delay and skewed distribution towards short functional connections in ASD than in TD, while a lower delay in E than in ASD and TD. Additionally, ASD had more short-distance connections, while E had more long-distance connections compared to TD. ASD and E significantly overlapped over short-distance connections within the temporal lobe. In summary, the proposed model illustrates that delay parameter and connection distance obtained from brain network data have the potential to objectively identify and associate co-occurring neurological conditions (e.g., ASD and E).**

***Index Terms*—Autism, Brain Network, Functional Connectivity, EEG, Epilepsy, Euclidean Distance, Brain Topology, Visibility Graph**

I. Introduction

EXPLORING brain network data and understanding brain functions via different data analytics techniques, such as efficient information exchange among different regions, is a challenging problem. Recent years have seen an increased number of research reports for the screening [1], [2], detection [3]–[5], management [6]–[10] and understanding [11]–[13] brain disorders such as Autism Spectrum Disorder (ASD). To dig deeper, the analysis of complex brain networks and their complex connections play a crucial role in analysing brain topology in disorders ASD and Epilepsy (E) [12], [14]. Brain functional connectivity (FC) serves as a means to study inter-regional communication of the brain in people with disorders as well as in Typical Developing (TD) individuals [15]. The neuro-computational models have already uncovered how the human connectome limits the cross-regional connectivity of the brain networks [16]–[19]. The topology of brain FC networks modelled using a single parameter-based probability model extracts anatomical distances (Euclidean) to explain coordination in brain regions [20]. The theory-based data investigation methods depict neighbouring brain areas are more likely to interact with each other, reducing the metabolic costs [21]. Simultaneously, they also maintain a few long-distance connections to accelerate data transmission. Thus, the data analytics model has revealed complex topology as a trade-off factor between constraints on anatomical distances and trends for clustered connections [16]. However, the studies have majorly focused on correlating regions with the anatomical distance but failed to provide information on connection distance-based alterations in the brain network and to compute the connectivity distances in case the brain signals are in the form of multivariate data.

The present paper aims to extend the work on brain data analysis methods and investigates how the alterations in the whole-brain FC can detect alteration in terms of connection among brain units/structures representing brain topologies, which leads to conditions like ASD and E and their co-occurrence [12]. A data-driven method that models the FC distances extracted from brain signal (i.e., EEG) is proposed to check the suitability of brain connections in detecting the neurological conditions (i.e., ASD, E, and TD) more precisely. This work uses graph-based algorithms to map brain signals into complex networks comprising edges and nodes and analyse modification in the edges using complex metrics. Here, in the case of multichannel EEG signals, each channel is considered a node, and the relation between the two channels is regarded as an edge. To form an edge, the association between the channels is computed via different parameters such as correlation coefficient, synchronisation likelihood, coherence, and mutual information [21]–[23]. Afterwards, a certain threshold value of the computed parameter is decided to consider the network's corresponding edges (>threshold value). The formulated graph can be analysed by extracting complex network features, such as clustering coefficient and characteristic path length [24]. However, all these methods are biased to threshold criteria leaving many brain patterns unexplored and even unnoticed.

One of the techniques, namely the Visibility Graph (VG), has the potential to overcome some of the shortcomings of the existing methods as outlined in [25]. It provides a connection (i.e., an edge) between two nodes by defining a visibility criterion between them. This contributes to the formulation of a graph (i.e., a network formed by nodes and edges connecting them) as described in section III-B1 [25].

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Since the brain signals represent orchestrated and complex interactions of correlating brain units/regions, the VG can map this complexity at the network level. The VG method allows the construction of graph networks from the acquired EEG signals. Therefore, the VG method provides a possible representation of the brain's structural/regional units in a graph format enabling the application of powerful graph theoretical metrics to study subtle patterns seen during the inter- and intra-unit (region/structure) communication in the brain which otherwise are difficult to study and compare.

The brain contains modulatory neurotransmitter systems with extensive projections that influence overall brain activity [26]. Disruptions in these systems are associated with various neuropsychiatric disorders [27]. By adjusting specific neural processes, these systems impact perception, cognition, and behaviour [28], [29]. This makes the VG method very powerful in capturing the spontaneous variability of brain signals, which is considered one of the brain's inherent physiological aspects. The VG method also allows these signals to be translated into a scale-free and random graph for further analysis to study the variability of the network.

The VG method can be extended to a multivariate form to construct a multiplex network with layers generated from multiple EEG channels. The multivariate VG mainly uncovers dependency among different layers of the multiplex network by describing and quantifying the interlayer synchronisations. This provides whole-brain connectivity information using the multiplex network formulated for each time instance of the multichannel EEG data. Relevant metrics extracted from the connectivity information can help in understanding neural alterations pertaining to different neurological conditions such as ASD, E and TD.

Based on this, the current work puts forward the following contributions:

- Propose a multivariate VG-based computational model of FC distance to analyse multichannel brain signals.
- Provide a probability density-based delay metric to reflect connection variations in predicting brain network topology of ASD, E, and TD.
- Provide a quantitative means to identify co-occurring neurological conditions (e.g., ASD with E) derived from multichannel brain signals.

The rest of the paper is organised as follows: section II summarises the existing literature on the topic while section III discusses the demographic and EEG data of participants, followed by a detailed description of multivariate VG-based complex network construction, validation parameters, simulated probabilistic network models, hypothesis framing for identifying network differences. Finally, sections IV, V and VI present the results, discussion and conclusion with the future scope of the proposed model.

II. Literature Review

Priorly, the researchers have worked on modelling brain connection distance to find out the neural markers leading to neuro-[degenerative/developmental] disorders [16], [30]. One of the data-driven modelling studies has brought forward the concept of the relationship between geometric distance, FC, and network topology to evaluate neurological conditions such as schizophrenia [16]. Another study investigated the balance between anatomical wiring cost and brain data complexity, suggesting that any disruption in wiring might contribute to neuropsychiatric disorders [31]. Researchers also successfully revealed the dependence of FC on the distance between different brain regions [32]. This dependence provided an estimation of neural complexity under a cognitive demand and metabolic cost of sustaining links between brain elements [33], [34]. Based on this concept, the present paper has proposed distance metrics-based algorithms to build complex networks and find out perturbations in brain connectivity of individuals with ASD and E.

Researchers have used neuroimaging and electrophysiological data such as Magnetic Resonance Imaging (MRI) and Electroencephalogram (EEG) to investigate brain connectivity under resting state and different experimental conditions [35]–[37]. Investigations using resting state have been more informative compared to a task-based state in understanding the alteration and synchronisation of brain regions. The variations in the interplay of different brain regions provide useful insights into understanding various neurological conditions such as ASD and E [34]. Transforming brain signals, such as EEG, into complex graph networks and extracting graph-based measures from them have shown the potential to reveal hidden information and patterns from these signals [38] to describe brain connectivity networks of individuals with ASD and E [24]. For example, a recent study constructed a complex brain network from fMRI data using graph-theory-based methods and utilised phenotype information of individuals with ASD as edge weights. The study computed the correlation coefficient of the resulting network and detected ASD with 70.4% accuracy [39]. A similar study reported that both over-connectivity and under-connectivity in different brain regions could differentiate ASD and TD individuals [40].

Researchers used VG algorithm to convert single-channel EEG into a complex network to extract parameters, namely average degree as features to classify ASD and TDs with high accuracy or to quantify network complexity [41]. Similarly, the VG was used to convert the brain univariate EEG dynamics into a complex network and classify epileptic signals with 100% accuracy using an SVM classifier [42]. Thus, the univariate series-based studies proved the VG approach is promising for transforming the brain signals into a graph network for better analysis of the pathological condition.

A. Computational Data Analytics Models and Limitations

The authors in [16] utilised an anatomical Euclidean distance (ED)-based model to evaluate the brain's FC in schizophrenia from fMRI data. The study compared connectivity with the anatomical distances and found excessive pruning of short connections as a reason for topological disturbances in schizophrenia [16]. Another study utilised the same anatomical ED-based model to investigate FC variations across the lifespan [43]. It concluded that FC reorganisation over a lifespan could be characterised using mean connection

TABLE I
DEMOGRAPHIC DATA OF THE PARTICIPANTS.

Measures		**ASD**	**E**	**TD**	**Statistical Test**		
Number of Participants		34	34	32		Value	*p-value
Male / Female Ratio		13:4	12:5	5:3	Chi-square (df)	0.92 (1)	0.53
Age (Years)		13.26 $\pm$ 3.4 (7-20 y)	14.21 $\pm$ 4.2 (8-20 y)	12.82 $\pm$ 2.4 (6-19 y)	t-test (df)	TD vs ASD: 3.32 TD vs E: 4.51	0.34
ADOS-2 Total Score		8.92 $\pm$ 1.23	-	-		-	-
MISIC (IQ)	Verbal	102.4 $\pm$ 7.3	104.5 $\pm$ 4.2	114.3 $\pm$ 12.9		TD vs ASD: 12.14 (33) TD vs E: 8.56 (33)	0.62 0.54
	Performance	105.2 $\pm$ 10.1	107.3 $\pm$ 6.3	108.7 $\pm$ 12.0		TD vs ASD: 12.14 (33) TD vs E: 8.56 (33)	0.43 0.36
	Full-scale	104.7 $\pm$ 9.2	107.6 $\pm$ 8.7	113.4 $\pm$ 13.2		TD vs ASD: 12.14 (33) TD vs E: 8.56 (33)	0.18 0.22

density and mean anatomical ED of the network. Following the same model, the authors in [44] proved that the distance metric in complex networks is a fundamental concept for interpreting the dynamical features of temporal networks.

In cases of ASD, it is found that connection length plays a major role in defining short- and long-distance FC in posterior cingulate and prefrontal cortex regions. However, from the literature, the majority of the model-based studies in ASD and E focus on short- and long-distance connections computed using the distance penalty metric among brain regions are limited in number. Moreover, there are no studies to quantitatively model the neural associations of both conditions. As a result, neuroscientists struggle to reproduce the findings and precisely diagnose co-existing neurological conditions such as ASD and E. The lack of a mathematical model motivates us to propose a simple exponential decay model that can find the variations in the brain FC via the distance penalty metric. The complex network from a multi-variate time series is tailored using the VG algorithm and Multivariate Euclidean Distance (MED) to detect brain topologies in ASD, E and TD.

B. Purpose

The goal of the study is to design a quantitative data-driven model for identifying altered connectivity in ASD and E conditions based on brain connectivity parameters. This paper puts forward a simple method, where the edge distance metric is computed using MED to find atypicality in brain networks. The proposed method is also applied to detect commonality and variability in brain connectivity of atypicalities (i.e., ASD and E conditions) with TD. The present paper utilised ED, despite strongly curved connections, as this metric proved to be a better one in capturing the variance of connections across the brain regions. Many connections in the brain are strongly curved (e.g., 15% of the prefrontal cortex connections are curved) and it becomes difficult to find the link length of such connections. In such cases, ED has outperformed other metrics like topological length and fibre length in representing the multi-factorial nature of network connectivity [30], [45]. Furthermore, a probabilistic model is utilised to explore how variation in the penalisation of long-distance connections can represent changes in the topological metrics of brain networks.

III. MATERIALS AND METHODS

A. Dataset Description

The data collection procedure was approved by the institutional ethical committee of Dr B R Ambedkar National Institute of Technology, Jalandhar 144 011, India (approval number: NITJ/EC 568,712,092,018) and carried out according to the APA standards. As summarised in Table I, thirty four participants with ASD (age range: 7–20 years, mean: 13.26 years) who fulfilled clinical diagnostic criteria as per DSM-5 and ICD-10, were selected for the present work. The hospital team conducted ASD diagnosis using the Autism Diagnostic Observation Schedule–2 (ADOS-2) tool, which took 30–60 minutes to investigate social and communication interaction. The mean ADOS-score value in ASD was 8.92$\pm$1.23. Thirty-four age- and IQ-matched participants with E condition (age range: 8–20 years, mean age: 14.21 years) and thirty-two TD (age range 6–19 years, mean age: 12.82 years) were also recruited. The hospital team provided additional data of the individuals with E condition who were instructed to stop any related medication and treatment for a period of a week. The IQ of the participants was evaluated using the Malin's Intelligence Scale for Indian Children (MISIC) scale. The individuals with ASD and E were found to have a similar IQ (mean difference: 3.56, t(33): 7.91, p: 0.08). The IQ was also compared with TD, and the difference was found insignificant among TD vs ASD (mean difference: 8.56, t(33): 12.14, p: 0.18) and TD vs E (mean difference: 5.83, t(33): 8.56, p: 0.22).

The subjects were checked for the exclusion criteria (i.e., any prior medication, medical history, language or cognition impairment, IQ>70). EEG signals with closed eyes were recorded for 30 seconds using the EEG-1200 machine (Neurofax, Nihon Kohden, Tokyo, Japan) following recording parameters listed in Table II. For the individuals with E condition, the signals were recorded from the epileptogenic zones corresponding to seizure and epileptiform activity. The data preprocessing was done using EEGLAB (e.g., *runica()* function) and visually to remove noises, eye blinks (>100 μV), and signal portions with large amplitudes ($> 3\times$ mean amplitude). The recording of the brain signals simultaneously from different brain regions is defined as multivariate time

TABLE II
EEG SIGNAL RECORDING PARAMETERS SET BY THE HOSPITAL UNIT

Parameters	Values
Electrode System	10-20 standard system
Sampling Frequency	128 Hz
Filters (in recording system)	0.5–70 Hz (Bandpass) & 50 Hz (Notch)
Reference	Right and Left Mastoid
Electrode & Impedance	Ag/AgCl & <10 KΩ
Recording Software	Neurofax, Nihon Kohden, Tokyo, Japan

series. To analyse the acquired multivariate data of 30 seconds per participant, 4 segments of 960 samples each were created.

B. Model Construction

In the present paper, brain networks were constructed using the proposed multivariate VG method and the extracted network metrics were validated using a traditional simulated probabilistic model.

1) Multivariate VG-based Complex Network Construction: The multivariate VG method was utilised to construct edges using MED for the visible links. The MED was advantageous as it could build VG-based networks for the brain signals both within and between the electrodes. This allowed the construction of complex networks for each electrode of interest (EoI) leading to multiplex networks for each time instance from different EoI. To attain the complex weighted graph network consisting of nodes, visible edges, and weights defined by ED, the steps listed below are followed:

a) Step 1: Each data-point in the time series (X) of an EoI is a node of the complex network such that, $X(t_k) = \{x(t_1), x(t_2), \ldots, x(t_N)\}; 1 \leq k \leq N$ with $N = \text{len}(X)$.

b) Step 2: Build edges between visible nodes for within and among EoI as per the visibility criteria (Eq. 1) [25]:

$$x(t_2) < x(t_1) + (x(t_3) - x(t_1))\frac{t_2 - t_1}{t_3 - t_1} \tag{1}$$

where, $x(t_1), x(t_2), x(t_3)$ are data values (i.e., nodes) at t_1, t_2, t_3 times.

c) Step 3: For multivariate series like EEG, each of the series (i.e., channels or EoI) yields a VG, giving a multi-layer graph whose layers are equal to the number of electrodes [25]. In such a multi-layered graph, the nodes are naturally aligned across different layers, and it is possible to form a complex network for differential layers (e.g., $X - Y$). As a result, the multi-layer graph effectively forms a multiplex network; that is, the nodes are aligned across layers based on timestamps with intra-connection weights defined by Eq. 2.

$$e_m(X) = \left(\frac{1}{n_X^2} \sum_{i=1}^{n_X} \sum_{j=1}^{n_X} \|x(t_i) - x(t_j)\|_2 \right) \tag{2}$$

Here, n is the number of visible nodes with $n \leq N$.

d) Step 4: Each graph layer has same number of nodes which facilitates the comparison of the graphs via edges. For finding the distance between visible nodes across layers, i.e., the link between the inter-layer nodes, an inter-ED (i.e., MED) is computed between any two nodes using Eq. 3 [46].

$$\begin{aligned} e_m(X,Y) = \frac{n_X n_Y}{n_X + n_Y} \Bigg(& \frac{2}{n_X n_Y} \sum_{i=1}^{n_X} \sum_{j=1}^{n_Y} \|x(t_i) - y(t_j)\|_2 \\ & - \frac{1}{n_X^2} \sum_{i=1}^{n_X} \sum_{j=1}^{n_X} \|x(t_i) - x(t_j)\|_2 \\ & - \frac{1}{n_Y^2} \sum_{i=1}^{n_Y} \sum_{j=1}^{n_Y} \|y(t_i) - y(t_j)\|_2 \Bigg) \end{aligned} \tag{3}$$

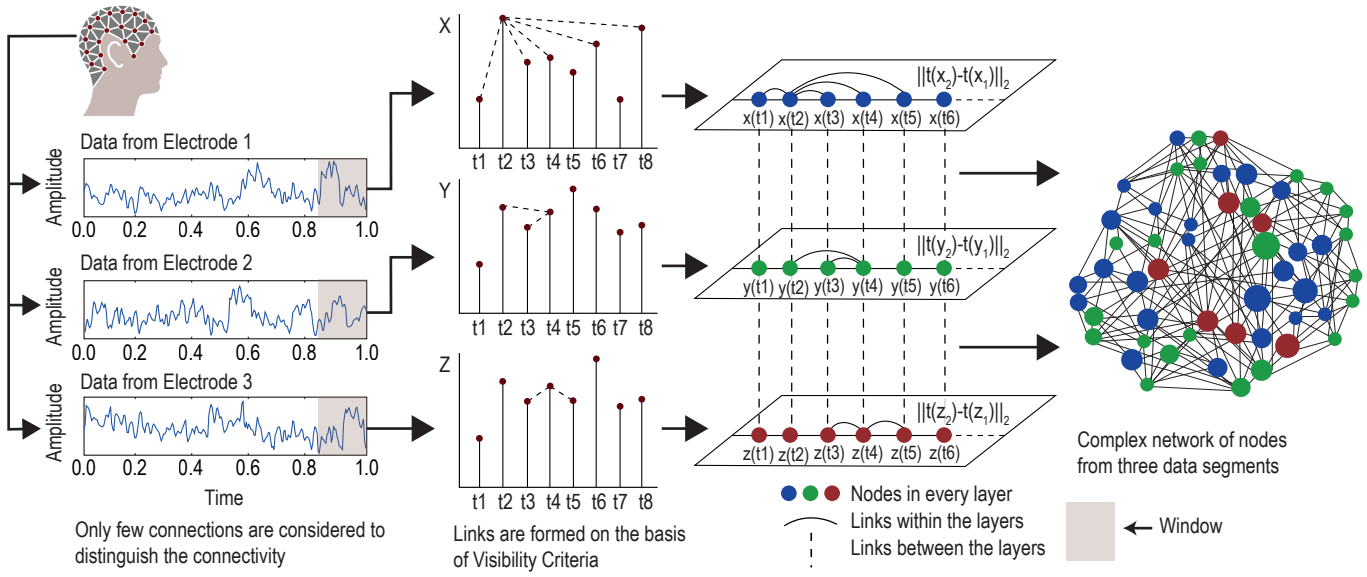

Fig. 1. Schematic diagram describing the construction of the multiplex network using the visibility graph method.

Here, X and Y represent time series of two EoI, $X = \{x(t_1), x(t_2), \ldots, x(t_N)\}$ and $Y = \{y(t_1), y(t_2), \ldots, y(t_N)\}$ with $x(t)$ and $y(t)$ as nodes, and $\| \ \|_2$ is the 2-norm.

If X and Y have same node distribution, then the parameter $e_m(X, Y)$ (as in Eq. 3) provides the inter-distance without considering any intra-distance such that $\|x(t_i) - x(t_j)\|_2 = 0$ and $\|y(t_i) - y(t_j)\|_2 = 0$.

If X and Y are not identical to each other, then both intra- and inter-distances are evaluated, respectively. Based on the median-split approach, the MED values are divided into short-distance and long-distance values [16]. Although there is no strict definition, the median split approach has given a more appropriate categorisation for FC. The steps to form the multiplex network from three data segments are diagrammatically shown in Fig. 1.

2) Validation Metrics: The topological properties of FC networks are analysed using the graph metrics that have already been used in brain network-based studies. Based on the edges computed between nodes as described in section III-B1, the following topological parameters are evaluated for participants of each group: (i) *global efficiency*, which measures network integration and is inversely related to average path length, (ii) *modularity*, which measures the decomposition of a network into a set of different densely intra-connected nodes and sparsely inter-connected groups of nodes or modules, (iii) *small-worldness*, which is a ratio of average path length to clustering coefficient and provides an estimation of complexity of brain networks, and (iv) *betweenness centrality*, which measures how many times a node is bridged in between strongly connected nodes, i.e., estimation of shortest paths in the network.

3) Simulated Probabilistic Network Model: To compute how variation in the distance can account for the variation in topological properties of the functional brain network, a probabilistic model is simulated based on edge connection probability and ED. A probabilistic model can be used to calculate the link probability between any two nodes as an exponentially decaying function of distance between those nodes [33]. This work has utilised this concept to discover the interplay between connection distances and topological aspects of the brain network organisation. The connection probability based on the visibility criterion can be given as:

$$P(X \leftrightarrow Y) = e^{\lambda(e_m(X,Y))} \tag{4}$$

where λ is the decay rate of the links/edges in the network. The large values of λ reflect a lack of long-distance connections in the brain, while small values reflect poor modular networks indicating inefficient brain connectivity. The larger values of the exponential parameter will reduce the connection probability of the two regions. The exponential model for a range of various values of parameter λ can generate networks with different degrees dictating connection probability between the nodes. Thus, the model with a spectrum of λ parameter values can help in comparing the neural profile of ASD, TD, and E groups of individuals.

4) Hypothesis Testing for Identifying Network Differences: For testing the networks, a null hypothesis is formed: all participants (ASD, E, and TD) from the three groups have the same delay with the distance in their connection strength. Thus, the null hypothesis is:

$$H_0 : \lambda_{ASD} = \lambda_E = \lambda_{TD}$$

The alternative was that at least one of the group participants had a different delay rate. The hypothesis is tested statistically using ANOVA and t-tests to determine whether we can detect the brain network variations induced by the connection probability function.

IV. Results

A. Functional Connection Probability and Connectivity Distance

The variation of connection probability with the connectivity distances of EoI is shown in Fig. 2A. The pooled data within each group reflect that connectivity proportion decays with the increasing distance in all participants. The variation in the mean values of the participants in all three groups provided a good approximation of the linear decay trend.

The initial overlap in Fig. 2A indicates that for a minimum connection distance, the connection probability depicts the existence of essential brain connectivity among individuals. The curves depict that an exponential function yielded a reasonable fit to the variation of connection probability density over different connectivity distances in ASD, E, and TD participants. For each subject, the distance between each pair of connected nodes is estimated and compiled as an empirical probability distribution of anatomical distance. As shown in Fig. 2A, the network topology is found to have asymmetric distance distribution for all the participants such that more skewness is seen towards short-distance connections. It is evident that the individuals with ASD showed more connectivity in short-distance compared to long-distance. Individuals with E condition showed greater strength between nodes separated by short distances which is attenuated for the ASD and TD individuals. The proportion of long-distance connections was greater for individuals with E condition compared to ASD and TD. The paired sample t-test reflected that mean connection distance in E condition (mean=58.2) was significantly higher compared to TD (mean=52.3, t(58)=4.32, p-value=0.001) and ASD (mean=45, t(58)=5.11, p-value=0.03) Here, the mean connection distance refers to the average ED of overall visible

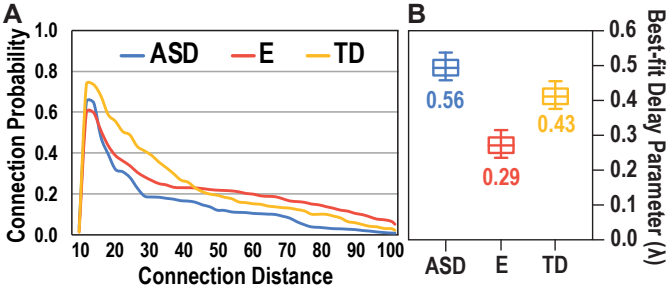

Fig. 2. A. Comparing connection probability density over connectivity distance in ASD, E and TD participants with best-fit values of connection delay parameter. B. Mean value of model-parameter (λ) in ASD, E and TD participants.

pairs of connected nodes for the different EoI in the graph. The curves in Fig. 2A show exponential delay that satisfies Eq. 4 for each group. The calculated best-fitting value of delay parameter (λ) significantly differentiates the three groups. As shown by the Box plots in Fig. 2B, a range of values for λ are attained in ASD, E, and TD. A paired-sampled t-test provided significant comparison among the participants with significantly higher values in ASD (mean=0.56$\pm$0.036) than TD (mean=0.43$\pm$0.054, t(58)=7.87, p-value=0.001) and E (mean=0.29$\pm$0.047, t(58)=11.31, p-value=0.02) conditions.

B. Connection Distance and Topological Metrics

ANOVA was used to evaluate the effect of connection distance and group on topological metrics. A 3 (group: ASD, E, TD) $\times$ 2 (distance: Short and Large) $\times$ 4 (lobes: Frontal, Parietal, Occipital, Temporal) ANOVA was designed with distance and lobes as within-subject factors and the group as a between-subject factor. The summary of the results is provided in Table III which shows that the main effect of distance, group, and lobs are much more significant (p-value$\geq$0.001) compared to other effects and interactions for the metrics defined in section III-B2.

TABLE III
SUMMARY OF 3 $\times$ 2 $\times$ 4 ANOVA IN ASD, E AND TD PARTICIPANTS

Interaction	F-Value			
	MD	GE	SW	BC
Distance	25.4*	18.7**	11.2**	8.9**
Group	16.8*	9.3*	13.4**	11.8**
Lobes	23.7*	20.6**	13.4**	15.9**

Legend– **MD**: Modularity, **GE**: Global Efficiency, **SW**: Small-Worldness, **BC**: Betweenness Centrality.

The Spearman correlation, as shown in Fig. 3, reflected that the between-subject variability in mean ED is strongly associated with the individual variations in the functional network topology. For TD participants, the mean connection distance was significantly correlated with modularity (r^2=-0.69, p-value=0.03), betweenness centrality (R^2=0.88, p-value=0.02), and global efficiency (R^2=0.88, p-value=0.01). An insignificant correlation with the small-world index (R^2=-0.002, p-value=0.41) reflects the robustness of the brain network to connection distance variations. Thus, the brain network in TD is less clustered, less modular, and more globally efficient with the increasing distance between different EoI.

In ASD, the mean connection distance was significantly correlated with modularity (R^2=-0.63, p-value=0.001), betweenness centrality (R^2=0.23, p-value=0.003), and small-worldness (R^2=0.42, p-value=0.037). An insignificant correlation with global efficiency (R^2=0.06, p-value=0.24) was found, which reflects a poor integrated network in ASD. The correlation reveals a more clustered and modular network with short-distance connections in ASD. In E participants, the connection distance was significantly negatively correlated with small-worldness (R^2=-0.57, p-value=0.003), modularity (R^2=0.74, p-value=0.02), betweenness centrality (R^2=0.40, p-value=0.01),

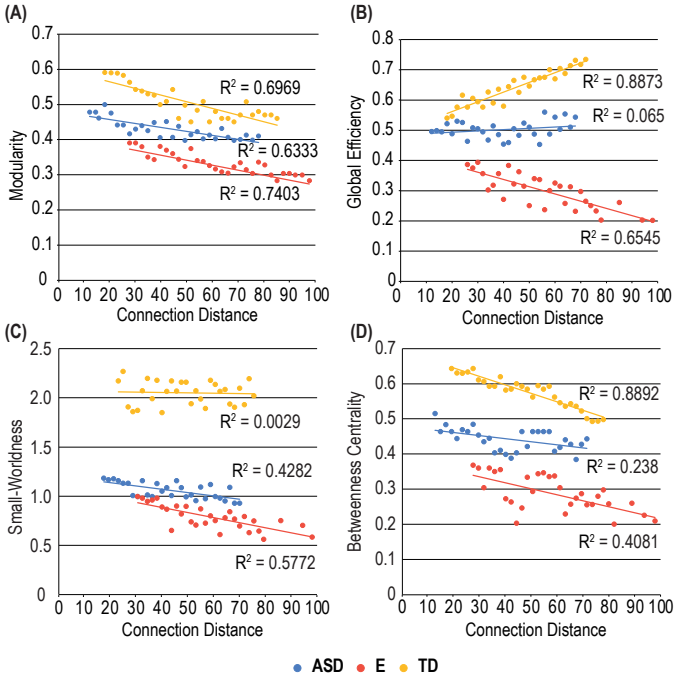

Fig. 3. Correlation of connection distance with brain topology metrics– Modularity (A), Global Efficiency (B), Small-world (C), and Betweenness Centrality (D) in ASD (blue), E (red), and TD (yellow) participants.

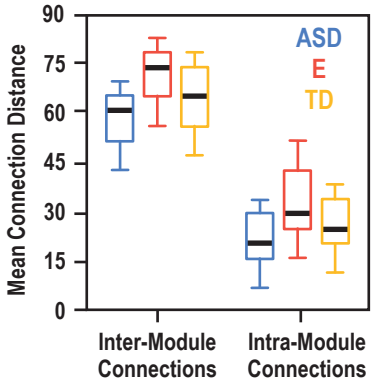

Fig. 4. Variation in mean intra-module and inter-module connectivity values with connection distance in ASD, E, and TD participants.

and global efficiency (R^2=0.65, p-value=0.001). It reveals that the brain network in E is, although less clustered, less modular, and more globally efficient with the increasing distance between different EoI, the connections are longer over the entire brain network compared to ASD and TD.

The mean proportion of short- and long-distance connections among all the participants of ASD, E, and TD groups is shown in Fig. 4. The strength of short-distance connections is high in ASD compared to E and TD. For the long-distance connections, E showed much more connections than TD and ASD. The inter-module mean connection distance was higher in the E (mean=69.4$\pm$15.24) than in TD (mean= 59.6$\pm$13.89; t(58)=23.67, p-value=0.001) and ASD (mean= 51.8$\pm$11.32; t(58)=18.9, p-value=0.02). The intra-module mean connection distance was lower in ASD (mean=23.81$\pm$11.6) compared

to TD (mean=29.62±10.4, t(58)=32.5, p-value=0.03) and E (mean=35.01±9.85, t(58)=29.8, p-value=0.02).

C. Hemispherical and Lobe-wise Connection Distance

Based on the presented definition of short- ($<$ 50 mm) and long-distance connections ($>$50 mm), out of 300 total connections, 135 short-distance and 165 long-distance connections satisfied the visibility criterion. In ASD, 48 long-distance and 24 short-distance connections have not shown any connectivity on applying the visibility criterion. In TD, 36 long-distance and 19 short-distance connections were found absent. In E, 38 short-distance and 24 long-distance connections were not visible out of the total connections. The comparison of the edge connections within different lobes in ASD, E, and TD individuals concerning connection distance is shown in Fig. 5.

In TD, the intra-module distance was 32.67±7.81 while the inter-module distance was 59.67±12.34. In E, the mean connection distance was 55.12±11.54 and 34.67±9.54 for the inter-module and intra-module, respectively. In ASD, the mean connection distance values were found lower in comparison to E and TD, such that the intra-module was 24±12.67 and the inter-module was 52±13.21.

The frontal and occipital lobes showed high edge density in ASD (Frontal mean= 0.35±0.12) compared to TD (mean=0.32±0.09, t(58)=11.32, p-value=0.01) and E (mean=0.26±0.19, t(58)=8.17, p-value=0.03). The temporal and parietal lobes have higher density in TD (Temporal mean=0.37; Parietal mean=0.38) compared to ASD (Temporal mean=0.32, t(58)=14.02, p=0.03; Parietal mean=0.34±0.09, t(58)=15.10, p-value=0.001) and E (Temporal mean= 0.29, t(58)=10.12, p=0.001; Parietal mean=0.27±0.09, t(58)=11.32, p-value=0.01). Among ASD and E participants, an association was found in the temporal lobe reflected by insignificant differences in the mean values (mean difference=0.0213, t(58)=, p-value=0.53). Among ASD and TD participants, an overlap was found in the occipital lobe such that there was no significant difference among both groups (mean difference: 0.02, t(58)=14.36, p-value=0.52).

D. Probabilistic Modelling of Brain Network

A probabilistic model was developed with the delay parameter (λ; $0 < \lambda < 1$) and it was tuned for the variation of topological metrics with connection lengths. After finding the best-fit values of λ (see Fig. 2B), the connection length of the complex network was computed for each topological metric of the brain network (see Table IV). The findings from the probabilistic model provide a proof-of-concept that abnormality in the brain network's topological properties of individuals with E condition can be determined through short-distance connections, whereas for ASD, it can be determined from long-distance connections.

TABLE IV
MEAN CONNECTION LENGTHS IN BRAIN NETWORKS

Metrics	**ASD** (λ)	**E** (λ)	**TD** (λ)
Global Efficiency	-	34.6±0.32 (0.31)	45.6±(0.40) (0.40)
Modularity	64.7±0.34 (0.53)	21.5±0.14 (0.24)	39.3±0.26 (0.45)
Small-Worldness	59.3±0.26 (0.57)	26.4±0.11 (0.28)	-
Betweenness-Centrality	68.9±0.52 (0.51)	23.5±0.20 (0.26)	37.5±0.21 (0.43)

V. DISCUSSION

The present paper aims to find a relationship between connection distance and topological properties of functional brain networks to predict the brain network topology. A computational model of the brain network topology is proposed and is exploited to associate the complex neural correlates and FC-based distances. The model is inspired by multivariate VG network algorithm and MED, which are utilised to map the EEG time series into a complex brain network. The topological properties based on MED were computed to find correlations between connection distances and functional brain topologies. A state-of-the-art probabilistic model is also utilised to find the delay rate (λ) in connection probability with the distance in brain regions. The topological properties were matched to a range of values of λ to find the connection length for different topological metrics, which can aid the identification of neurological conditions more accurately. It is worth noting that the effect of sampling rates on the estimation of the topological properties from the multiplex graphs generated using the VG method is negligible (data not shown).

Information transmission in intra- and inter-regional brain units is key to the typical functioning of brain circuitry, leading to correct behavioural and perceptual outcomes. The transmission is precisely governed by the exact firing of neurons at appropriate timings, forming active neuronal networks. For important tasks related to perceptual, motor and cognitive functions, delay can lead to several intra- and inter-regional communication anomalies causing brain disorders [47]. One way to find these anomalies is to identify the connection distance among brain units which helps characterise the topological structure of inferred brain networks [48]. Computing long- and short-range connections (i.e., connection distances) and degrees of connection of brain regions can shed light on the efficiency of intra- and inter-regional communication [49]. For example, with a growing number of long-distance connections, a network's global efficiency increases and local efficiency decreases, as observed in the case of individuals with E conditions. On the other hand, when the number of short-distance connections grows, a network's local efficiency increases and global efficiency decreases, as observed in the case of individuals with ASD conditions. Therefore, a balance between long- and short-distance connections is needed for a locally and globally efficient network [50], as observed in the case of TD individuals. The VG method captures these phenomena quite well, as in the case of long-distance connections, more EEG time points are visible from other relatively farther points, while fewer EEG time points are visible in the case of a higher number of short-distance connections.

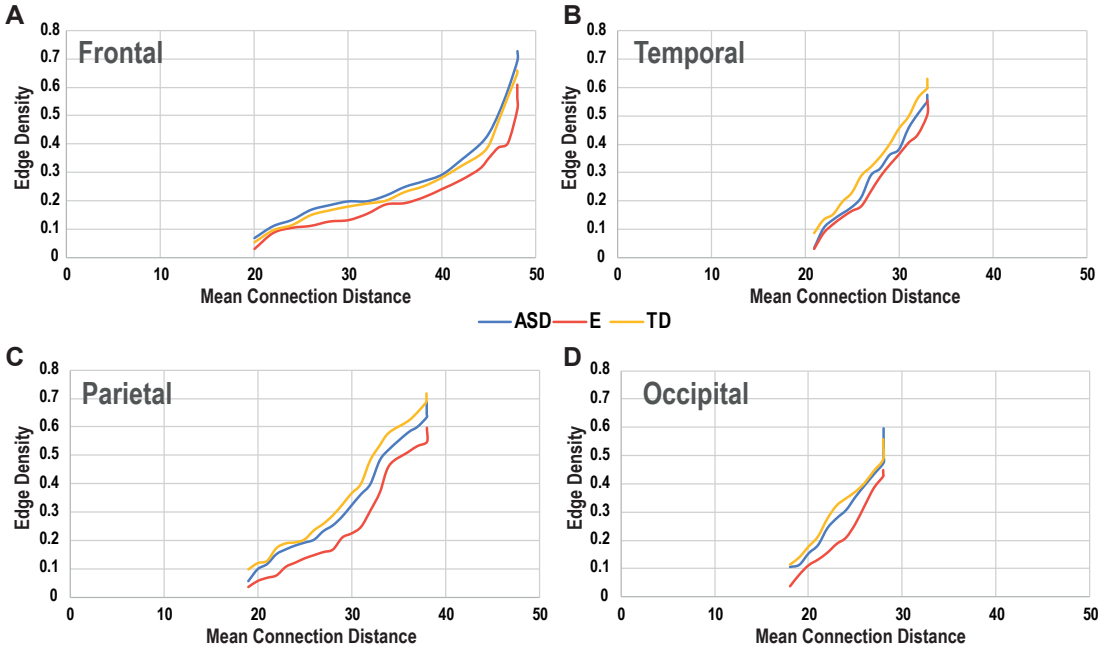

Fig. 5. Mean edge density with connection distance based on visibility criterion in (A) Frontal, (B) Temporal, (C) Parietal and (D) Occipital lobes in ASD, E and TD participants.

A. Contribution

The present paper quantitatively revealed the brain network topology that can identify ASD and E conditions by exploring the association of complex neural correlates and FC-based distances. It has demonstrated the objective marker to identify ASD and extended the existing literature [23], [51] by evaluating the range of λ values in identifying the disorder. The results reflect that the ASD network profile is skewed towards short-distance connections. A total of 117 long-distance and 111 short-distance connections have shown visible connectivity, whereas E individuals have 97 short-distance and 141 long-distance connections in the visible category. Thus, in the future, ASD can be identified by extracting topological properties over long-distance connections only. In comparison, the network profile for individuals with E can be identified by computing the topological properties for short-distance connections since the network has higher long-distance connections. Thus, the presented quantitative evaluation in this work contributed to investigating the extent to which variations in the distance of FC can explain the variations in the network topology of ASD, E, and TD.

B. Comparison with Related Work

The multivariate weighted VG method put forward in this paper proves to be robust and efficient in providing the edges compared to the traditional method, which depends upon $(n(n-1)/2)$ links. Based on the connections following visibility criteria among all the participants (ASD, E, and TD), a skewed distribution with connections towards short-distances is found, which favours that efficient functioning in brain network is biased towards short-distance connections [52], [53]. However, ASD is characterised by higher short-distance and lower long-distance connections, whereas E condition possesses high long-distance connections and low short-distance connections. Analysing FC with connection distances provides strong evidence of neural differences underlying ASD and E conditions. The best-fitting values of the delay parameter (λ) indicated significant group differences between the participants. The value of λ is 0.56 in ASD, 0.43 in TD, and 0.29 in E condition. This finding is in line with a study that has differentiated between three sub-populations revealing λ = 0.6, 0.8, and 1 under certain neuropathologies [33]. The variation in λ values leads to the rejection of the null hypothesis and suggests that brain connectivity in individuals with ASD, E, and TD function at different delay rates or penalties. It favours the conclusion that diagnosis-by-distance can evaluate the neural mechanisms underlying disorders like ASD [51], [54]. Thus, the delay parameter (λ) has the potential to explore altered neurological conditions.

The variability of extracted topological properties with connection distance in different EoI has also differentiated all the conditions. ASD individuals have reduced modularity, small-worldness, and betweenness-centrality without any rise in global efficiency among more distant regions. The TD individuals possess lower modularity and betweenness centrality with an increase in global efficiency that results in a network with a small-worldness topology. The probability of the connection between different nearby EoI is higher, but it declines sharply with the increasing distance. On comparing ASD and E participants, common FC is found for short-distance within the temporal lobe, whereas variability in both the groups is detected for short- and long distances. The connection probability over short distances has also reflected the association between both conditions, whereas the different delay rates and connectivity distribution in other EoI for

both conditions have reflected the variability, which has the potential to untangle both conditions.

The higher number of short-distance connections in ASD indicated modular and clustered networks in participants with ASD compared to E. The comparison of modular connections further revealed more densely connected intra-module nodes in participants with ASD compared to E condition. The individuals with ASD demonstrated an early decay (i.e., high λ values) as a function of distance within the short-distance EoI (i.e., within the frontal, parietal, occipital, and temporal lobes), while a faster decay in the long-distance inter-module connections (e.g., from frontal to temporal and frontal to occipital lobes). The loss of long-distance connections indicated inefficient global and nodal brain network topology in ASD. Like the TD group participants, the individuals with ASD showed greater strength of FC between EoI separated by short distances and poor strength for EoI with long-distance. The TD group brain network topology comprises of strong short-distance connections supporting clustered and modular topology and a higher number of long-distance connections among inter-module hubs in different brain areas. This balanced topology of connections in TD favours the previous theoretical studies indicating the distribution of a few long-distance connections among a large number of short-distance connections [23], [39]. The correlation of the topology metrics and distance-based links reveals that higher global efficiency in the TD group can be attributable to the existence of strong long-distance connections between different EoI. The exponential probability distribution showed more long-distance connections in the E group and more short-distance connections in the TD group.

VI. Conclusion

The present paper has quantitatively extended the research on analysing neural connections and their distances in revealing brain architecture, their interactions and associated brain diseases. The proposed model incorporates the multivariate VG algorithm and ED to quantitatively analyse resting-state brain networks using EEG signals in terms of delay and connection distance parameters that reflected variation in the probability distribution of brain connections. In ASD, a higher delay rate and more skewed distribution towards short-distance functional connections are reported, whereas, in E, a lower delay and more long-distance connections are found compared to TD. Furthermore, the model illustrated a significant overlap over short-distance connections within the temporal lobe. Thus, the presented model can process brain data via delay parameter and connection distance with the potential to identify neurological disorders like ASD and E. Future studies focusing on structural and FC dynamics are required to provide better quantification of ASD and E conditions.

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References

[1] T. Ghosh *et al.*, "Artificial intelligence and internet of things in screening and management of autism spectrum disorder," *Sustain. Cities Soc.*, vol. 74, p. 103189, 2021.

[2] S. Ahmed *et al.*, "Toward machine learning-based psychological assessment of autism spectrum disorders in school and community," in *Proc. TEHI*, 2022, pp. 139–149.

[3] T. Akter, M. H. Ali, M. S. Satu, M. I. Khan, and M. Mahmud, "Towards autism subtype detection through identification of discriminatory factors using machine learning," in *Proc. Brain Inform.*, 2021, pp. 401–410.

[4] M. Biswas *et al.*, "An xai based autism detection: the context behind the detection," in *Proc. Brain Inform.*, 2021, pp. 448–459.

[5] T. Wadhera and M. Mahmud, "A deep concatenated convolutional neural network-based method to classify autism," in *Proc. ICONIP*, 2023, pp. 1–12.

[6] A. Sumi *et al.*, "fassert: a fuzzy assistive system for children with autism using internet of things," in *Proc. Brain Inform.*, 2018, pp. 403–412.

[7] M. H. Al Banna *et al.*, "A monitoring system for patients of autism spectrum disorder using artificial intelligence," in *Proc. Brain Inform.*, 2020, pp. 251–262.

[8] S. Ahmed *et al.*, "Ci in detection and support of autism spectrum disorder," in *Artificial Intelligence in Healthcare: Recent Applications and Developments*. Singapore: Springer, 2022, pp. 179–197.

[9] M. Mahmud *et al.*, "Towards explainable and privacy-preserving artificial intelligence for personalisation in autism spectrum disorder," in *Proc. HCII*, 2022, pp. 356–370.

[10] T. Hughes-Roberts, V. Cui, M. Mahmud, and D. J. Brown, "Leveraging virtual reality and machine learning as mediated learning tools for social skill development in learners with autism spectrum condition," in *Proc. HCII*, 2022, pp. 231–240.

[11] T. Wadhera and M. Mahmud, "Influences of social learning in individual perception and decision making in people with autism: A computational approach," in *Proc. Brain Inform.*, 2022, pp. 50–61.

[12] ——, "Brain networks in autism spectrum disorder, epilepsy and their relationship: A machine learning approach," in *Artificial Intelligence in Healthcare: Recent Applications and Developments*. Singapore: Springer, 2022, pp. 125–142.

[13] ——, "Brain functional network topology in autism spectrum disorder: A novel weighted hierarchical complexity metric for electroencephalogram," *IEEE J. Biomed. Health Inform.*, pp. 1–8, 2023, doi: 10.1109/JBHI.2022.3232550.

[14] J. Liu *et al.*, "Complex brain network analysis and its applications to brain disorders: a survey," *Complexity*, vol. 2017, 2017.

[15] S. Schipul, T. Keller, and M. Just, "Inter-regional brain communication and its disturbance in autism," *Front. Syst. Neurosci.*, vol. 5, p. 10, 2011.

[16] A. F. Alexander-Bloch *et al.*, "The anatomical distance of functional connections predicts brain network topology in health and schizophrenia," *Cereb. Cortex*, vol. 23, no. 1, pp. 127–138, 2013.

[17] R. Bakhtiari *et al.*, "Computational model of excitatory/inhibitory ratio imbalance role in attention deficit disorders," *J. Comput. Neurosci.*, vol. 33, no. 2, pp. 389–404, 2012.

[18] S. Guo *et al.*, "Anatomical distance affects functional connectivity in patients with schizophrenia and their siblings," *Schizophr. Bull.*, vol. 40, no. 2, pp. 449–459, 2014.

[19] D. Meedeniya and I. Rubasinghe, "A review of supportive computational approaches for neurological disorder identification," in *Interdisciplinary Approaches to Altering Neurodevelopmental Disorders*. IGI Global, 2020, pp. 271–302.

[20] P. E. Vértes *et al.*, "Simple models of human brain functional networks," *Proc. Natl. Acad. Sci.*, vol. 109, no. 15, pp. 5868–5873, 2012.

[21] D. Kakkar *et al.*, "Diagnostic assessment techniques and non-invasive biomarkers for autism spectrum disorder," *Int. J. E-Health Med. Commun.*, vol. 10, no. 3, pp. 79–95, 2019.

[22] P. Lo Giudice *et al.*, "Leveraging network analysis to support experts in their analyses of subjects with mci and ad," *Med. Biol. Eng. Comput.*, vol. 57, no. 9, pp. 1961–1983, 2019.

[23] F. V. Farahani, W. Karwowski, and N. R. Lighthall, "Application of graph theory for identifying connectivity patterns in human brain networks: a systematic review," *Front. Neurosci.*, vol. 13, p. 585, 2019.

[24] T. Wadhera and D. Kakkar, "Multiplex temporal measures reflecting neural underpinnings of brain functional connectivity under cognitive load in autism spectrum disorder," *Neurol. Res.*, vol. 42, no. 4, pp. 327–337, 2020.

[25] L. Lacasa, B. Luque, F. Ballesteros, J. Luque, and J. C. Nuno, "From time series to complex networks: The visibility graph," *Proc. Natl. Acad. Sci.*, vol. 105, no. 13, pp. 4972–4975, 2008.

[26] T. Pfeffer, A.-E. Avramiea, G. Nolte, A. K. Engel, K. Linkenkaer-Hansen, and T. H. Donner, "Catecholamines alter the intrinsic variability of cortical population activity and perception," *PLoS Biol.*, vol. 16, no. 2, p. e2003453, 2018.
[27] G. Shafiei, Y. Zeighami, C. A. Clark, J. T. Coull, A. Nagano-Saito, M. Leyton, A. Dagher, and B. Mišić, "Dopamine signaling modulates the stability and integration of intrinsic brain networks," *Cereb. Cortex*, vol. 29, no. 1, pp. 397–409, 2019.
[28] C. Cecchetto, M. Mahmud, and S. Vassanelli, "Anesthesia effect on single local field potentials variability in rat barrel cortex: Preliminary results," in *Proc. EMBC*, 2015, pp. 4721–4724.
[29] M. Mahmud and S. Vassanelli, "Differential modulation of excitatory and inhibitory neurons during periodic stimulation," *Front. Neurosci.*, vol. 10, p. 62, 2016.
[30] F. Cauda *et al.*, "Hubs of long-distance co-alteration characterize brain pathology," *Hum. Brain Mapp.*, vol. 41, no. 14, pp. 3878–3899, 2020.
[31] A. Perinelli, D. Tabarelli, C. Miniussi, and L. Ricci, "Dependence of connectivity on geometric distance in brain networks," *Sci. Rep.*, vol. 9, no. 1, pp. 1–9, 2019.
[32] A. Cerqueira, D. Fraiman, C. D. Vargas, and F. Leonardi, "A test of hypotheses for random graph distributions built from eeg data," *IEEE Trans. Netw. Sci. Eng.*, vol. 4, no. 2, pp. 75–82, 2017.
[33] D. Fraiman and R. Fraiman, "An anova approach for statistical comparisons of brain networks," *Sci. Rep.*, vol. 8, no. 1, pp. 1–14, 2018.
[34] D. Kakkar *et al.*, "Influence of emotional imagery on risk perception and decision making in autism spectrum disorder," *Neurophysiology*, vol. 51, no. 4, pp. 281–292, 2019.
[35] G. Brihadiswaran *et al.*, "Eeg-based processing and classification methodologies for autism spectrum disorder: A review," *J. Comput. Sci.*, vol. 15, no. 8, 2019.
[36] D. Haputhanthri *et al.*, "An eeg based channel optimized classification approach for autism spectrum disorder," in *Proc. MERCon*, 2019, pp. 123–128.
[37] ——, "Integration of facial thermography in eeg-based classification of asd," *Int. J. Autom. Comput.*, vol. 17, no. 6, pp. 837–854, 2020.
[38] A. Walden and L. Zhuang, "Constructing brain connectivity group graphs from eeg time series," *J. Appl. Stat.*, vol. 46, no. 6, pp. 1107–1128, 2019.
[39] S. Parisot *et al.*, "Disease prediction using graph convolutional networks: application to autism spectrum disorder and alzheimer's disease," *Med. Image Anal.*, vol. 48, pp. 117–130, 2018.
[40] A. Pascual-Belda, A. Díaz-Parra, and D. Moratal, "Evaluating functional connectivity alterations in autism spectrum disorder using network-based statistics," *Diagnostics*, vol. 8, no. 3, p. 51, 2018.
[41] T. Wadhera and M. Mahmud, "Computing hierarchical complexity of the brain from electroencephalogram signals: A graph convolutional network-based approach," in *Proc. IJCNN*, 2022, pp. 1–6.
[42] S. Supriya, S. Siuly, H. Wang, J. Cao, and Y. Zhang, "Weighted visibility graph with complex network features in the detection of epilepsy," *IEEE Access*, vol. 4, pp. 6554–6566, 2016.
[43] M. Cao *et al.*, "Topological organization of the human brain functional connectome across the lifespan," *Dev. Cogn. Neurosci.*, vol. 7, pp. 76–93, 2014.
[44] Y. Shimada, Y. Hirata, T. Ikeguchi, and K. Aihara, "Graph distance for complex networks," *Sci. Rep.*, vol. 6, no. 1, pp. 1–6, 2016.
[45] S. Oligschläger *et al.*, "Gradients of connectivity distance are anchored in primary cortex," *Brain Struct. Funct.*, vol. 222, no. 5, pp. 2173–2182, 2017.
[46] K. Yu *et al.*, "Individual morphological brain network construction based on multivariate euclidean distances between brain regions," *Front. Hum. Neurosci.*, vol. 12, p. 204, 2018.
[47] R. Hari and L. Parkkonen, "The brain timewise: how timing shapes and supports brain function," *Philos. Trans. R. Soc. B: Biol. Sci.*, vol. 370, no. 1668, p. 20140170, 2015.
[48] Q. Cai, Z.-K. Gao, Y.-X. Yang, W.-D. Dang, and C. Grebogi, "Multiplex limited penetrable horizontal visibility graph from eeg signals for driver fatigue detection," *Int. J. Neural Syst.*, vol. 29, no. 05, p. 1850057, 2019.
[49] S. Sannino, S. Stramaglia, L. Lacasa, and D. Marinazzo, "Visibility graphs for fmri data: Multiplex temporal graphs and their modulations across resting-state networks," *Netw. Neurosci.*, vol. 1, no. 3, pp. 208–221, 2017.
[50] J. Zhang, J. Xia, X. Liu, and J. Olichney, "Machine learning on visibility graph features discriminates the cognitive event-related potentials of patients with early alzheimer's disease from healthy aging," *Brain Sci.*, vol. 13, no. 5, p. 770, 2023.
[51] L. L. Gollo *et al.*, "Fragility and volatility of structural hubs in the human connectome," *Nat. Neurosci.*, vol. 21, no. 8, pp. 1107–1116, 2018.
[52] D. Meunier, R. Lambiotte, A. Fornito, K. Ersche, and E. T. Bullmore, "Hierarchical modularity in human brain functional networks," *Front. Neuroinformatics*, vol. 3, p. 37, 2009.
[53] T. Wadhera, "Brain network topology unraveling epilepsy and asd association: Automated eeg-based diagnostic model," *Expert Syst. Appl.*, vol. 186, p. 115762, 2021.
[54] Z. Long, X. Duan, D. Mantini, and H. Chen, "Alteration of functional connectivity in autism spectrum disorder: effect of age and anatomical distance," *Sci. Rep.*, vol. 6, no. 1, pp. 1–8, 2016.

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