IEEE SPMB 2020

NEW YORK INSTITUTE OF TECHNOLOGY

Machine Learning Approach to Diagnose Schizophrenia Based on Effective Connectivity of Resting EEG Data

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Schizophrenia

Schizophrenia is a chronic and severe psychotic disorder that affects how a person thinks, feels, and behaves.

- People with schizophrenia fail to understand what is real.

Prevalence: ~1.1% of the US population

Exact cause: Unknown, but it could be a combination of

1) Genetics
2) Environment
3) Altered brain chemistry and structure

A core deficit of schizophrenia: failure of effective functional integration within and between brain areas

Electroencephalography (EEG)

Scalp electroencephalography (EEG) : Neuroimaging technique to measure the brain's electrical activity by non-invasive scalp electrodes.

EEG technique is popular because it is

1) Non-invasiveness
2) Accessible
3) Low cost

EEG is promising to identify relevant biomarkers to diagnose various mental and neurological disorders such as schizophrenia, depression, autism, epilepsy, dementia, and Alzheimer's.

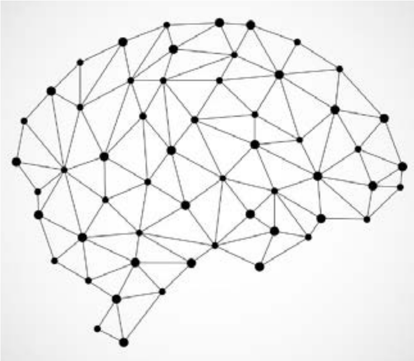
Diagnosing Schizophrenia

The mental abnormalities in schizophrenia can be reflected in brain network.

- Measuring brain network ability can improve understanding of disruption in brain connectivity underlying schizophrenia.

Two methods to measure brain connectivity are

1) Functional connectivity: reflects the undirected statistical dependencies of signals from different brain regions
    a) cross-correlation
    b) coherency
    c) phase lag index measures



2) Effective connectivity: reflects the directed information flow through neurons, as opposed to *functional* connectivity

Effective Connectivity

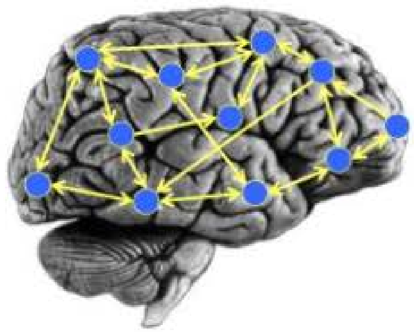
Effective connectivity must meet four requirements to be useful for measuring brain connectivity:

1) Independence of *a priori* definitions and models

2) The ability to detect non-linear interactions across brain function

3) The ability to detect effective connectivity even if there is a wide distribution of interaction delays between the two signals

    signals may move between brain areas through multiple pathways with different conduction delays



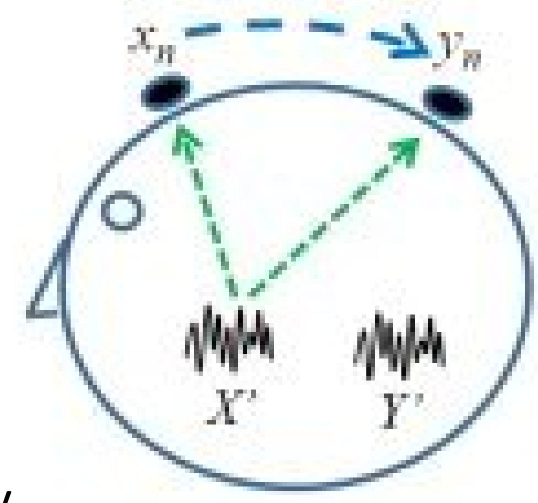
4) Robustness against linear cross-talk between signals

Transfer entropy (TE): Measuring the time-directed transfer of information between two random processes, meet four requirements

A useful approach for the quantification of effective connectivity

Transfer Entropy (TE)

Suppose X= (x_1, x_2, …, x_N) and Y= (y_1, y_2,…, y_N) originating from two different brain regions.



$$T_{Y,X} = H(X_{i+t}|X_i) - H(X_{i+t}|X_i, Y_i)$$
$$= \sum p(X_{i+t}, X_i, Y_i) \log_2 \frac{p(X_{i+t}|X_i, Y_i)}{p(X_{i+t}|X_i)}$$

Transfer entropy measures the reduction in the uncertainty in X_{i+t} when the information about X_i *and* Y_i are given

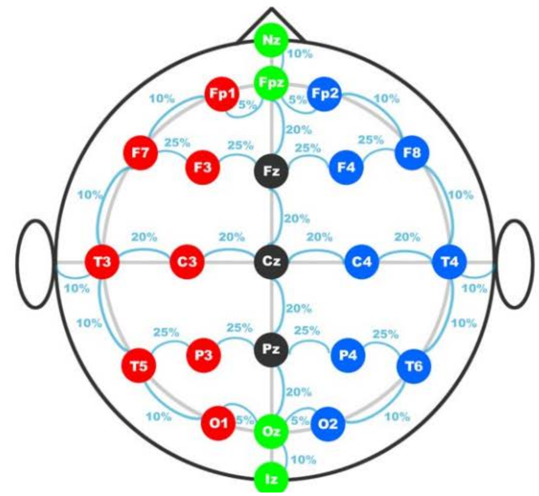
Symbolic transfer entropy (STE) estimates TE by using a method of symbolization.

STE is convenient, robust, and computationally efficient

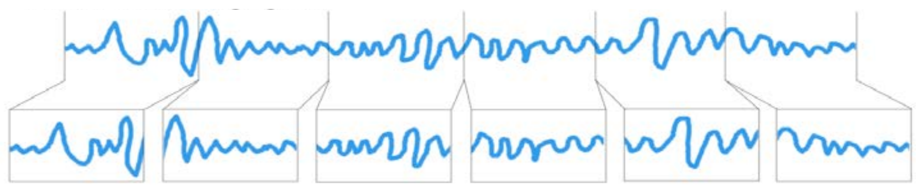
Apply STE to EEG signals

1) Decompose resting EEG data measured with 20 electrodes into 5 frequency bands:

   δ (1Hz -4Hz), θ(4Hz-8Hz), α (8Hz-13Hz), β (13Hz-30Hz), and γ (30Hz-50Hz)



2) At each frequency band divide the EEG signal into non-overlapping segments of 10 sec .



3) For each segment, the STE is computed between each two EEG electrodes

4) The average of the STEs among all EEG segments is considered as the final STE between each two electrodes

Brain Network Properties

8 brain network properties at each frequency band were investigated :

1) clustering coefficients for each node (EEG electrode) (20 features)

2) global-efficiency (1 feature)

3) local-efficiency (20 features)

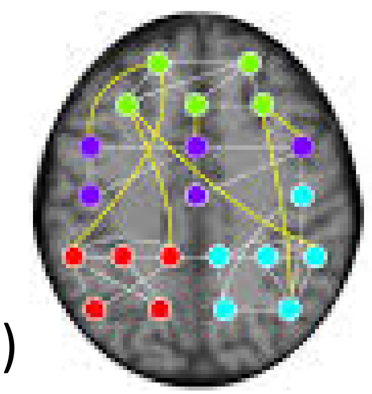
4) characteristic-path (1 feature)

5) shortest-path-length between each two nodes (380 features)

6) density (1 feature)

7) eccentricity (20 features)

8) node-strength (20 features)



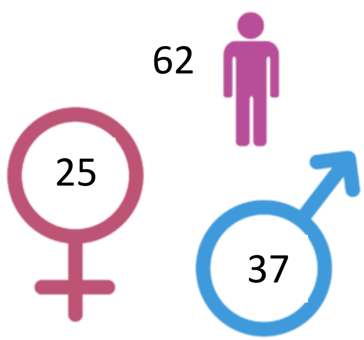
The total numbers of features for all 5 frequency bands: N_c=463×5= 2315

Database

3.5 min eye closed resting EEG data

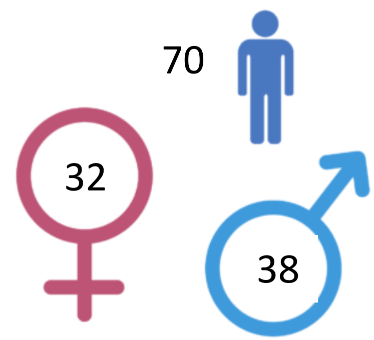
- EEG signal was band-pass-filtered [0.5 Hz-50 Hz]
- EEG artefacts were then removed using wavelet enhanced ICA (wICA) algorithm

Schizophrenic patients



age [years]: avg. = 37.27, std = 8.98, min = 17, max = 56

Healthy controls



age [years]: avg. = 37.74, std = 16.57, min = 18, max = 81

Machine Learning Algorithm

Training data: 80% of the samples in each class

Test data: The remaining 20% of the samples in each class

Feature selection algorithm: Relief

selects the features that have

- the maximum similarity in neighboring data samples in one class
- the maximum difference in neighboring data samples in different classes

Relief algorithm is noise-tolerant and robust to feature interactions

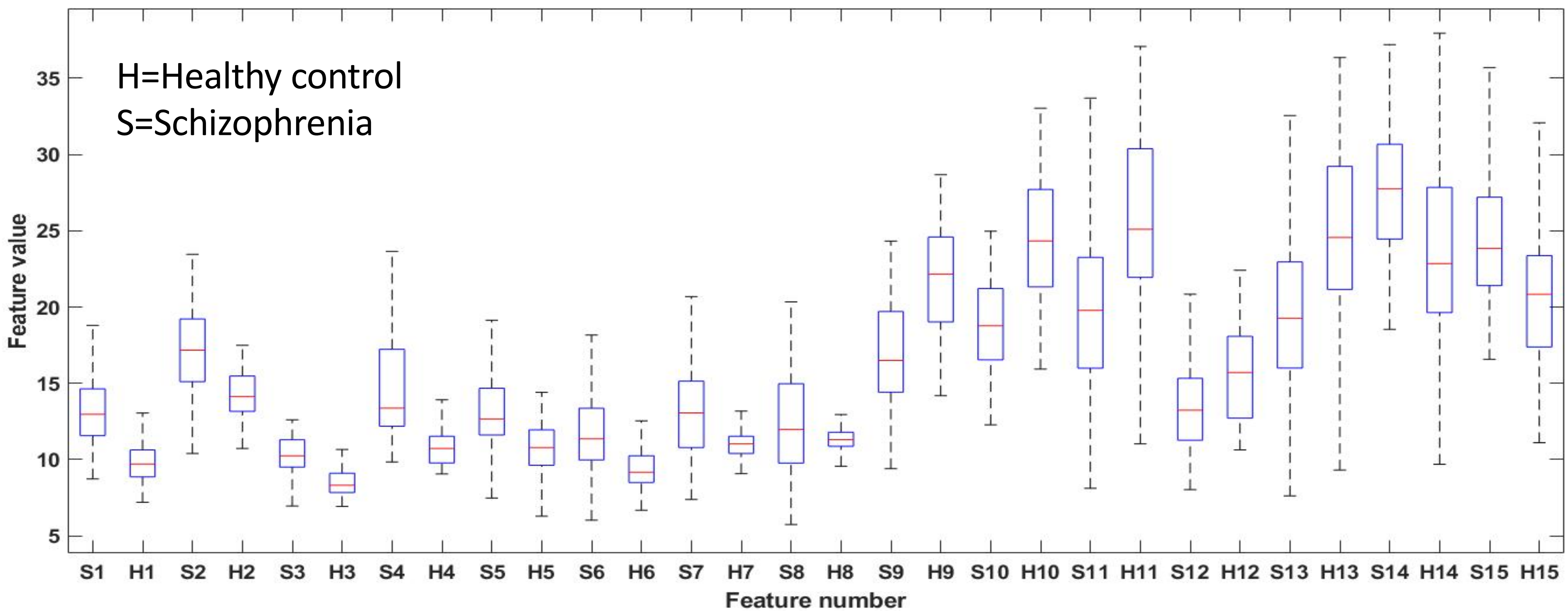
Selected Features

Feature #	Frequency Band	Shortest Path Length
1	δ	O1 and Oz
2	δ	O1and O2
3	θ	O1and Oz
4	θ	O1 and O2
5	θ	O2 and O1
6	α	O1 and O2
7	β	O1 and O2
8	β	O2 and O1
9	θ	C4 and T4
10	θ	P4 and T4
11	δ	F7 and F8
12	α	F8 and T4
13	δ	F8 and F7
14	δ	Fz and T3
15	δ	T3 and F3

Selected brain regions:

- Occipital areas (features 1-8).
- Centro-Temporal (features 9)
- Parieto-Temporal (feature 10)
- Frontal areas (features 11 & 13)
- Fronto-Temporal (feature 12, 14, and 15)

Selected Features



The median of 10 features (features 1-8, 14-15) are significantly higher (*p*-value ≤0.05) for SCZs than HCs using Wilcoxon rank sum test

Classification Performance

Classifier	Sensitivity	Specificity	Total Accuracy
SVM	**100**	**92.86**	**96.15**
KNN	**100**	**92.86**	**96.15**
RF	**100**	**85.71**	**92.31**
GNB	**83.33**	**92.86**	**88.46**
LDA	**83.33**	**92.86**	**88.46**

SVM: Support Vector Machine

KNN: K Nearest Neighbors

RF: Random Forest

GNB: Gaussian Naïve Bayes

LDA: Linear Discriminant Analysis

Classification performances:

SVM and KNN: 96.15% (Highest)

RF: 92.31%

GNB and LDA : 88.46%.

High classification performance across different classification algorithms

- The selected features are highly discriminating between the two classes

Consistency with previous studies

From previous studies:

1) From diffusion tensor imaging (DTI): shortest path length and clustering coefficient parameters can discriminate anatomical changes in neuron for SCZ patients

SCZ patients displayed comparatively lower clustering coefficient and longer path lengths

2) The volume of the occipital lobe is decreasing in SCZ patients

3) disruptions in fronto-parieto-temporal connections

4) bilateral reduction in grey matter volume of the temporal lobes

The combination of ML and STE results in a significant improvement in the ability to characterize schizophrenia with small relevant features

Thank You!