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Structural and Functional Brain Networks: From Connectome to Major Depression

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Introduction

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Connectome — concept of the human brain as a large-scale complex network

- Functional Connectome (FC) - a comprehensive map of correlated brain regions
- Structural Connectome (SC) - a comprehensive map of anatomical white matter connections in brain

Major Depression — a serious mental disorder

- So far, no biological tests confirm major depression
- The current knowledge indicates that the pathophysiology of depression may be distributed across many brain regions and circuits.

We are interested in finding the relationship between brain connectivity and major depression

Data

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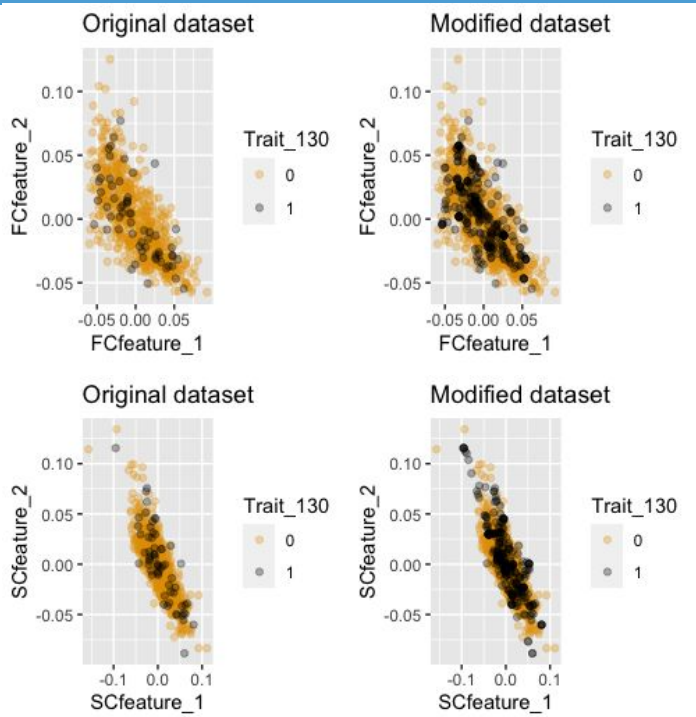
The Human Connectome Project (HCP) : 1206 adults

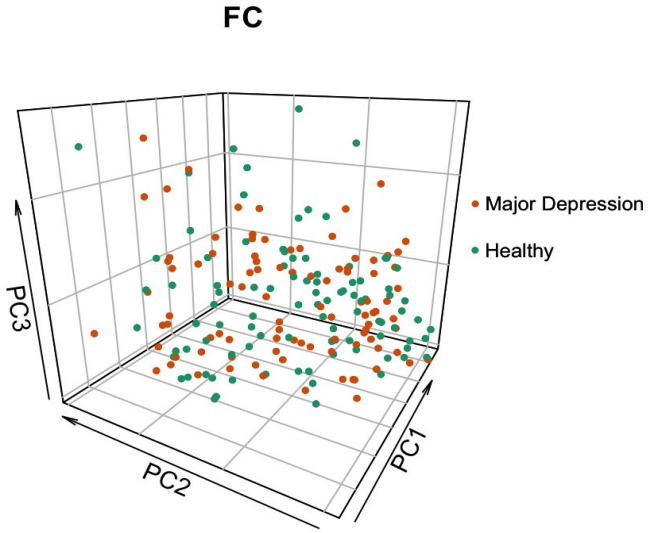
- FC and SC: two 68 x 68 connectivity matrices for each subject
- Tensor PCA (TNPCA)
  - Each subjects has 60 PC scores for FC and 60 PC scores for SC
- 175 traits mearsured for each subject
  - Major Depression (Yes/No)
  - Number of depressive symptoms (0-9)

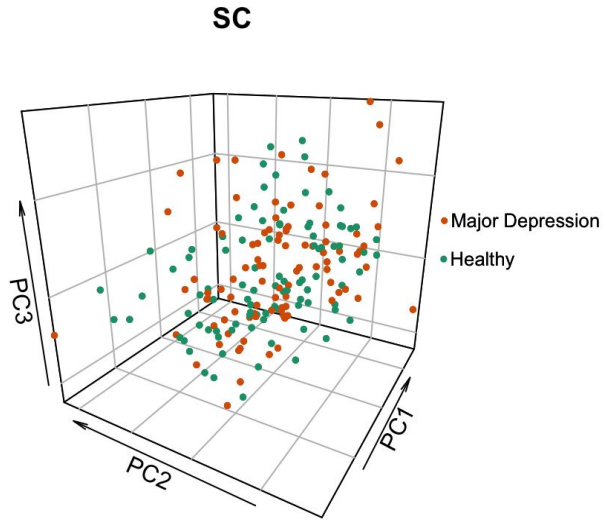
Oversampling

- Imbalanced dataset (95/1028)
- generate 200 synthetic samples using SMOTE



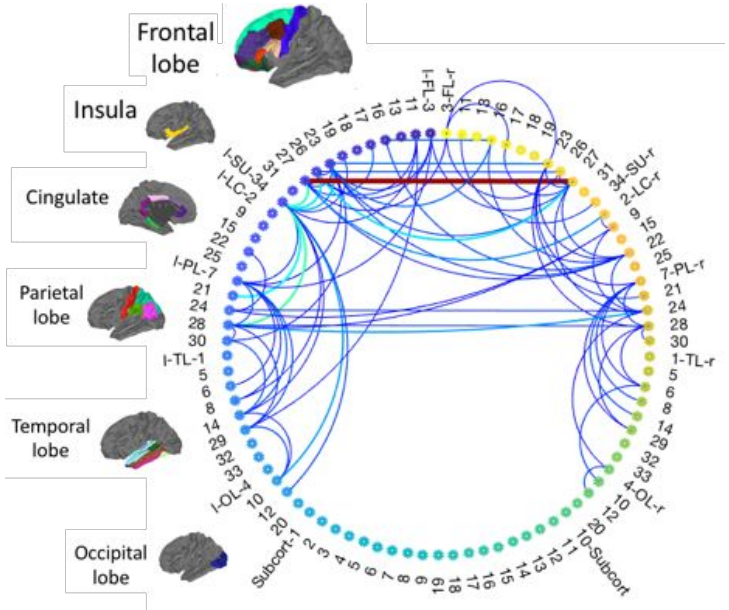
PCA scores and traits



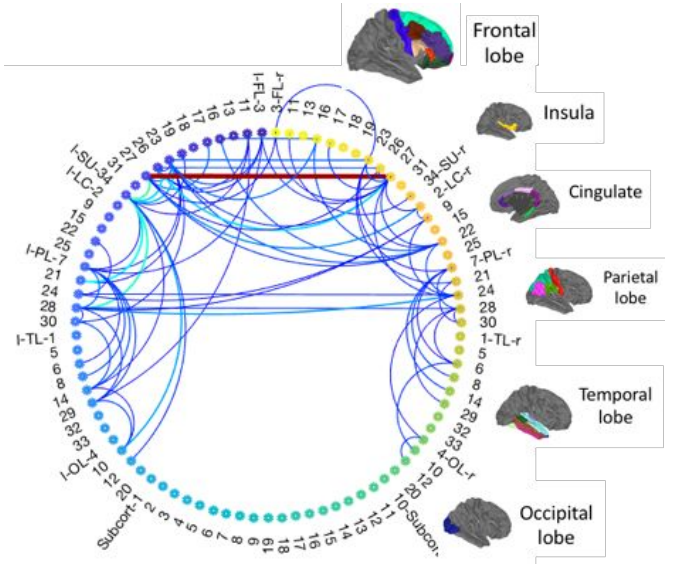


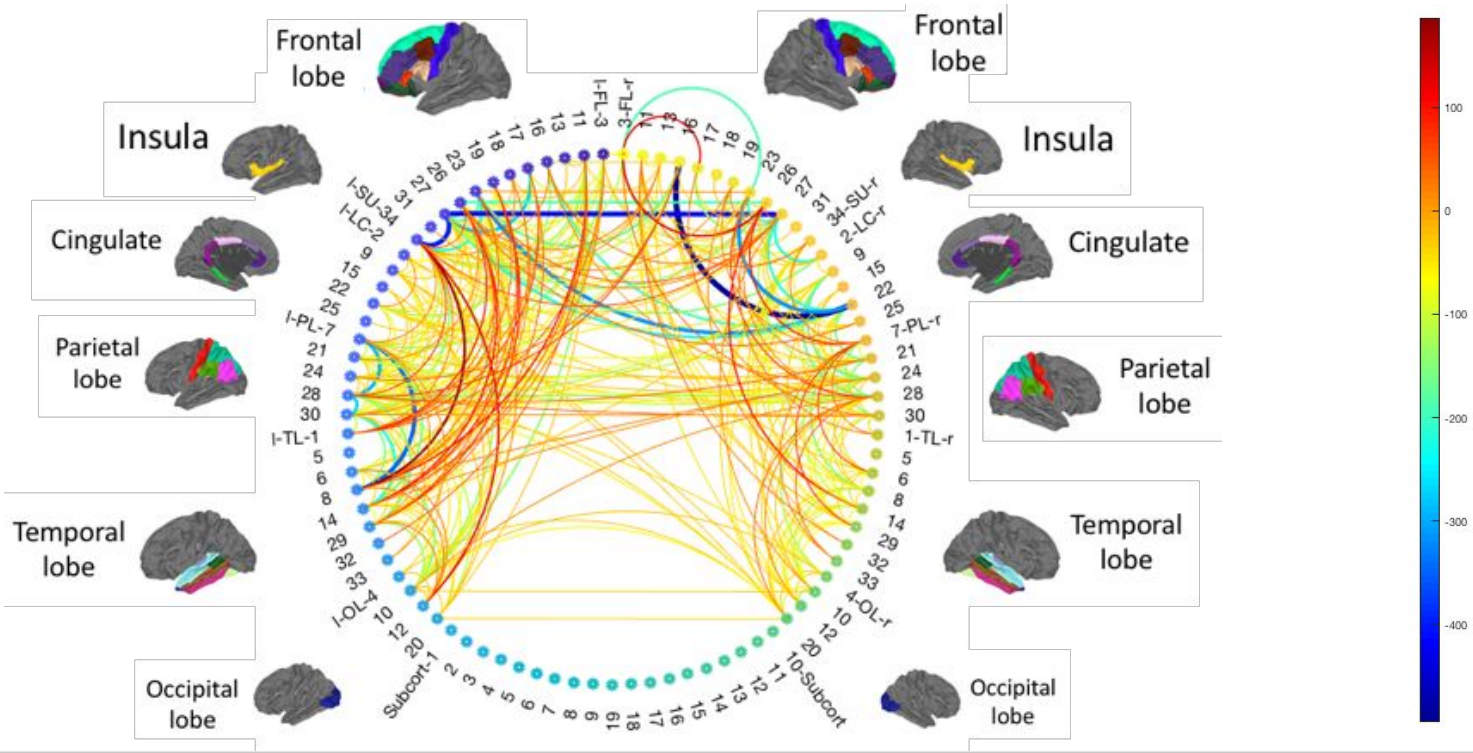
- Each group contains 95 subjects
- Performed Maximum Mean Discrepancy Test
  - Not enough evidence to say the distributions are different

Trait_130 no-depression (mean count, threshold 0.1)

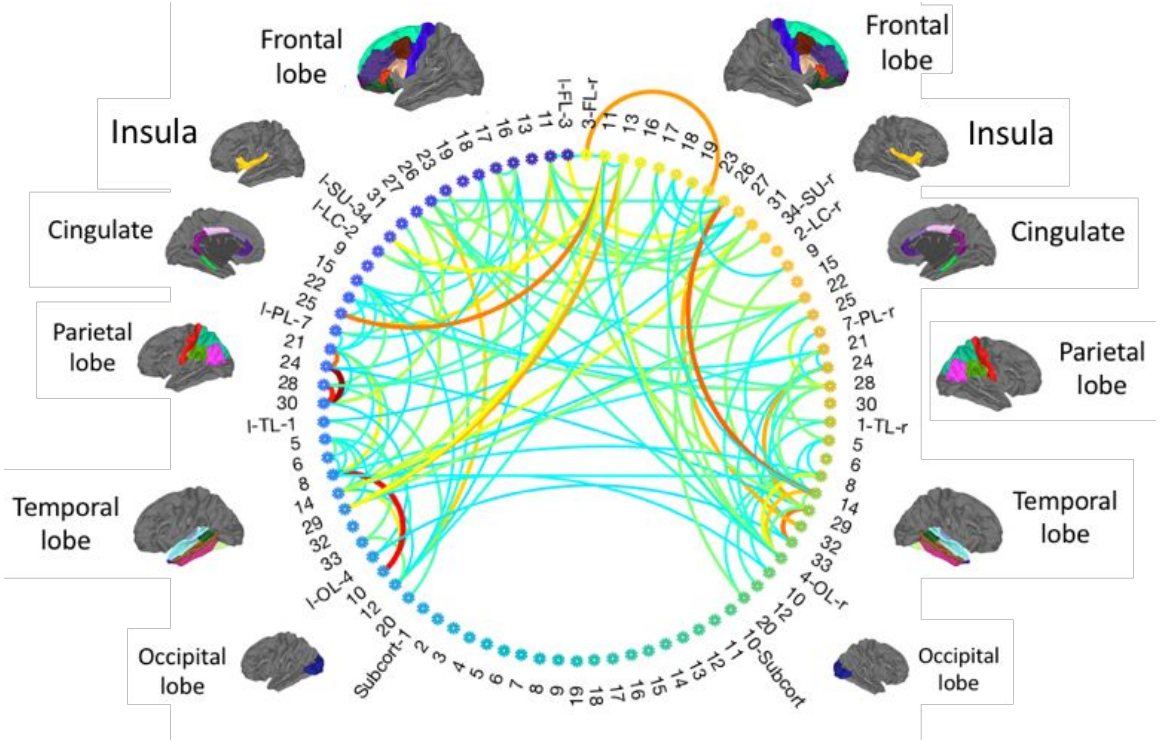


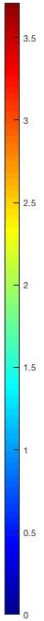
Trait_130 depression (mean count, threshold 0.1)





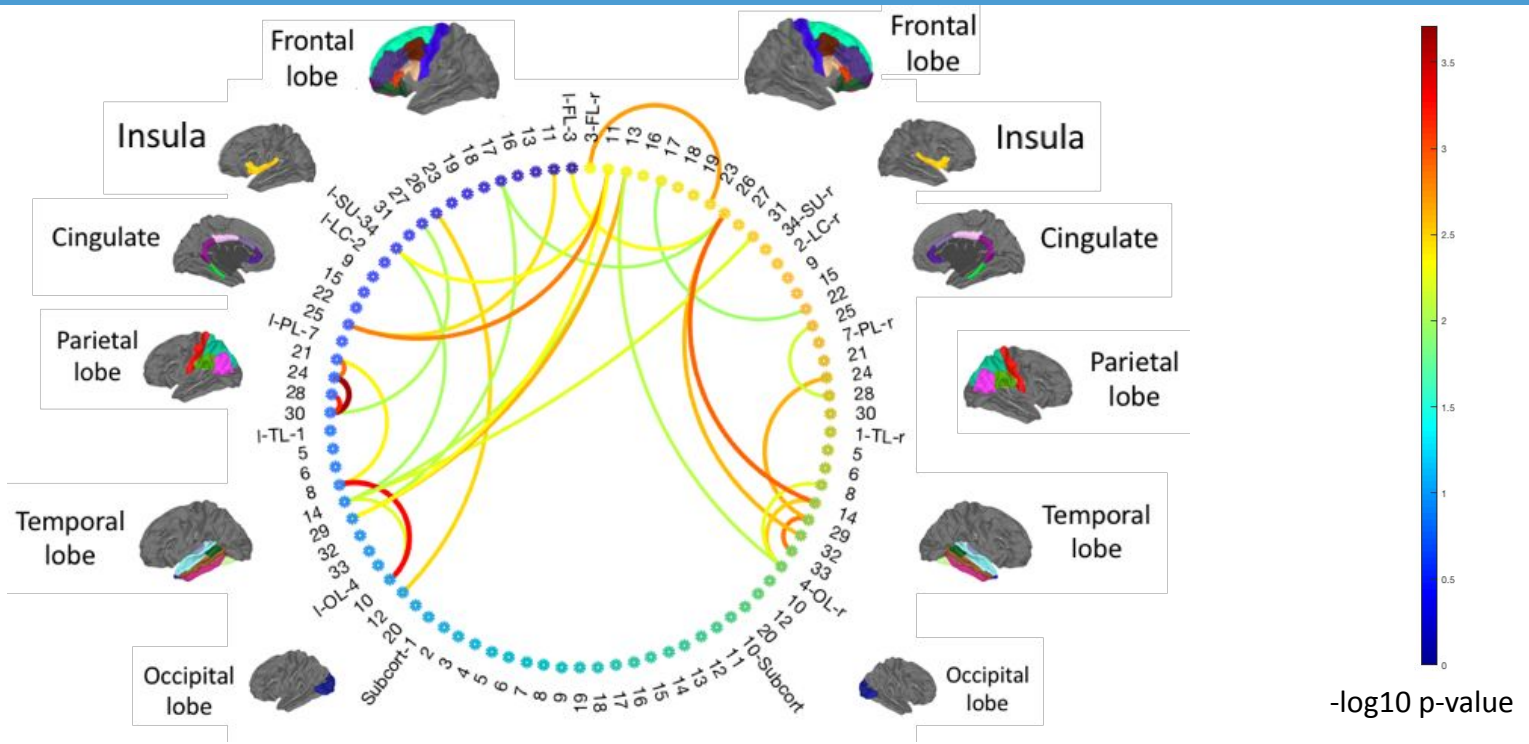
Trait_130 depression, SC network difference, threshold 0.1





HCP: depression trait
p-values ≤ 0.05
edge number = 120

-log10 p-value



HCP: depression trait
p-values ≤ 0.01
edge number = 29

-log10 p-value

Modeling

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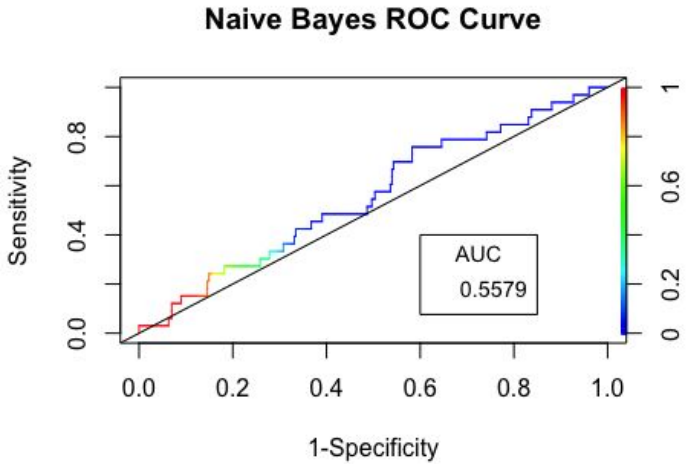
	Accuracy	Specificity	Sensitivity	AUC
Logistic Regression	80.30%	86.75%	21.21%	0.4692
LDA	81.19%	88.41%	15.15%	0.4714
Naïve Bayes	72.84%	77.81%	27.27%	0.5579



Penalized Regression

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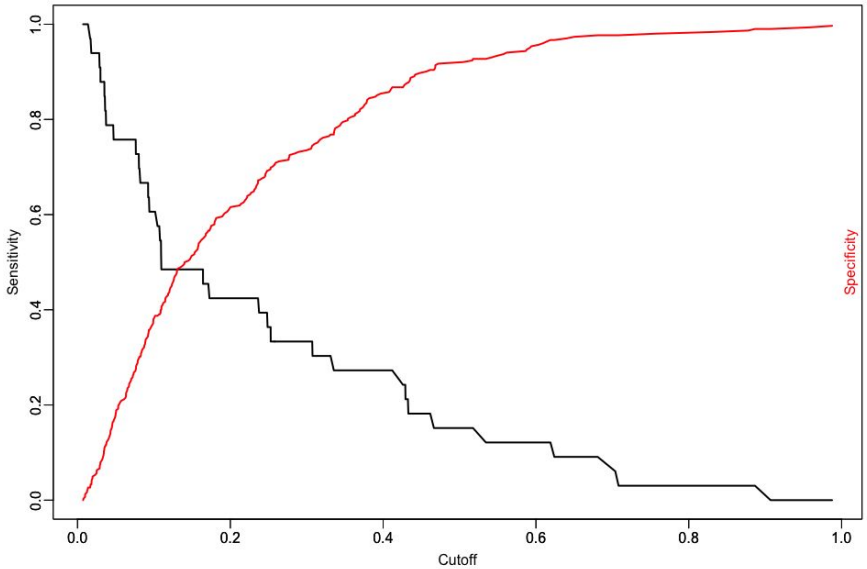
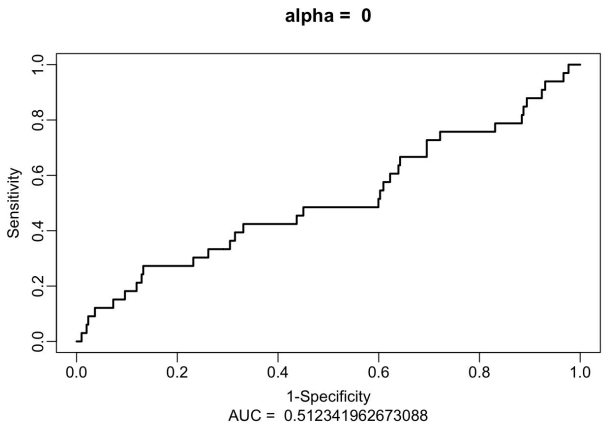
Ridge Regression: Cutoff v.s. sensitivity/specificity

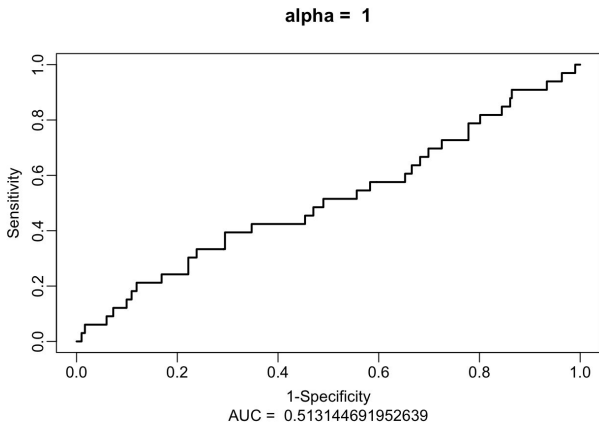


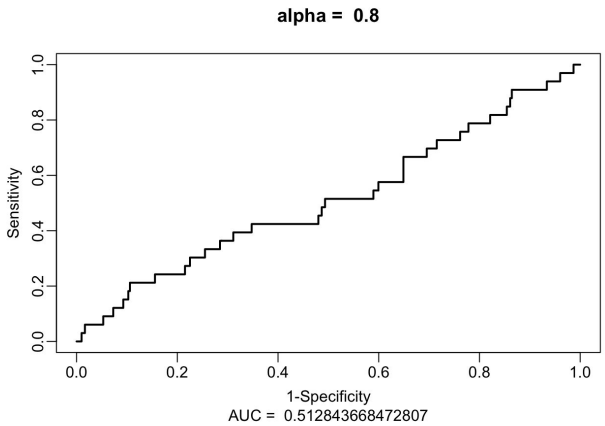
Threshold = 0.4

Prediction \ Reference	0	1
0	259	24
1	43	9

Ridge, Lasso and Elastic Net







Ridge, Lasso and Elastic Net

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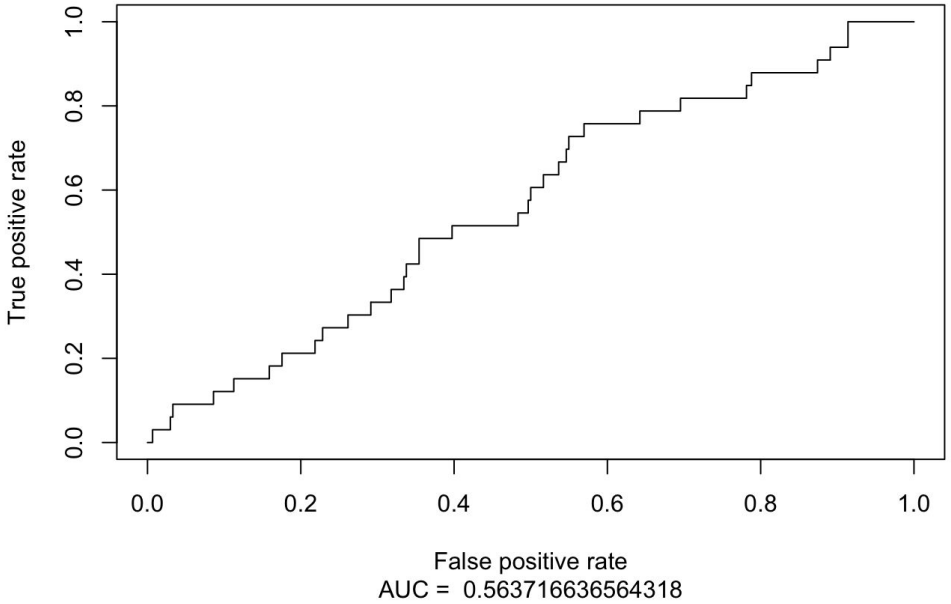
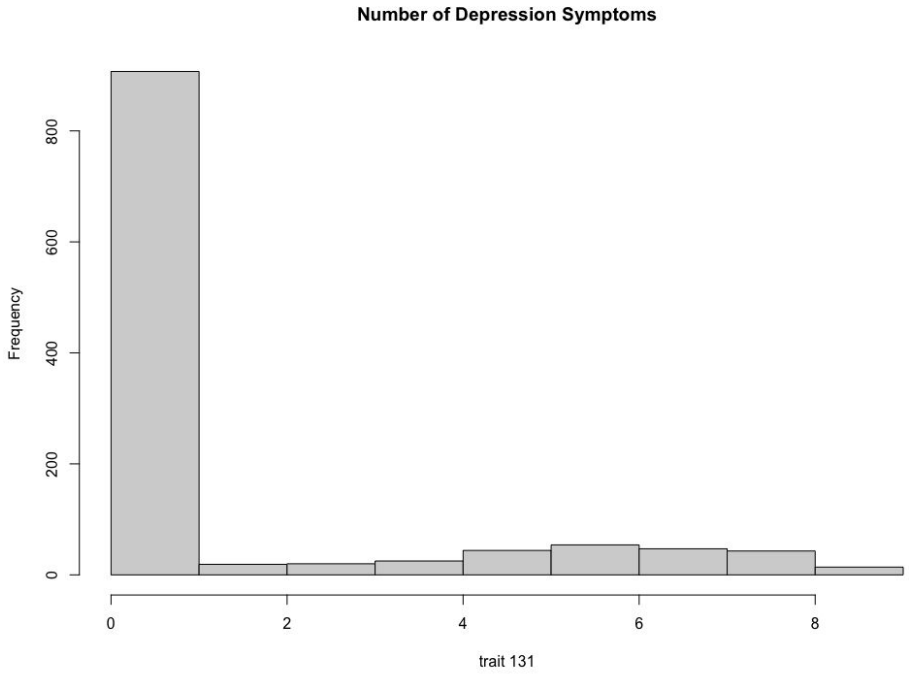
	Accuracy	Specificity	Sensitivity	AUC
alpha = 0	80%	85.76%	27.27%	0.5123
alpha = 1	74.63%	80.13%	24.24%	0.5131
alpha = 0.8	80.9%	87.42%	21.21%	0.5128

SVM



Prediction \ Reference	0	1
0	264	29
1	38	4

Regression: Number of Depression Symptoms



	MSE
Ridge	6.5
LASSO	6.60
SVM	9.24

Major Depression : Binary Classification

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Model: Decision Tree & Random Forest

Training Method: Cross Validation (10 fold)

Objective Function: Optimize Accuracy

Feature Selection:

- **Experiment 1: FC Feature (total 60)**
- **Experiment 2: SC Feature (total 60)**
- **Experiment 3: FC+SC Feature (total 120)**

Decision Tree Metric: AUC (Area Under Curve)

Major Depression : Decision Tree

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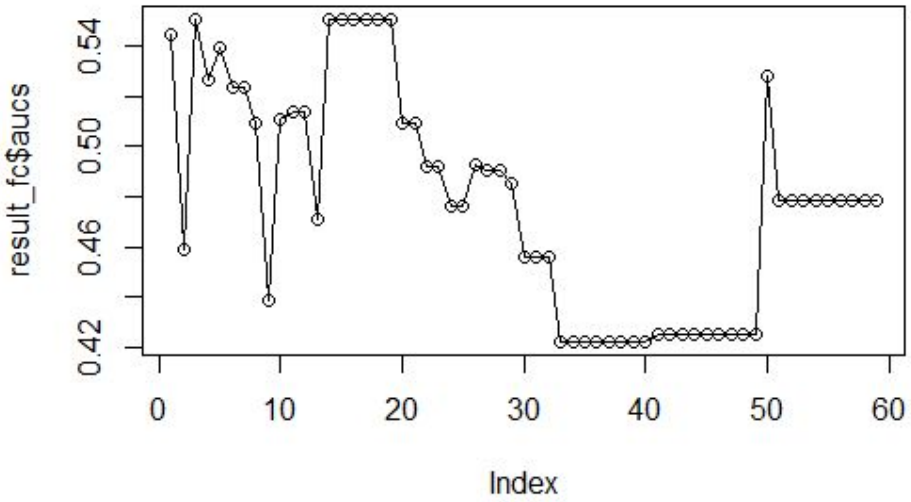
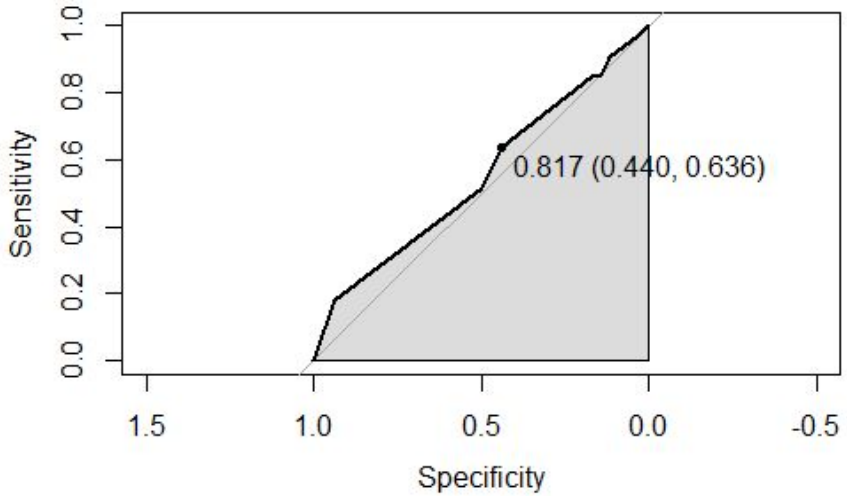
Experiment 1: FC Feature Feature number for best performance :14

number of features versus AUC





Major Depression : Decision Tree

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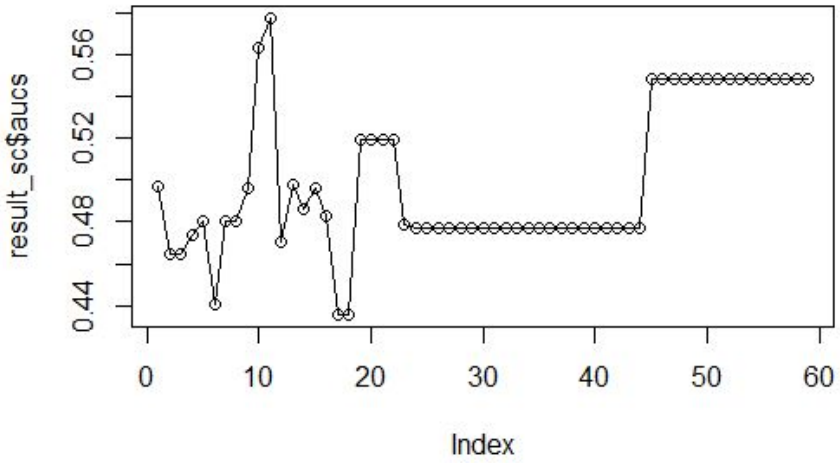
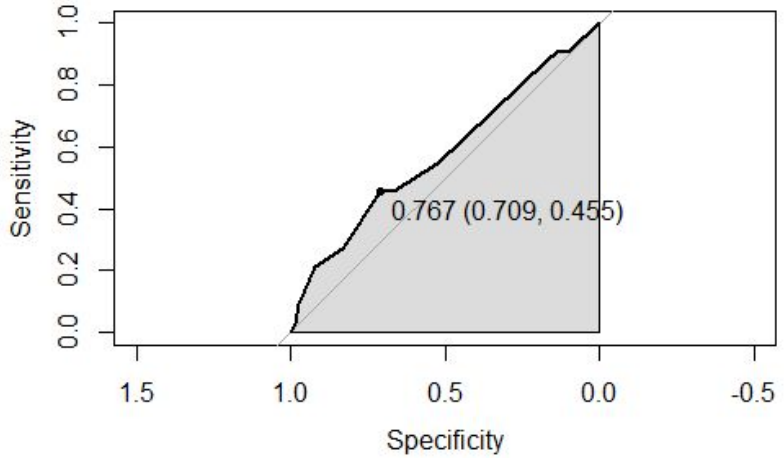
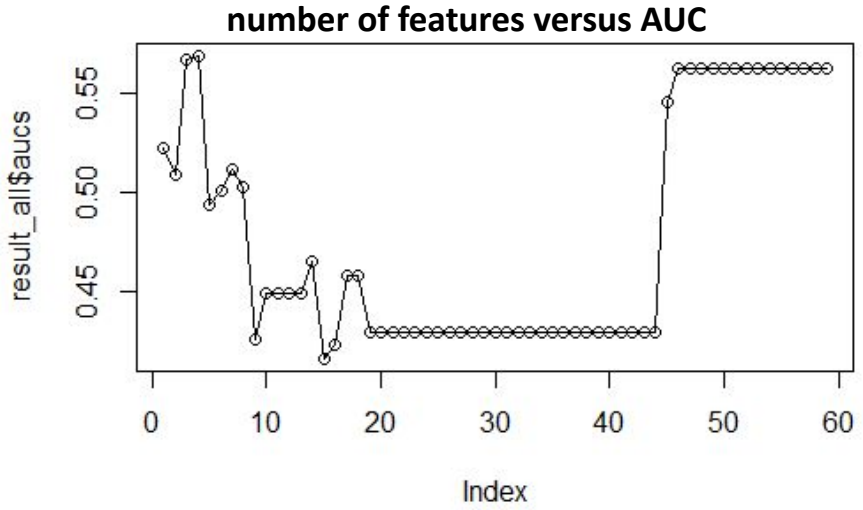
Experiment 2: SC Feature **Feature number for best performance: 11**

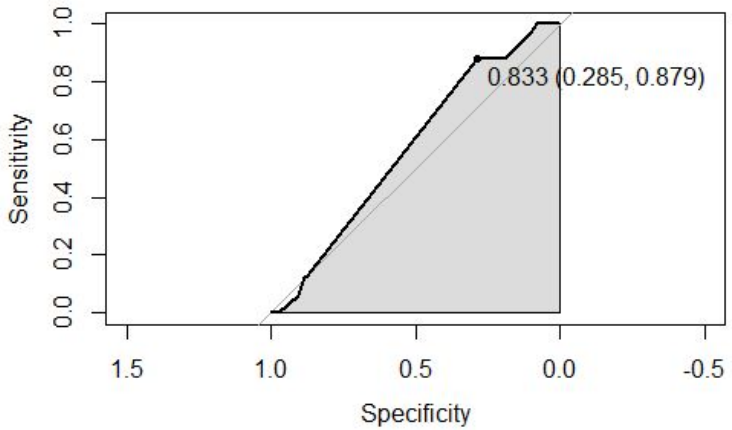
number of features versus AUC





Experiment 3: FC+SC Feature Feature number for best performance: 4 or 44+





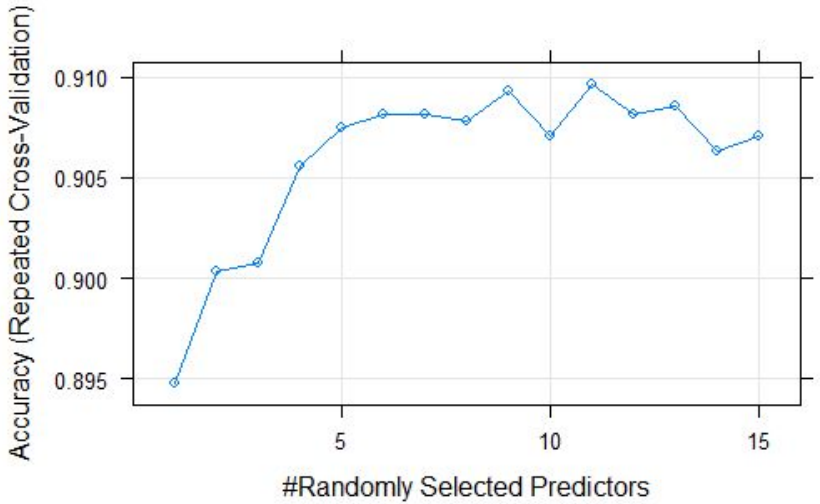
Summary

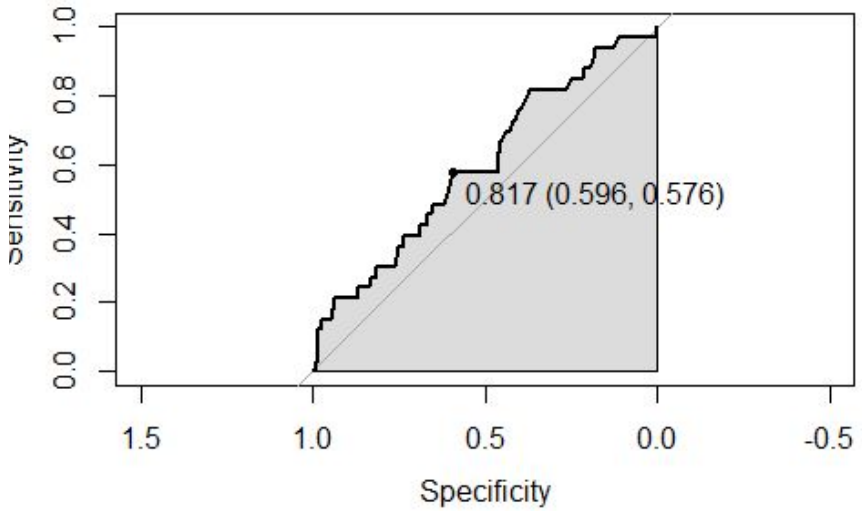
	FC	SC	FC+SC
AUC	0.55	0.578	0.569
Accuracy	0.460	0.684	0.343
Threshold	0.817	0.767	0.833

Major Depression : Random Forest

Experiment 1: FC Feature Method: Grid Search Best performance: mytry=11

number of mtry versus accuracy





Major Depression : Random Forest

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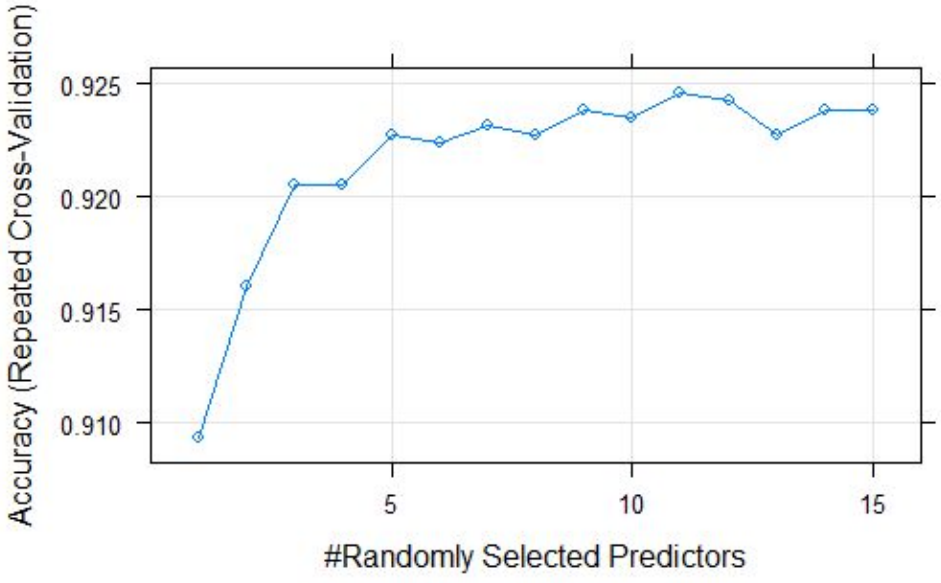
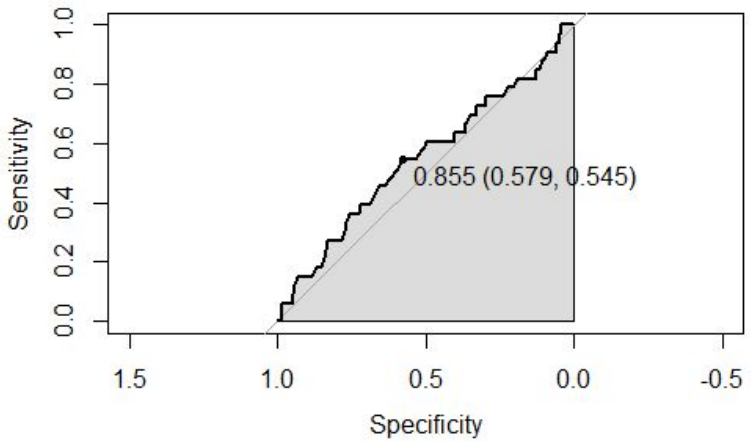
Experiment 2: SC Feature **Method: Grid Search** **Best performance: mytry=11**

number of mtry versus accuracy





Major Depression : Random Forest

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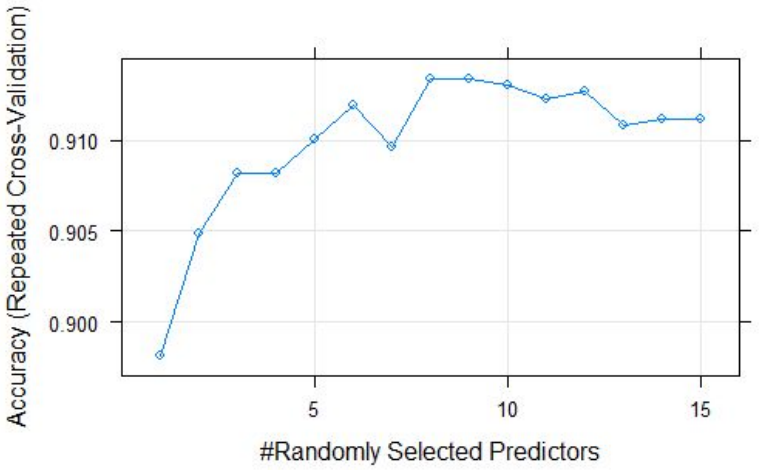
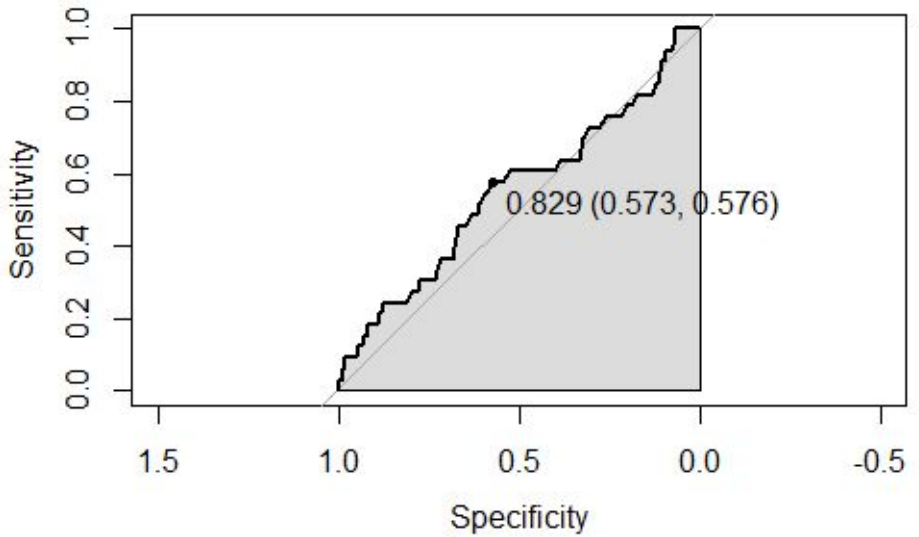
Experiment 3: FC+SC Feature **Method: Grid Search** **Best performance: mytry=9**

number of mtry versus accuracy





Summary

	FC	SC	FC+SC
AUC	0.600	0.549	0.551
Accuracy	0.594	0.576	0.573
Threshold	0.817	0.855	0.829

Number of Depression Sympotoms : Regression

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Model: Regression Tree & Random Forest Metric: MSE

Random Forest

FC	SC	FC+SC
7.58	7.03	6.52

Regression Tree

FC	SC	FC+SC
1.573	1.798	1.897

Discussion

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1. Through hypothesis testing, we didn't observe significant differences in the distribution of the brain PC scores among subjects having a low versus high value for depression.

2. Using multiple machine learning approaches, prediction accuracy was at slightly above chance level for depression, which is in line with literature including a recent similar large-scale study done in 10,343 healthy individuals from UK Biobank (PMID: 31858985).

3. The lack of consistency and generalizability among published studies of brain connectome and depression is likely, at least partly, due to differences in symptom profiles, sample characteristics, dissimilar definition of ROI, different methods for measurement and power of analytical tools.

4. Dissecting the relationship between the brain structural and functional connectome and mental health traits, in the long run, will improve diagnostics, prevention and treatment of mental disorders.

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Thank you !