Machine Learning and Feature Selection Analysis on Dynamic Connectivity Signatures in Neural Networks Engaged for Emotion Regulation

## **Motivation and objectives**

#### Major Depressive Disorder (MDD)

- Characterized by persistent low mood, loss of interest, and inability to regulate emotions
- 2017: estimated 3.2 million adolescents aged 12-17 (13.3% of demographic) experienced at least one major depressive episode

#### Difficult to diagnose consistently

- Few conclusive biomarkers

#### Objective

- Determine whether remitted subjects can be quantitatively distinguished from healthy subjects based on their dynamic signatures and phenotypic data

#### Table 1. DSM-IV-TR Criteria for Major Depressive Disorder

Five or more of the following symptoms should be present daily or for most of the day for at least 2 weeks:

- · At least one symptom is depressed mood or anhedonia
- · Changes in appetite or weight
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- · Fatigue or loss of energy
- · Feelings of guilt or worthlessness
- · Difficulty thinking, concentrating, or making decisions
- · Suicidal ideation or suicide attempts

DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Source: Reference 8.

## **Data collection**

105 healthy subjects24 subjects in remission from MDD

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- 2 increased Emotional Response trials
- 2 decreased Emotional Response trials

#### **Phenotypic Data**

- Beck Depression Inventory
- Early Adolescent Temperament Questionnaire
- Multidimensional Anxiety Scale for Children





### fMRI data processing

					fM	IRI d	data						Pr	oba	abili	isti	ooolean netwo	ork	•	Dynamic signature
Time series													List of possible solutions (boolean networks) that explain fMRI time series						Adjacency matrix [a <sub>ij</sub> ]	
F	R_V1_ROI R_M	IST_ROI R	V6_ROI R	V2_ROI R	V3_ROI F	V4_ROI R_V	/8_ROI	R_4_ROI F	R_3b_ROI F	R_FEF_ROI R	PEF_ROI R	55b_ROI R_	V3A_ROI R_F	RSC_ROI R_P	OS2_ROI R	V7_ROI R_I	l			
R_V1_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
R_MST_ROI	0	0	0	0.25	0	0	0	0	0	0	0	0	0	0	0	0	-			
V2 ROI	1	0	0	0.20	0	0	0	0	0	0	0	0	0	0	0	0				
V3_ROI	0	0	0	0.25	0	0	0	0	0	0	0	0	0	0	0	0	1			
V4_ROI	0	0	0	0.25	1	0	0	0	0	0	0	0	0	0	0	0				
V8_ROI	0	0	0	0.5	0	0	0	0	0	0	0	0	0	0	0	0	8			
4_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
3b_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-			
PEF ROI	0	0	0	0	0	0 0.16	0	0	0	0	0	0	0	0	0	0				
55b ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
V3A_ROI	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	<i>II C i</i>	. •	1 • • • • • • • • •
RSC_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		# Of 1.	tım	ies node i is input to nod
POS2_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	<b>a –</b>			
V7_ROI	0	0	0	0	0	0	0.5	0	0	0	0	0	1	0	0	0	$u_{ii}$ –		ш	
PS1_ROI	0	0	0	0.25	0	0 0.33	33333333333333333	0	0	0	0	0	0	0	0	0	l j		₩ (	OT INDUIS FOR NOAE 1
3B_ROI	0	0	0	0.25	0	0 0.00	0	0	0	0	0	0	1	0	0	0	<b>J</b>			- <u>j</u> j j
O1_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1			
02_ROI	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	"D '	
PIT_ROI	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0			<b>~</b> _	
T_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
1_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
SL_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	_			
CV ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
TV ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
Pm_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-			
m_ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				
POS1 ROI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				

#### **Dynamic signature network graphs**



- Betweenness centrality +



### **Conserved components**

 Amygdala-hippocampal complex component conserved across over 75% of healthy and remitted dynamic signatures, for both increased and decreased response



 Basal ganglia component (pallidum, putamen) conserves across over 70% of healthy dynamic signatures and over 75% of remitted dynamic signatures, for both response types



## **Conserved components**

Amygdala-Hippocampal complex

- Formation of episodic memories in response to stimuli
- Cognitive appraisal, emotional response



Basal ganglia

Reward system, decision making



# Data used for machine learning

#### **Network characteristics**

- 16 per dynamic signature, e.g. assortativity coefficient, density, number of articulation points **Motif occurrences** 
  - 32 motifs per dynamic signature: size of 3 vertices, within subgraph of second order connectivity to Hippocampus regions

#### Phenotypic data

- Only 13 of 531 variables used; remainder all had missing values

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Total of 203 features per subject

# **Dimensionality reduction and clustering**



### **Principal Component Analysis**



### **Hierarchical clustering**





#### **Feature Selection**

Recursive Feature Elimination with a Logistic Regression model

- Selected 30%, 50%, and 80% of features



### **Next steps**

- Search for motifs of different sizes in whole dynamic signatures
- Use Support Vector Machines for classification
- Potentially analyze more phenotypic data

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