Sensing Psychosis
Toward Robust Computational Phenotypes in Severe Mental Illness

Justin Baker
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Sensor Networks

Feature Extraction

Latent Construct Models

Motors & Actuators

Feedback
Sensor Networks

Feature Extraction

Latent Construct Models

Motors & Actuators

Feedback

Build model
Mixtures and mixed-membership models, time-series models, generalized linear models, factor models, Bayesian nonparametrics

Infer hidden quantities
Markov chain Monte Carlo, variational inference, Laplace approximation

Criticize model
Performance on a task, prediction on unseen data, posterior predictive checks

Apply model
Predictive systems, data exploration, data summarization

DATA

REVISE MODEL

Sensor Networks
Feature Extraction
Latent Construct Models
Motors & Actuators
Feedback
Sensor Networks
Feature Extraction
Latent Construct Models
Motors & Actuators
Feedback
Sensor Networks
Feature Extraction
Latent Construct Models
Motors & Actuators
Feedback
Development of Brain Risk States

- Healthy Trajectory
- Risk Trajectory
- Association network excitatory synapses
- Deficient myelination
- Reduced interneuron activity
- Excessive excitatory pruning
- Association network inhibitory synapses

Age (years)
Development of Brain Risk States

**Genetics, Neuroimaging, and Behavior**

- >2500 Healthy Individuals
- >1000 Individuals with Psychotic Illness
- >250 with MRI

Insel 2010
Healthy
n=100

Baker et al. 2014, JAMA Psychiatry
Psychosis
n=100

Baker et al. 2014, JAMA Psychiatry
Development of Brain Risk States

Risk for Psychosis

Polygenic Risk for SZ
North-American Prodromal Longitudinal Sample (NAPLS)
McLean Early Psychosis Program

Insel 2010
Development of Brain Risk States

Sensitive Periods

Unimodal networks
Heteromodal networks
Association networks

Excitatory Pruning
Myelination
Inhibitory Growth

Insel 2010
Individual Brains are Different
Individualized ROIs

Atlas-based ROIs

Schizophrenia

Bipolar Disorder

Wang et al., Molecular Psychiatry, 2019
Behavioral Assessment is Challenging and Human Resource Intensive

- Training can take months (~30 hours training, often spread out over several weeks)
- Administration and scoring takes 3-4 hours per participant.
- Highly Subjective
- Poor inter-temporal, inter-rater reliability
Covariance of Item-level Symptom Reports

N=1137
Distance between points signifies similarity in symptom profiles at time of evaluation using standard measures (PANSS, MADRS, YMRS, SCID).
Our illnesses have huge heterogeneity in presentation, which could obscure differences in biology based on group comparisons.

Unless we are capturing this heterogeneity accurately, scale will not help.
Latent Variable Approach to Psychiatric Construct Definition
Latent Variable Approach to Psychiatric Construct Definition
Latent Variable Approach to Psychiatric Construct Definition
Q1 What brought you into the hospital?
Q2 Has anything in particular been on your mind recently?
Q5 What are your goals for this hospitalization?
Q6 How are people treating you here?
Q7 How’s the food been?
Q8 How’s your mood?
Q9 How’s your thinking?
Q10 How’s your energy?
Q11 How many hours have you slept?
Q12 How’s your self-confidence now compared to usual for you?
Q1  What brought you into the hospital?
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Q12 How’s your self-confidence now compared to usual for you?

![Images of facial expressions with correlation coefficients]

**Unusual Thought Content (PANSS)**
- Q2: r=-0.744
- Alone: r=0.752

**Depression (BPRS)**
- Alone: r=0.656

**Delusions (PANSS)**
- Q12: r=0.680

**Negative Symptoms (PANSS)**
- Q12: r=-0.578
What brought you into the hospital?
Has anything in particular been on your mind recently?
What are your goals for this hospitalization?
How are people treating you here?
How’s the food been?
How’s your mood?
How’s your thinking?
How’s your energy?
How many hours have you slept?
How’s your self-confidence now compared to usual for you?
Voice as a psychiatric VS?
Voice as a psychiatric VS?

PANSS Negative Total
PANSS Suspiciousness
PANSS Neg Blunted Affected
PANSS Neg Emotional Withdrawal
PANSS Neg Social Withdrawal
PANSS Neg Speech Flow
PANSS Gen Depression
BPRS Depression
BPRS Bizarre Behavior
BPRS Blunted Affect
BPRS Emotional Withdrawal

Constricted Vowel Space

Typical Vowel Space

Expanded Vowel Space

Speech Signal

Speech Processing

Formant Tracking

Vector Quantization

Vowel Space Assessment

Vowel Space Ratio

Formant 1 (Hz)
Expressivity as a psychiatric VS?

Item-level Symptom Severity with Facial Expressivity

Alone Time

- M1 apparent sadness
- M3 tension
- P P6 suspiciousness
- P N2 emotional withdrawal
- P N7 stereotyped thinking
- P G9 unusual thought content
- P G12 lack of judgment and insight
- P G16 social avoidance
- B2 anxiety
- B5 guilt
- B7 elevated mood
- B16 blunted affect
- B17 emotional withdrawal
- B19 tension
- B22 distractibility

$R$ (correlation)

Entire Interview

- M3 tension
- M5 appetite
- P P6 suspiciousness
- P N2 emotional withdrawal
- P N4 social withdrawal
- P N7 stereotyped thinking
- P G9 unusual thought content
- P G16 social avoidance
- B2 anxiety
- B3 depression
- B5 guilt
- B7 elevated mood
- B16 blunted affect
- B17 emotional withdrawal
- B21 excitement
- B23 motor hyperactivity

$R$ (correlation)
Relationship of Automatic and Conventionally Acquired Measures
Syndromes change over time

Sensitive Periods

- Unimodal networks
- Heteromodal networks
- Association networks

Excitatory Pruning
Myelination
Inhibitory Growth
Syndromes change over time

![Graph showing manic and depressed episodes over time](image)
Intensive Longitudinal Case Series in Bipolar Disorder
“Deep Phenotyping”

- Multimodal, multi-time scale behavioral recordings robust to changes in exposome, development, and illness fluctuations.
Deep Phenotyping in Severe Mental Illness

- Started in early 2016
- Continuous monitoring of 15 individuals with chronic forms of bipolar disorder and schizophrenia in real-world settings and serial study visits.
- Randy Buckner (Harvard), JP Onnela (HSPH)
Individual Participant Study Timeline

GeneActiv
Beiwe
TestMyBrain
Study Visit

12 months of enrollment

Sensors and Behaviors Assessed

TMB Neurocognitive Web Battery

PANSS, YMRS, MADRS, MCAS

LATENT CONSTRUCTS

Energy Level (perceived)
Activity Level (measured)
Energy Expended
Amount of Sleep (perceived)
Amount of Sleep (measured)
Processing Speed
Rate and Quantity of Speech
Rate and Quantity of Movement
Presence of Mania
Presence of Psychosis
A. NON-AFFECTIVE AFFECTIVE

B. Individual Participant Study Timeline

GeneActiv
Beiwe
TestMyBrain
Study Visit

C. Sensors and Behaviors Assessed

TMB Neurocognitive Web Battery
PANSS, YMRS, MADRS, MCAS

D. Latent Constructs

Energy Level (perceived)
Activity Level (measured)
Energy Expended
Amount of Sleep (perceived)
Amount of Sleep (measured)
Processing Speed
Rate and Quantity of Speech
Rate and Quantity of Movement
Presence of Mania
Presence of Psychosis

E. File System and Pipeline Architecture – “PHOENIX”

F. Quality Control and Study Management

Deep Phenotyping Dashboard
37yo F with schizoaffective / bipolar disorder over 165 days of continuous monitoring and serial MRI

Confronts family about childhood abuse
Moves in with partner
Therapist moves away

Proposes to partner
Goes up on antidepressant
Anniversary

170 days of clinical evolution
37yo F with schizoaffective / bipolar disorder over 165 days of continuous monitoring and serial MRI

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170 days of clinical evolution

1000 days of clinical evolution
37yo F with schizoaffective / bipolar disorder over 165 days of continuous monitoring and serial MRI

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Clinical Scales
GPS
Activity
Calls
Texts
Voice
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37yo F with schizoaffective / bipolar disorder over 165 days of continuous monitoring and serial MRI

2016-02-12

2016-07-28

Daily Surveys

Clinical Scales

GPS

Activity

Calls

Texts

Voice
37yo F with schizoaffective / bipolar disorder over 165 days of continuous monitoring and serial MRI

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Clinical Scales
- GPS
- Activity
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Daily Surveys
- 2016-02-12
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- Goes up on antidepressant
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- Confronts family about childhood abuse
- Moves in with Partner
- Therapist moves away

170 days of clinical evolution

1000 days of clinical evolution
Six Individuals with Mental Illness
Automated, minimal-burden, continuous assessment of community and social functioning in individuals with severe mental illness.
Significant Locations
Two years of Geospatial Recording
Significant Locations
Two years of Geospatial Recording

Location classes (most to least common)
Any Given Sunday
Two years of Geospatial Recording

Location classes (most to least common)
Any Given Sunday
Two years of Geospatial Recording

Location classes (most to least common)
Any Given Sunday
Two years of Geospatial Recording

Location classes (most to least common)
Activity classification with wearable sensors

Brushing teeth

Smoking

Taking Meds

Combing Hair

Washing Hands

Drinking

Cherian et al. Pervasive Health’17, May 23–26, 2017, Barcelona, Spain
Learning a Behavioral State Space

depth
video

image
manifold

manifold
coordinates

Johnson et al, 2016
Building Behavioral Fingerprints

A

Class
benzo
antidepressant
antipsychotic

Drug
alprazolam
diazepam
bupropion
phenelzine
chlorpromazine
clozapine
haloperidol
risperidone
atomoxetine
venlafaxine
citalopram
fluoxetine
methamphetamine
methylphenidate
modafinil
controls

B

Dose

C

Position

Speed

 Scalars

D

Length & Height

E

MoSeq

Distance From Center (mm)

Speed (mm/s)

Length (mm)

Height (mm)

Percent usage

Syllable ID

0.0 1.0 4.0 9.0
Predicting Drug Identity

K-Means, Scalars

AR-HMM
Predicting Drug Identity and Dose

**Scalars**

- alprazolam 0.5
- alprazolam 2.0
- atomoxetine 0.25
- atomoxetine 2.0
- bupropion 0.5
- bupropion 10.0
- bupropion 40.0
- chlorpromazine 0.25
- chlorpromazine 1.0
- citalopram 0.25
- citalopram 10.0
- clozapine 0.25
- clozapine 10.0
- control 0
- diazepam 0.5
- diazepam 2.0
- fluoxetine 0.5
- fluoxetine 10.0
- fluoxetine 30.0
- haloperidol 0.1
- haloperidol 6.0
- modafinil 12.5
- modafinil 20.0
- phenelzine 0.25
- phenelzine 2.5
- risperdone 0.25
- risperdone 1.0
- venlafaxine 10.0
- venlafaxine 2.5

**AR-HMM**

- alprazolam 0.5
- alprazolam 2.0
- atomoxetine 0.25
- atomoxetine 2.0
- bupropion 0.5
- bupropion 10.0
- bupropion 40.0
- chlorpromazine 0.25
- chlorpromazine 1.0
- citalopram 0.25
- citalopram 10.0
- clozapine 0.25
- clozapine 10.0
- control 0
- diazepam 0.5
- diazepam 2.0
- fluoxetine 0.5
- fluoxetine 10.0
- fluoxetine 30.0
- haloperidol 0.1
- haloperidol 6.0
- modafinil 12.5
- modafinil 20.0
- phenelzine 0.25
- phenelzine 2.5
- risperdone 0.25
- risperdone 1.0
- venlafaxine 10.0
- venlafaxine 2.5
Device

EHR

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<th>Last</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
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<th>13</th>
<th>14</th>
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<th>16</th>
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<tbody>
<tr>
<td>Meds (3)</td>
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<tr>
<td>Metoprolol (Lopressor)</td>
<td>100 mg PO now</td>
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<tr>
<td>Captopril (Capoten)</td>
<td>12.5 mg Q8 hrs</td>
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<tr>
<td>Digoxin (Lanoxin)</td>
<td>0.125 mg = 1 tablet PO QD</td>
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<tr>
<td>Furosemide (Lasix)</td>
<td>40 mg PO Q6 hrs</td>
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| PRNs (4) |     |     |     |     |     |     |     |     |     |
| Acetaminophen | 650 mg PO Q6 hours |     |     |     |     |     |     |     |     |
| Colace (Docusate) | 100 mg PO Q12 hrs |     |     |     |     |     |     |     |     |
| Lorazepam (Ativan) | 1 mg IV Q8 hrs |     |     |     |     |     |     |     |     |
| Morphine Sulfate | 1-2 mg IV Q2 hrs |     |     |     |     |     |     |     |     |
- Real time recordings of wrist actigraphy and medication administration times reflected in the electronic health record
Taking Meds

Lorazepam 1mg PO
Power Spectral Density of Human Movement over 24 hours
Power Spectral Density of Human Movement over 24 hours
Power Spectral Density of Human Movement over 24 hours
Power Spectral Density of Human Movement over 24 Min
Power Spectral Density of Human Movement over 24 Min
Power Spectral Density of Human Movement over 3 min
Power Spectral Density and Raw Accelerometry over 3 minutes as Exercise Epoch is Ending
Using **Behavioral Variation** to Understand the Brain and Disease

10 seconds of behavioral changes

1000 days of behavioral changes
Using Behavioral Variation to Understand the Brain and Disease
Latent Variable Approach to Psychiatric Construct Definition
Questions?

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