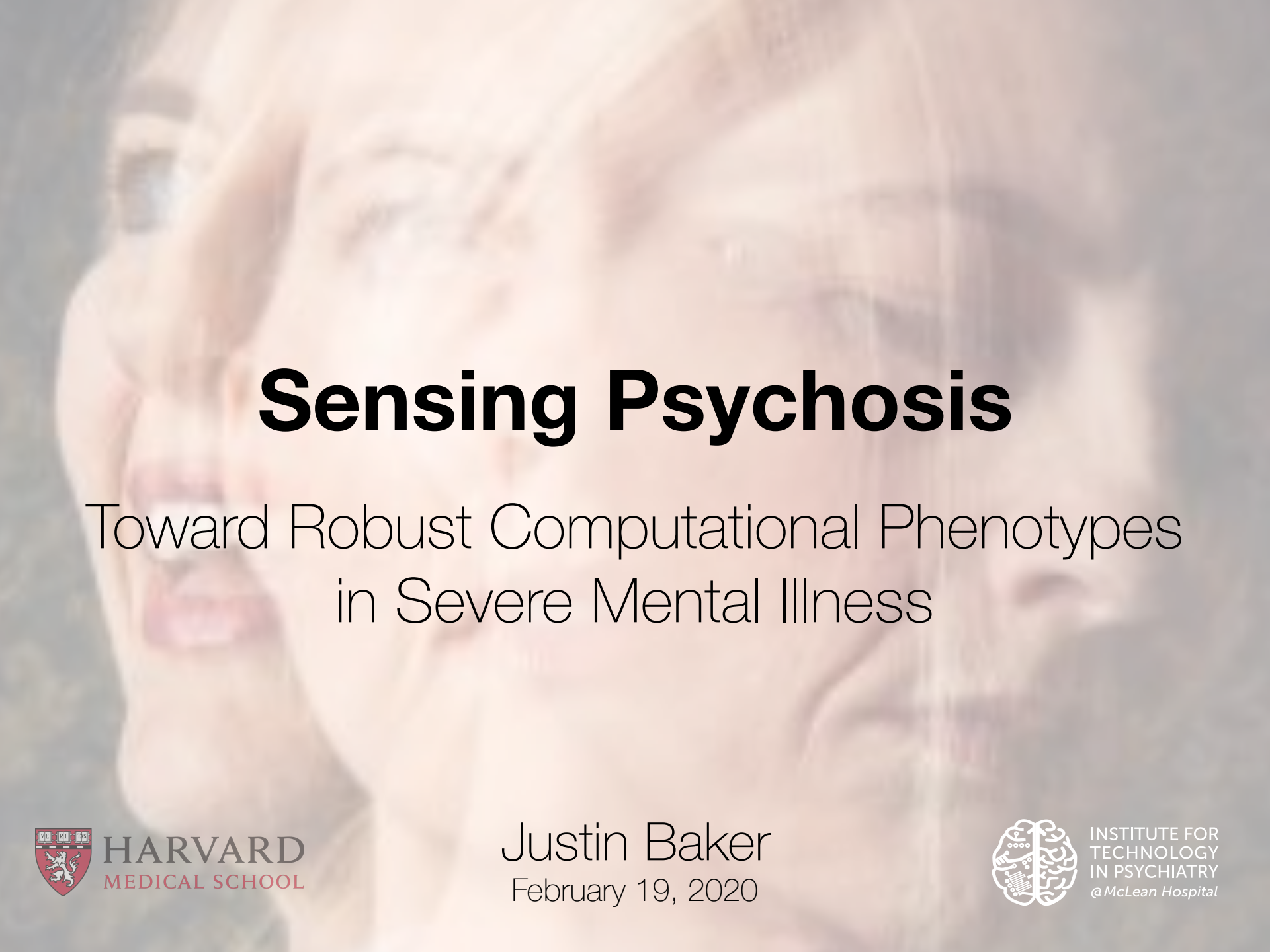


# Sensing Psychosis

## Toward Robust Computational Phenotypes in Severe Mental Illness


HARVARD MEDICAL SCHOOL

Justin Baker

February 19, 2020

INSTITUTE FOR TECHNOLOGY IN PSYCHIATRY
@McLean Hospital

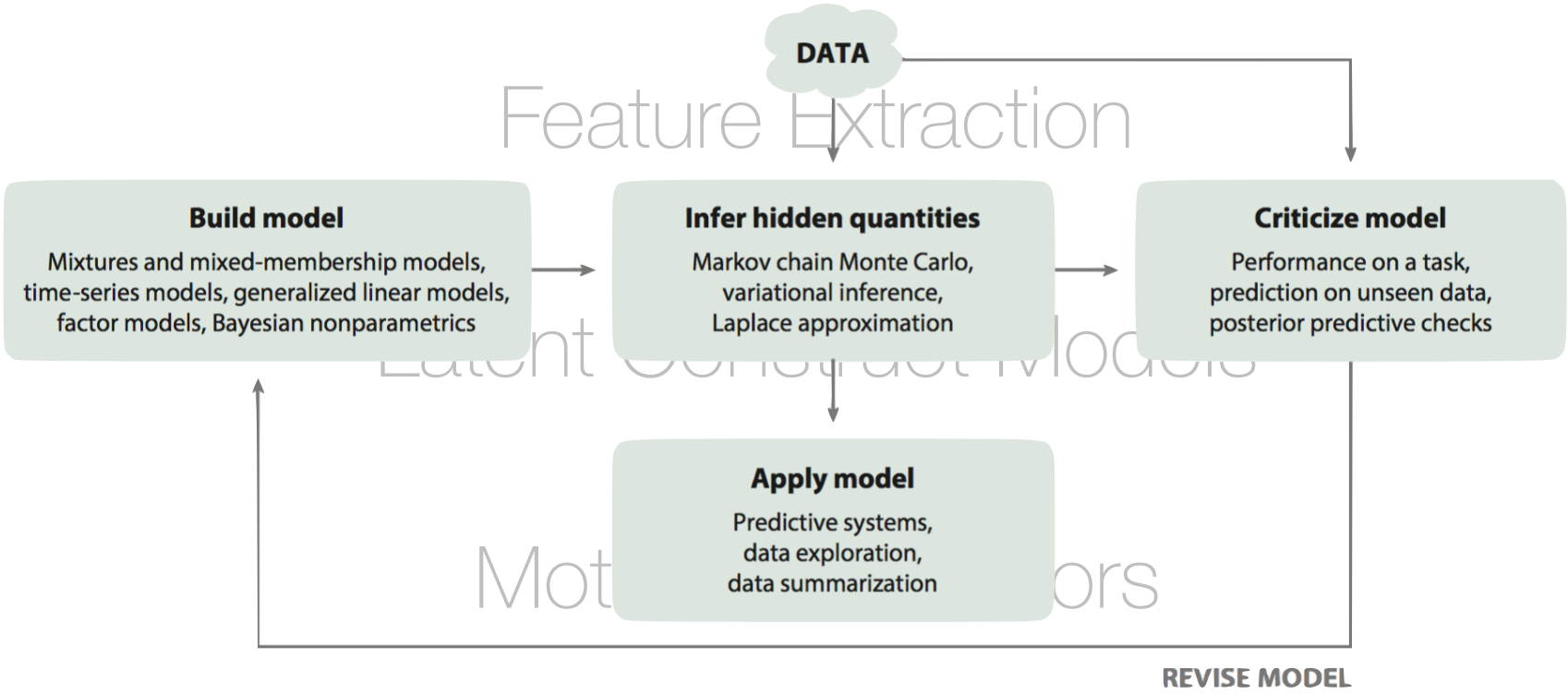
Sensor Networks

Feature Extraction

Latent Construct Models

Motors & Actuators

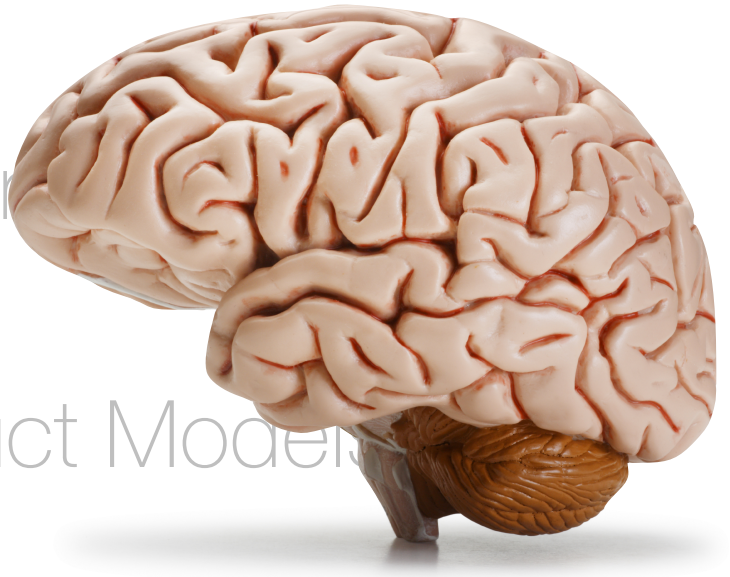
Feedback




*Box, 1976; Blei, Ann Rev Statistics, 2016*

Sensor Networks

Feature Extr



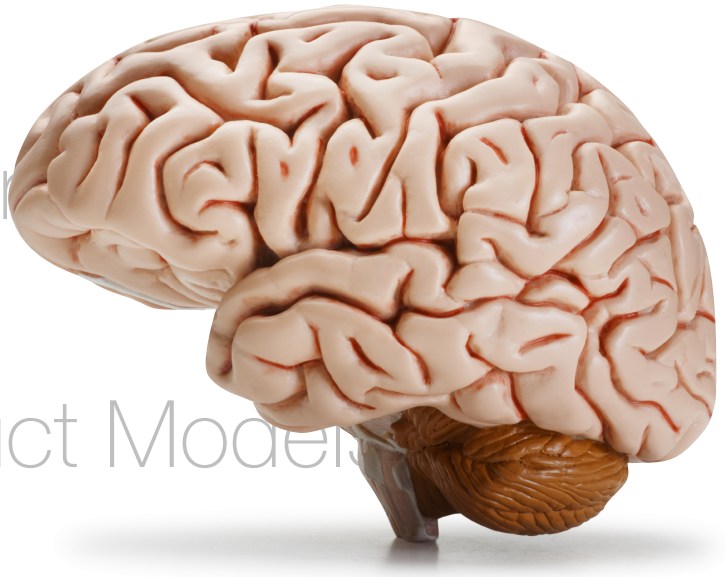
Latent Construct Model

Motors & Actuators

Feedback

Sensor Networks

ure Extr



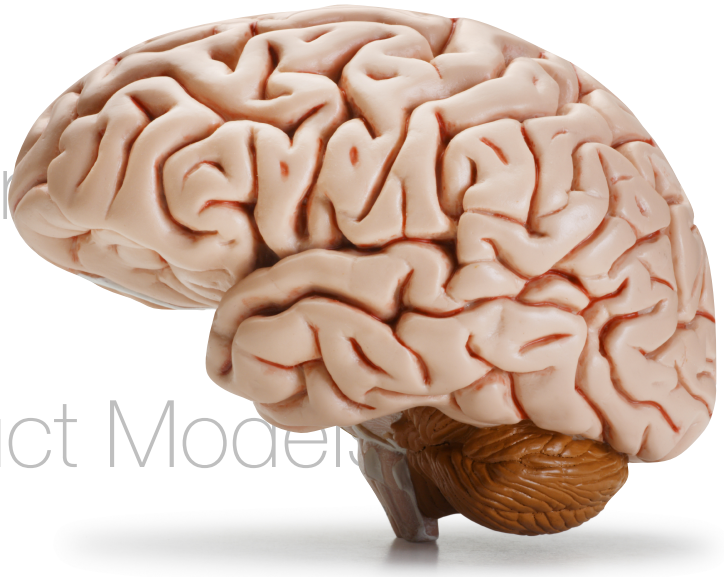
Construct Model

Motors & Actuators

Feedback

Sensor Networks

ure Extr



Construct Model

Motors & Actuators

eedback

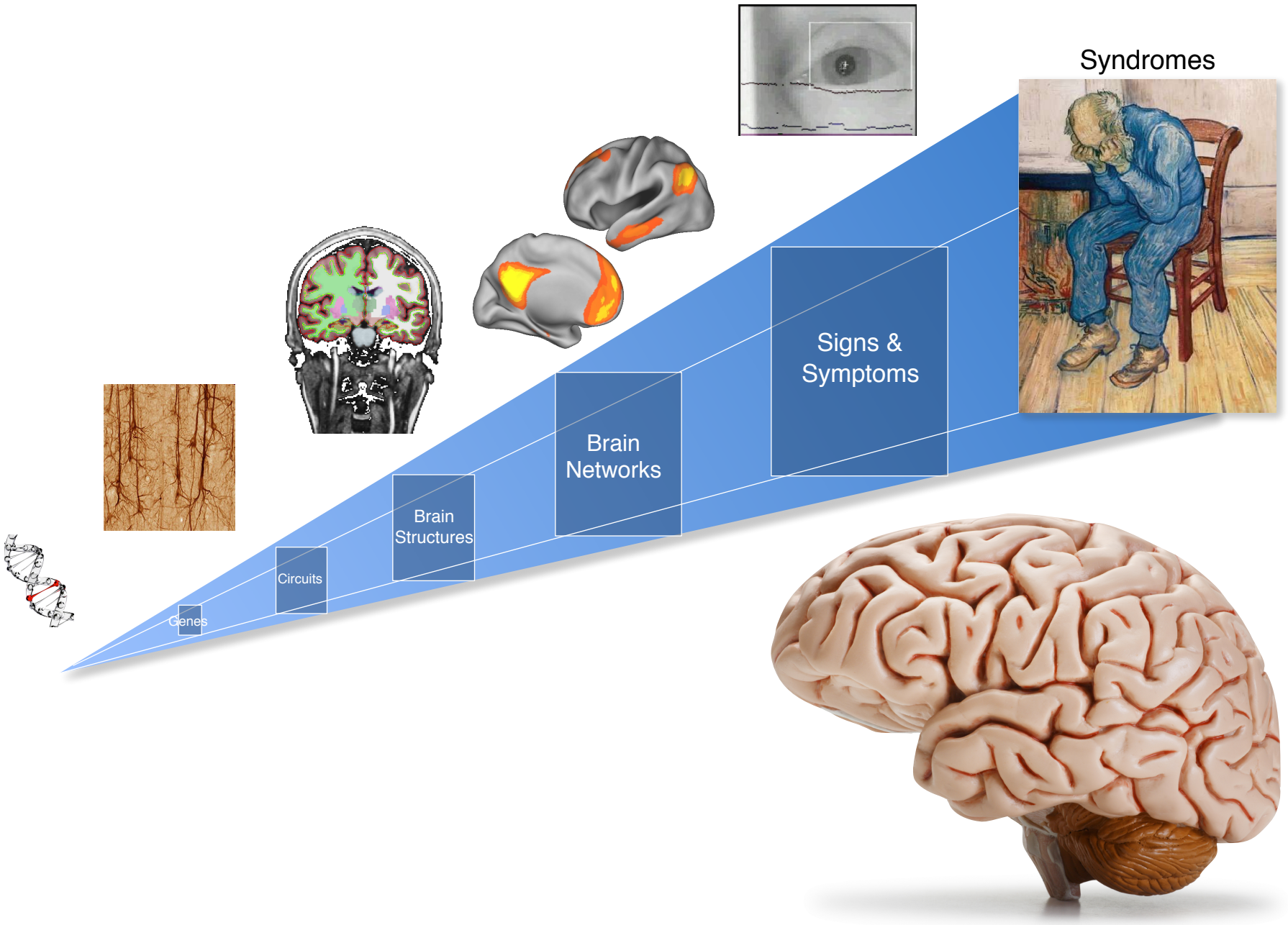
Sensor Networks

Feature Extraction

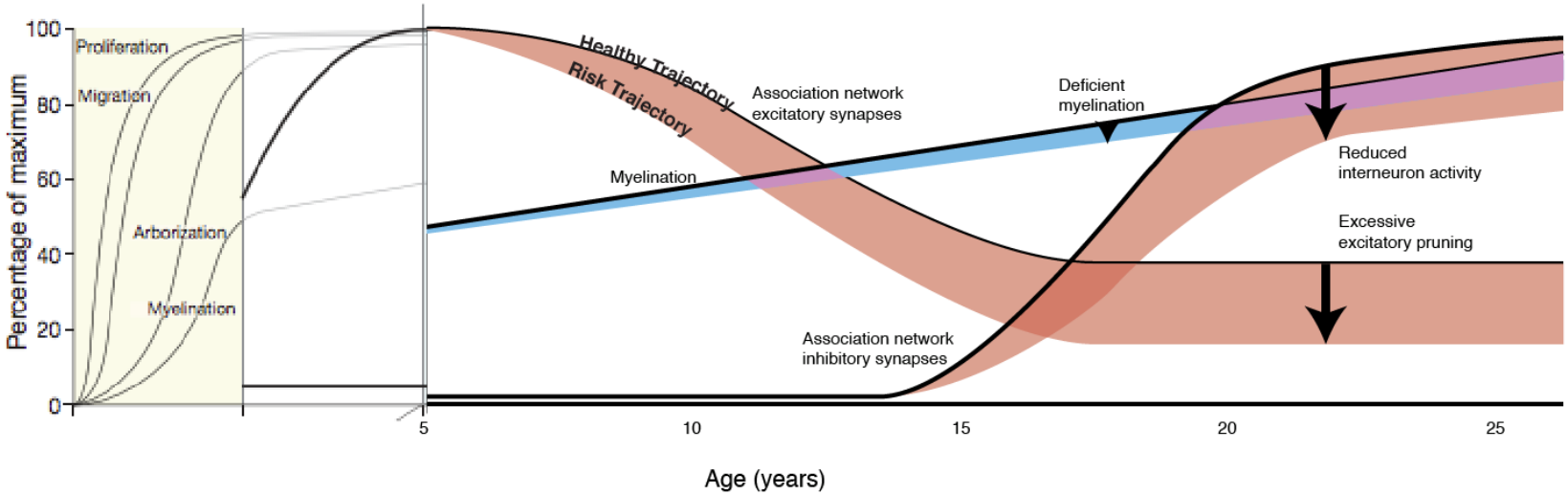
Latent Construct Models

Motors & Actu

Feedback

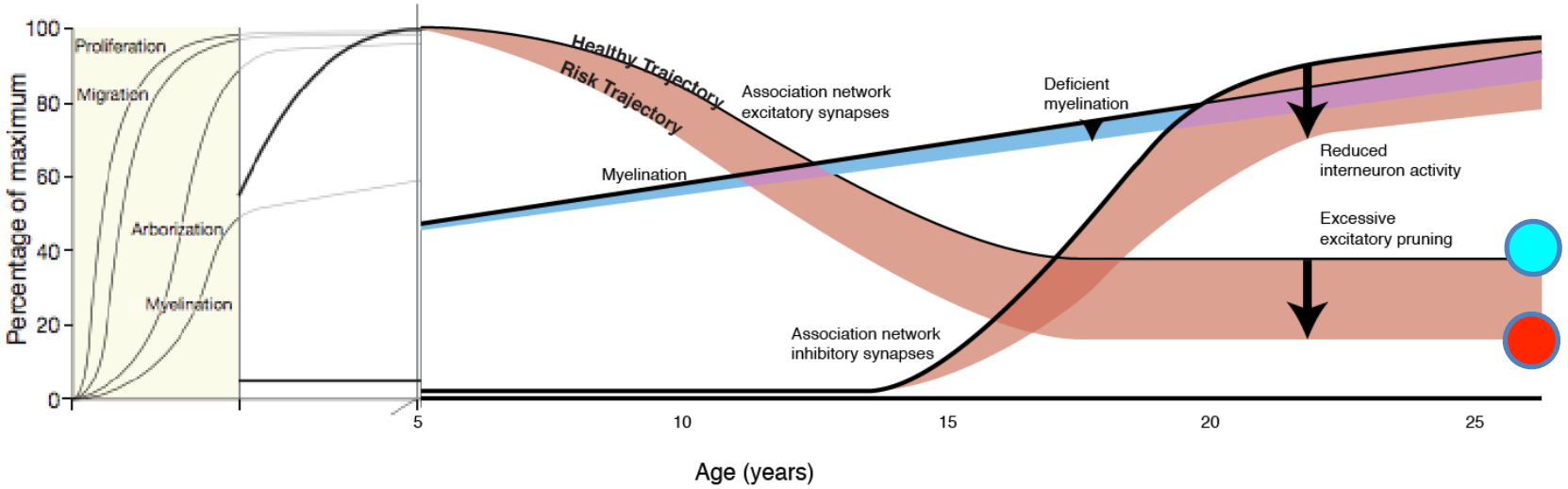

Syndromes
Signs & Symptoms
Brain Networks
Brain Structures
Circuits
Genes

# Development of Brain Risk States



Insel 2010

# Development of Brain Risk States

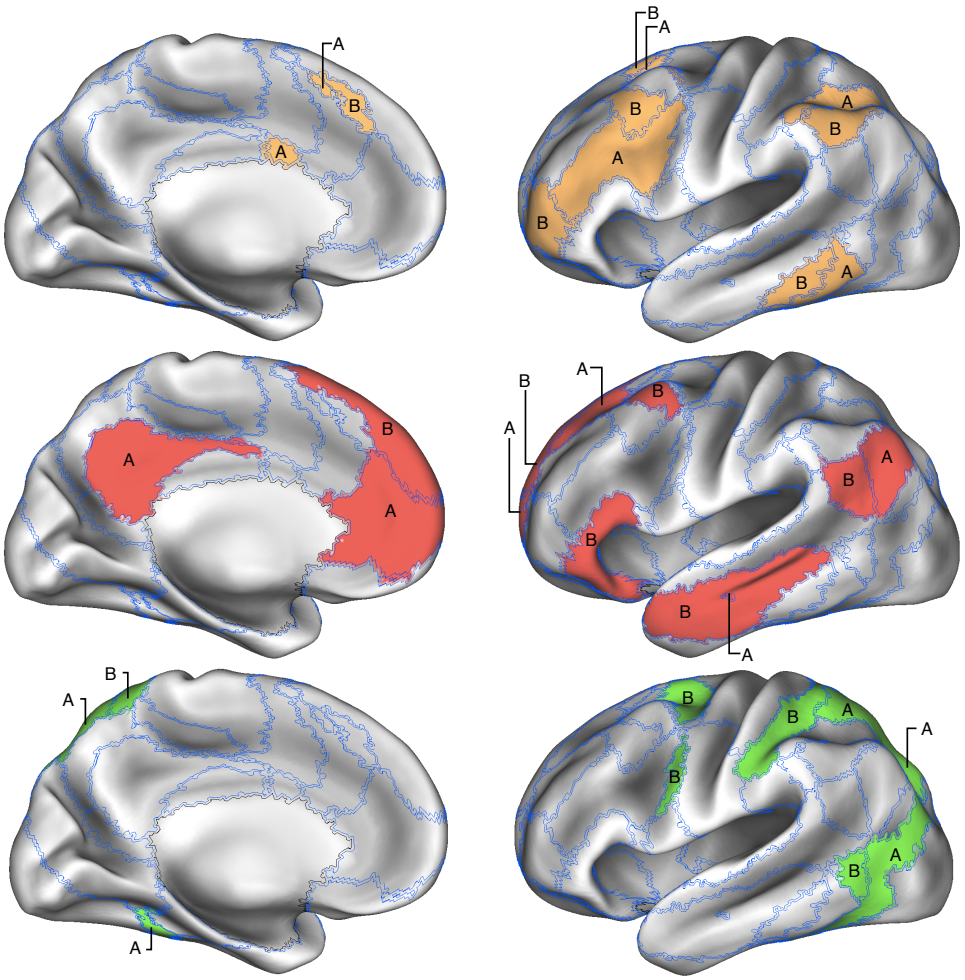



**Genetics, Neuroimaging, and Behavior**

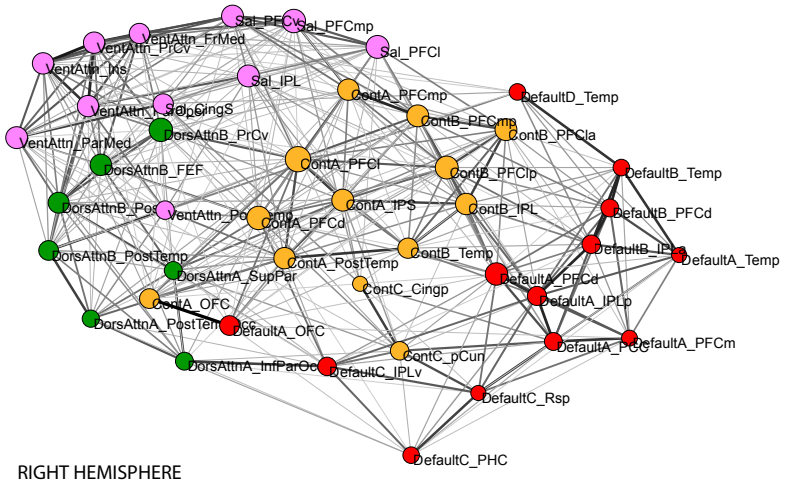
- >2500 Healthy Individuals
- >1000 Individuals with Psychotic Illness

  >250 with MRI

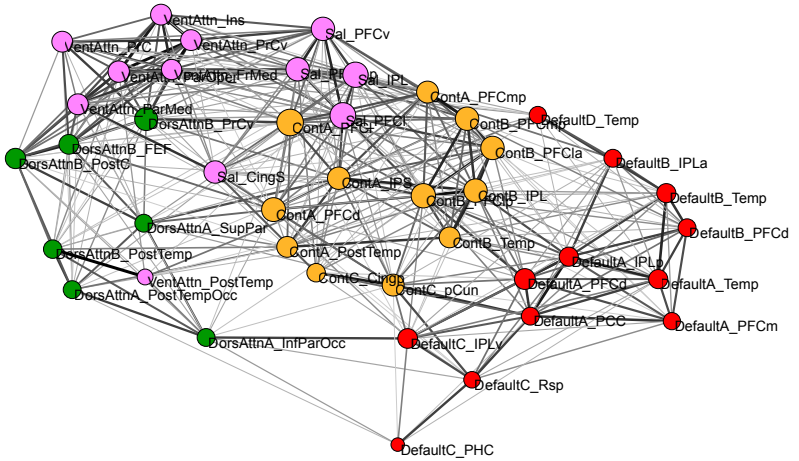
Insel 2010



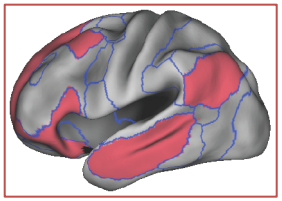

LEFT HEMISPHERE



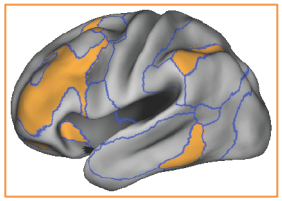

RIGHT HEMISPHERE



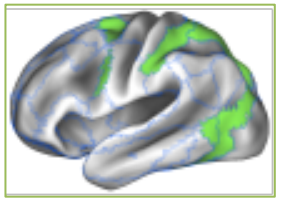
Default Network



Executive "Control"

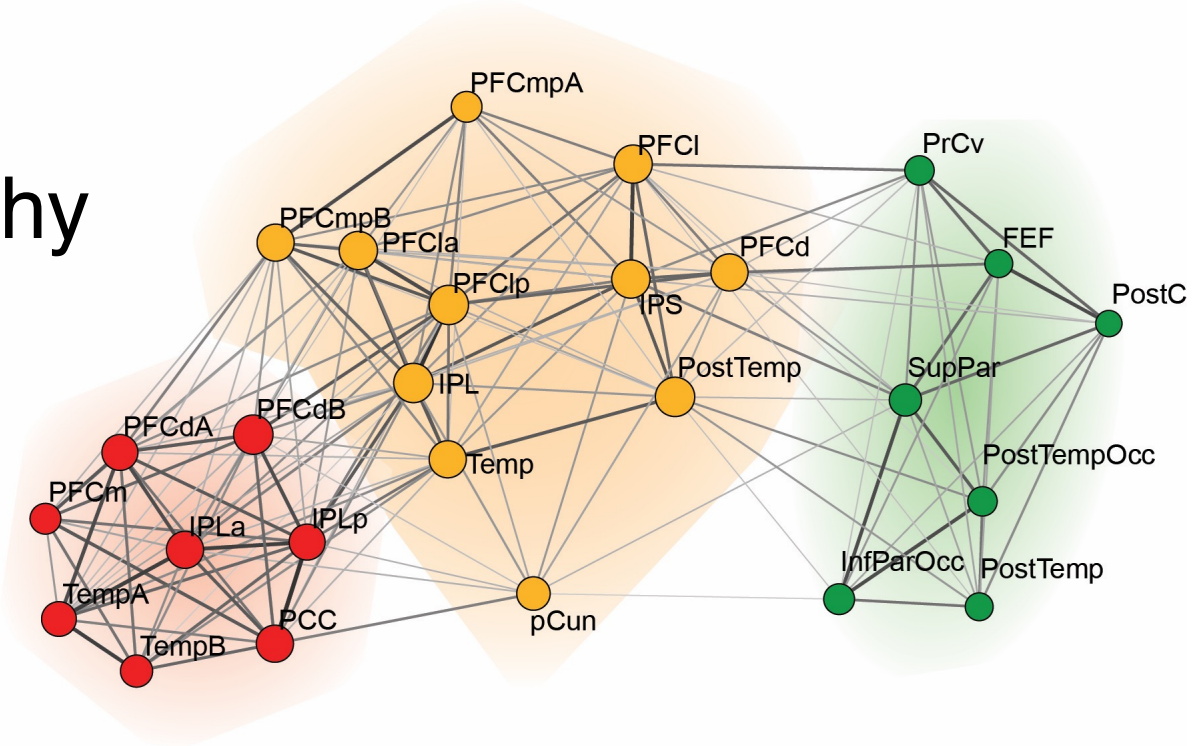


Attention Network



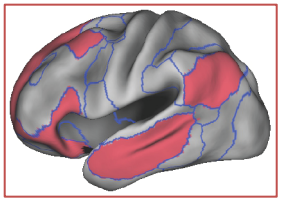
# Healthy

n=100

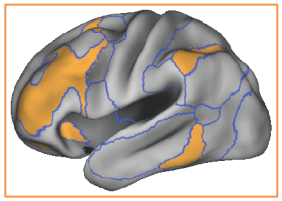



Baker et al. 2014, JAMA Psychiatry

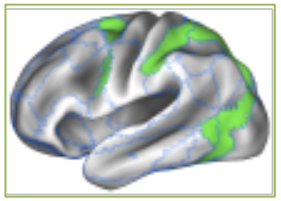
Default Network



Executive "Control"

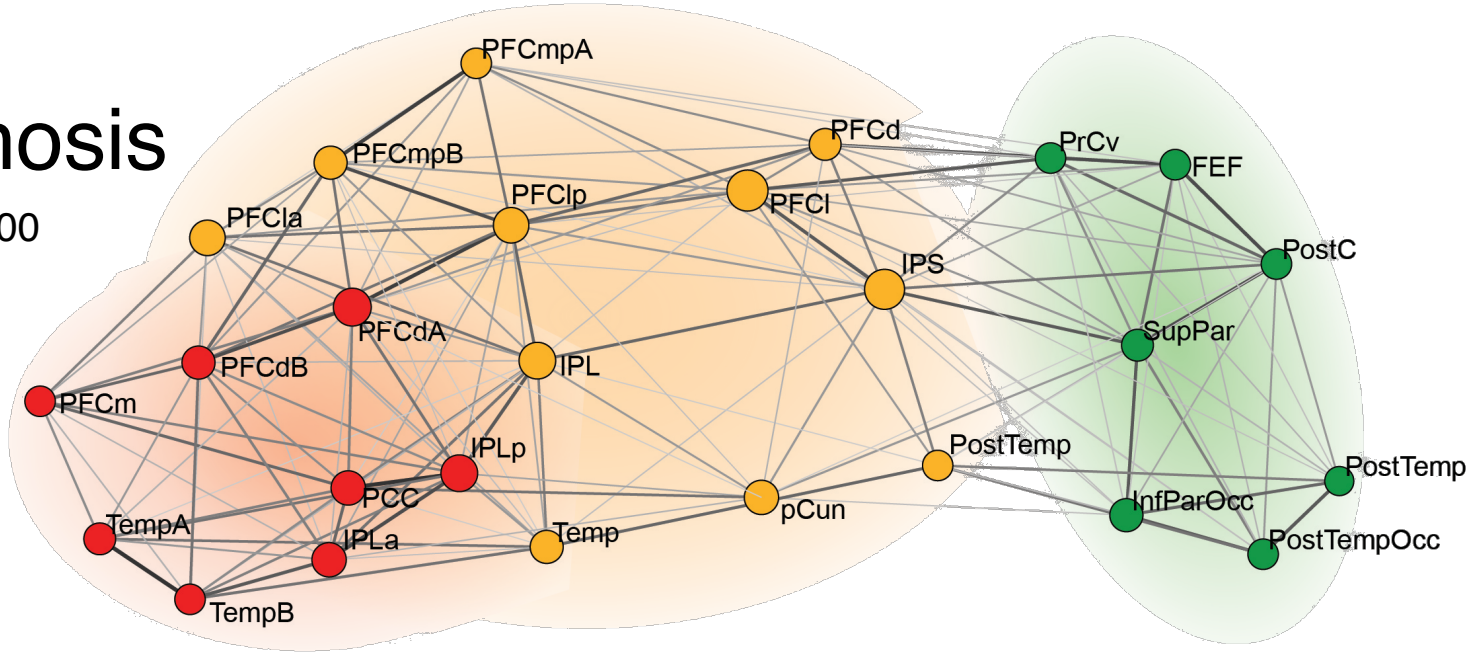


Attention Network



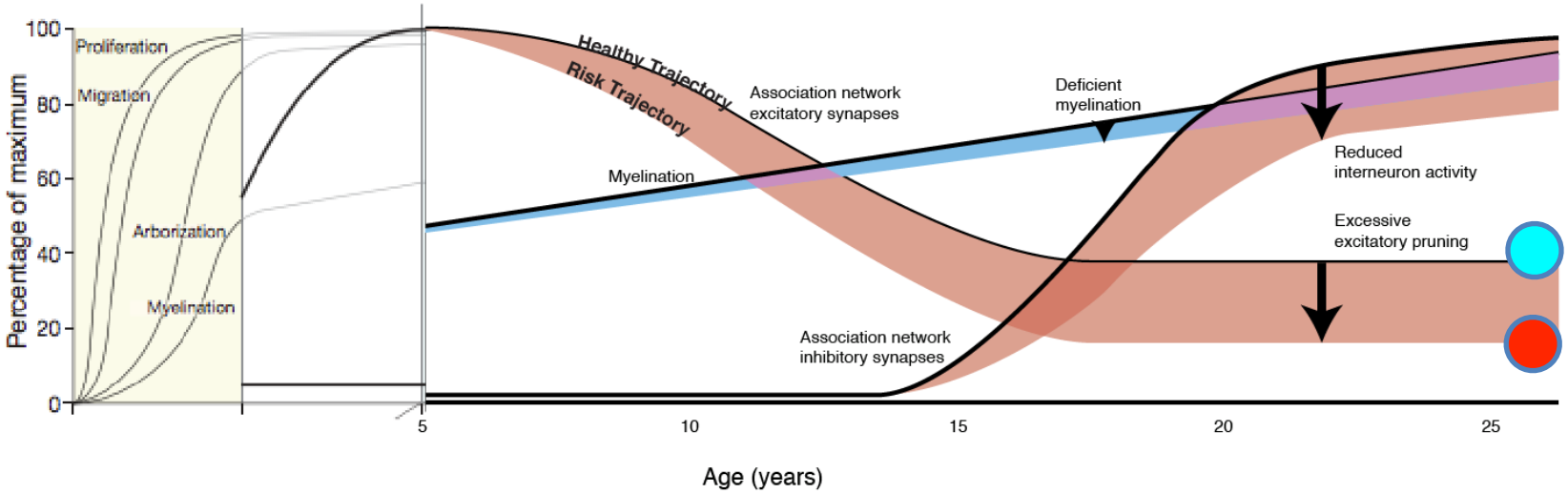
# Psychosis

n=100




Baker et al. 2014, JAMA Psychiatry

# Development of Brain Risk States




**Risk for Psychosis**

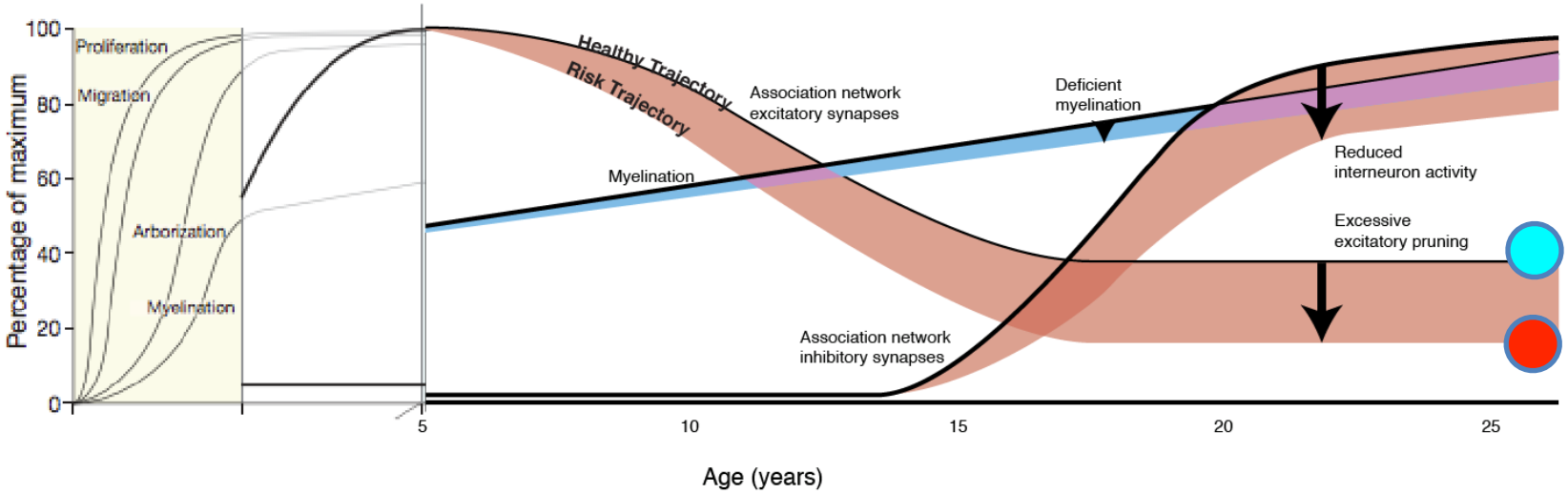
Polygenic Risk for SZ

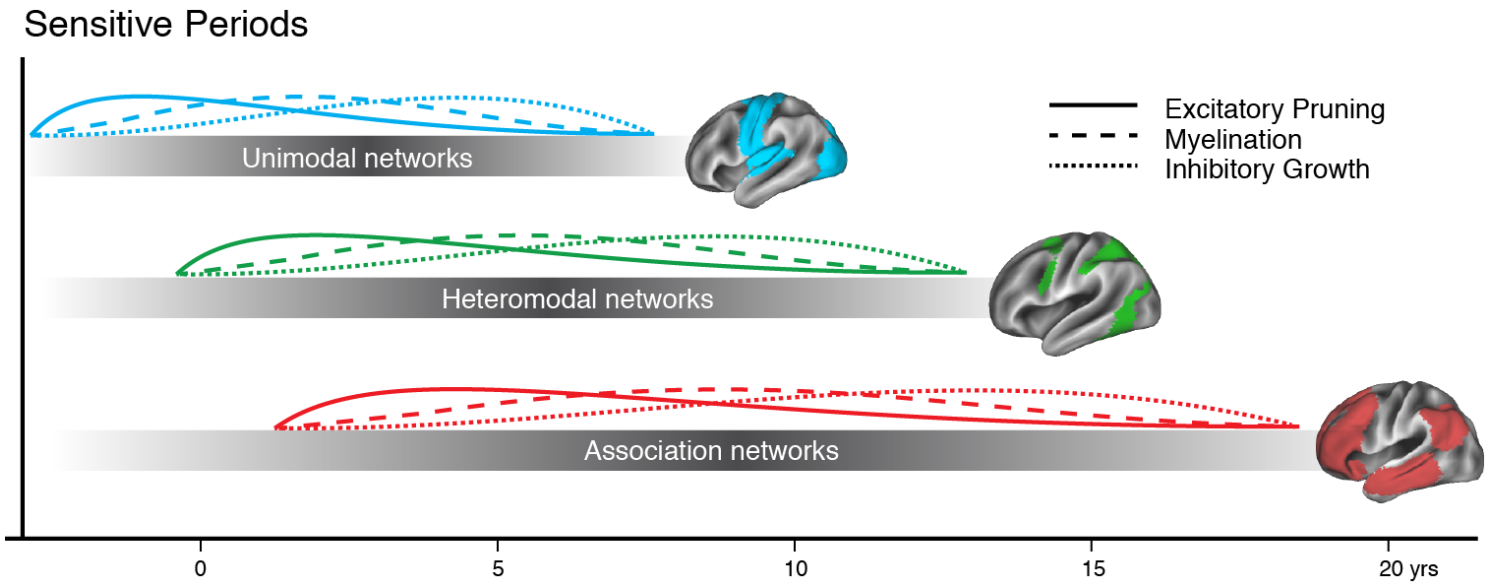
North-American Prodromal Longitudinal Sample (NAPLS)

McLean Early Psychosis Program

Insel 2010

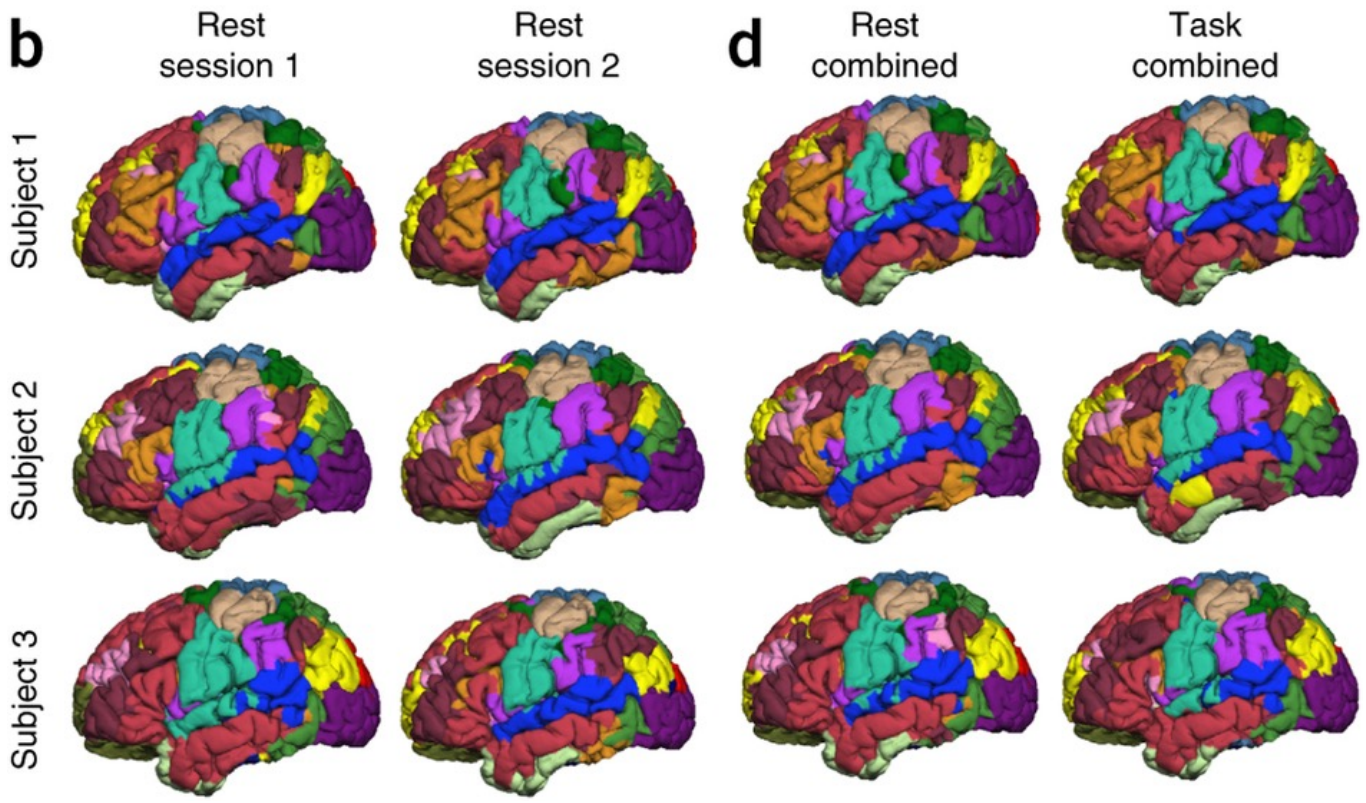
# Development of Brain Risk States

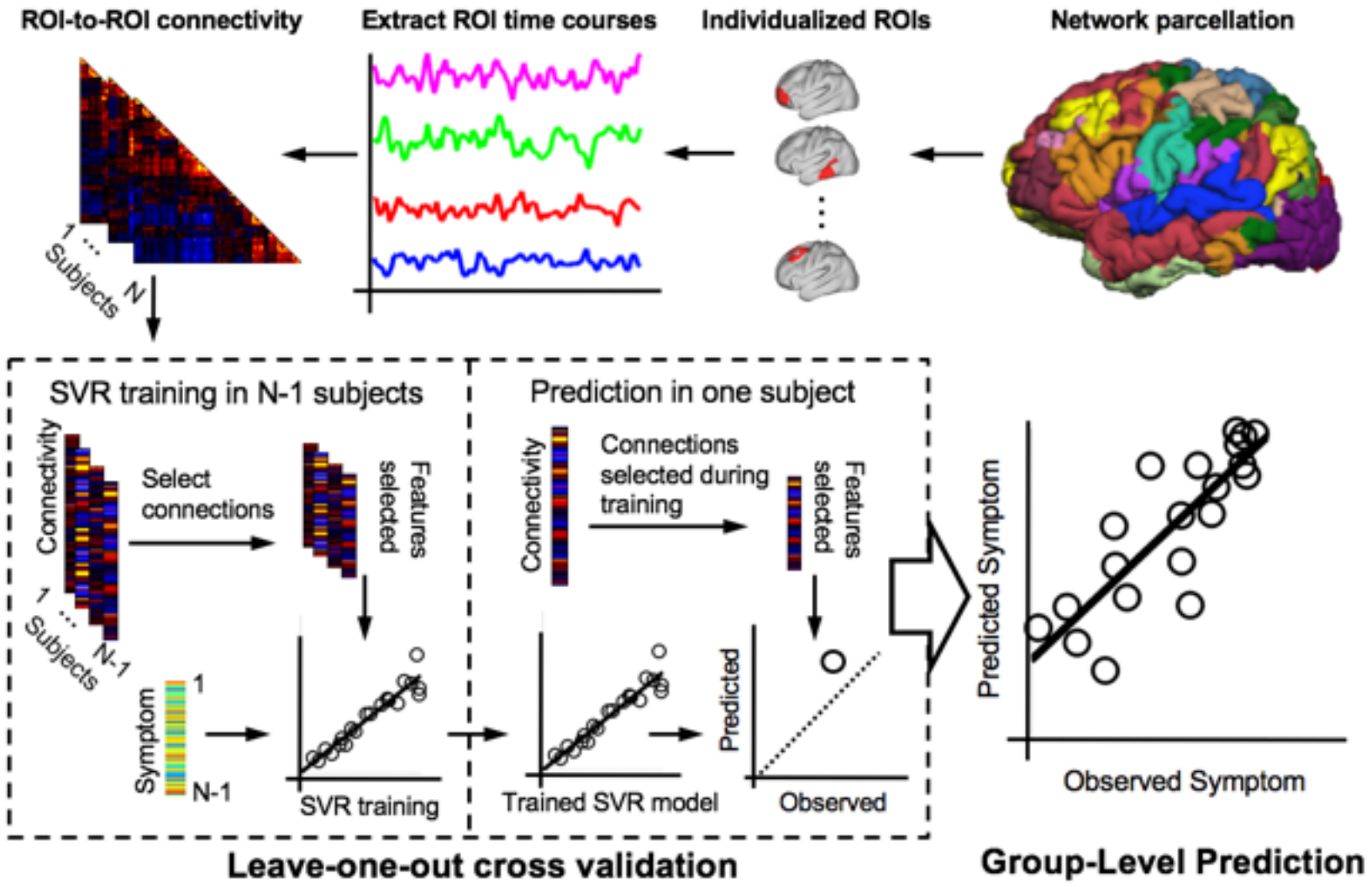


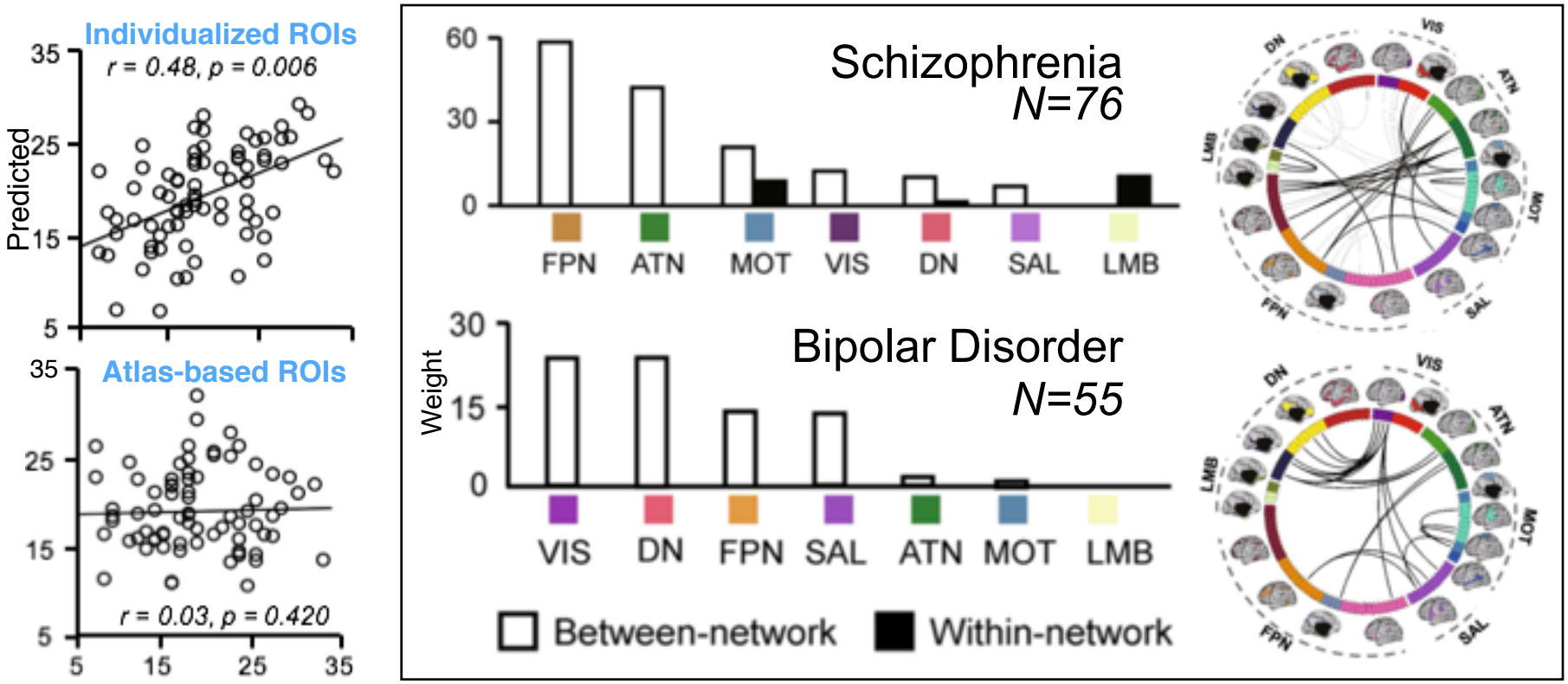

Insel 2010

# Individual Brains are Different






Wang et al., Molecular Psychiatry, 2019




Wang et al., Molecular Psychiatry, 2019

Sensor Networks

ure Extraction

onstruct Models

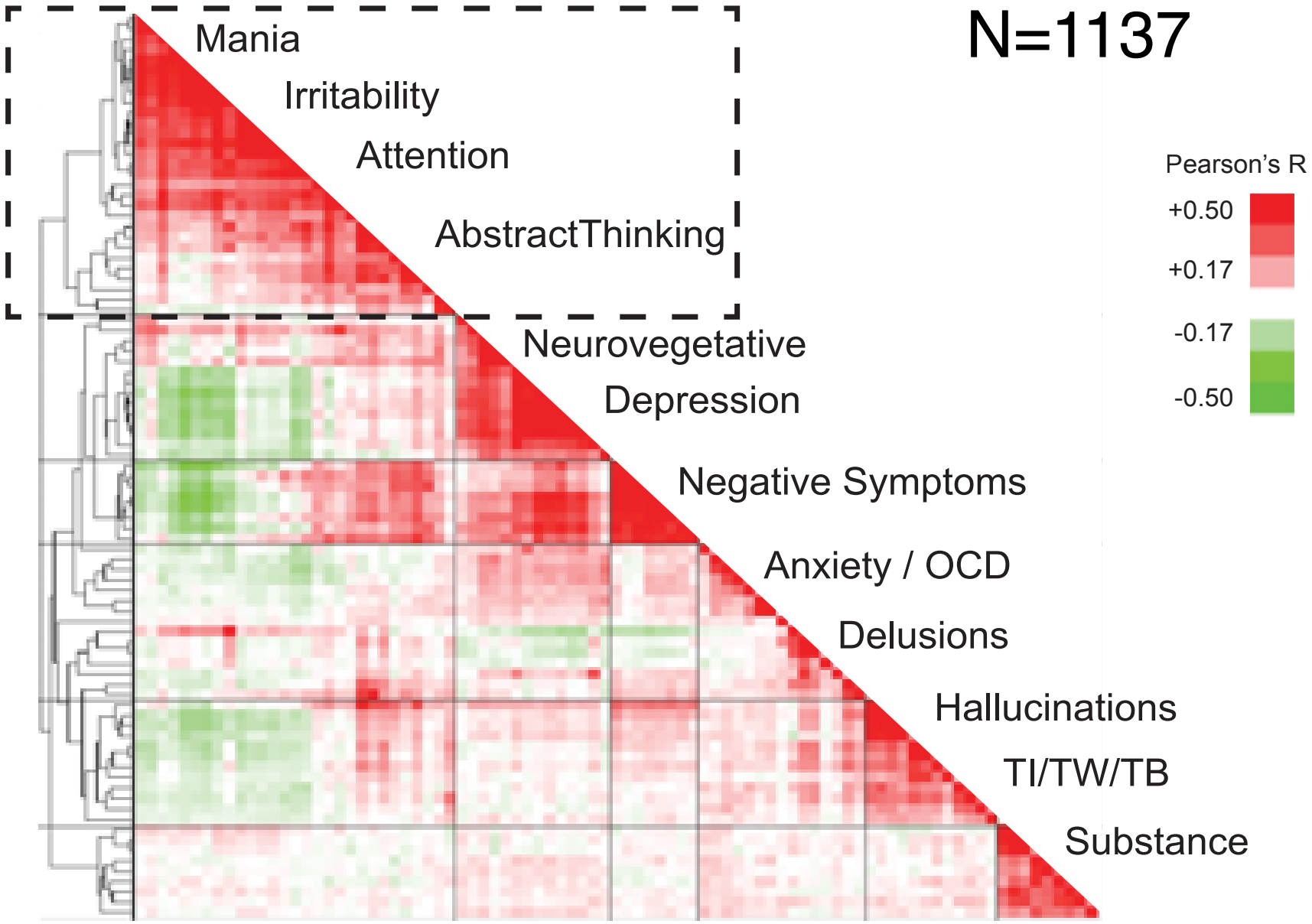
Motors & Actu

Feedback

# Behavioral Assessment is Challenging and Human Resource Intensive

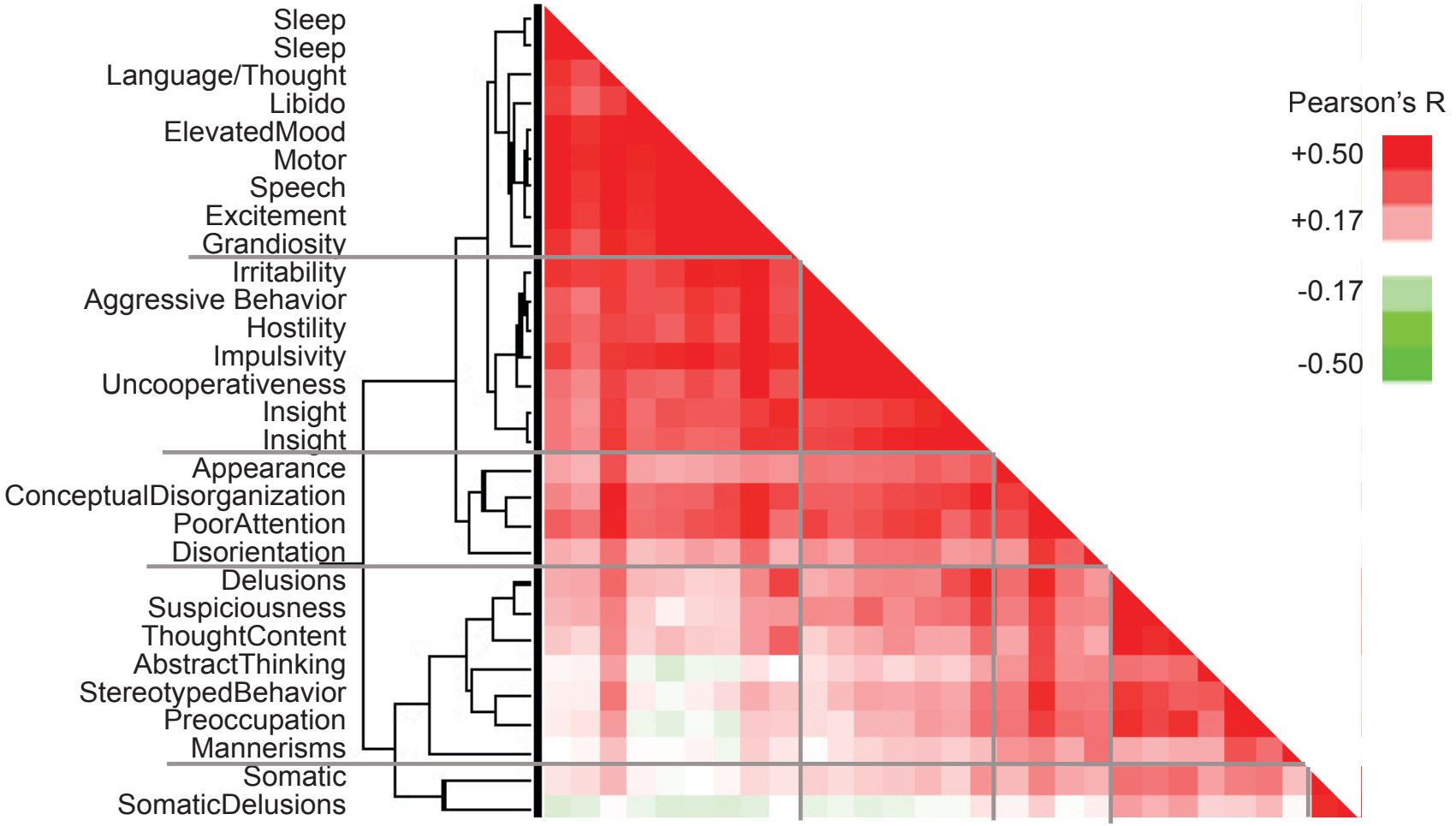
- Training can take months (~30 hours training, often spread out over several weeks)
- Administration and scoring takes 3-4 hours per participant.
- Highly Subjective
- Poor inter-temporal, inter-rater reliability

# Covariance of Item-level Symptom Reports



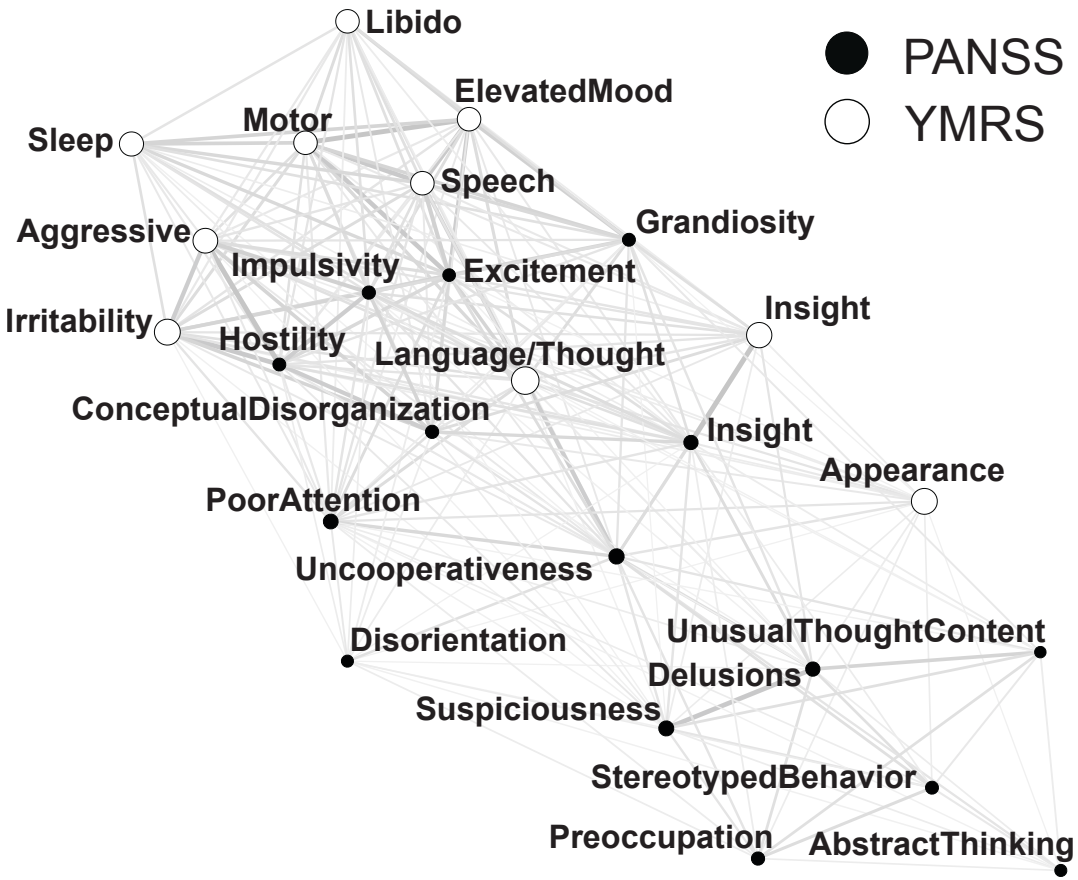
# Covariance of Item-level Symptom Reports

N=1137

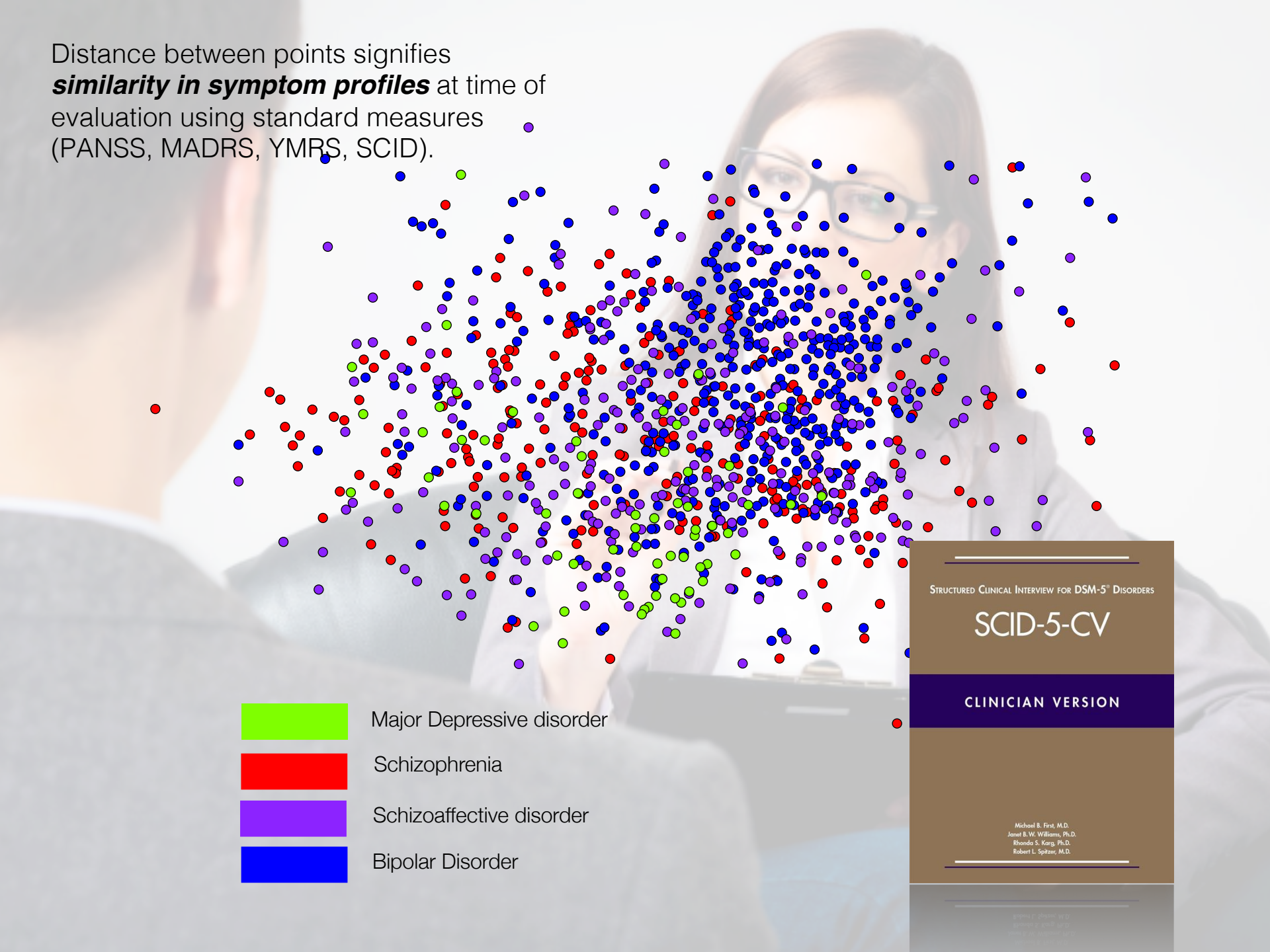


# Covariance of Item-level Symptom Reports

N=1137



Distance between points signifies ***similarity in symptom profiles*** at time of evaluation using standard measures (PANSS, MADRS, YMRS, SCID).



# Capturing **Real World Heterogeneity**

## Phenomics: the next challenge

*David Houle*, Diddahally R. Govindaraju‡ and Stig Omholt§||*

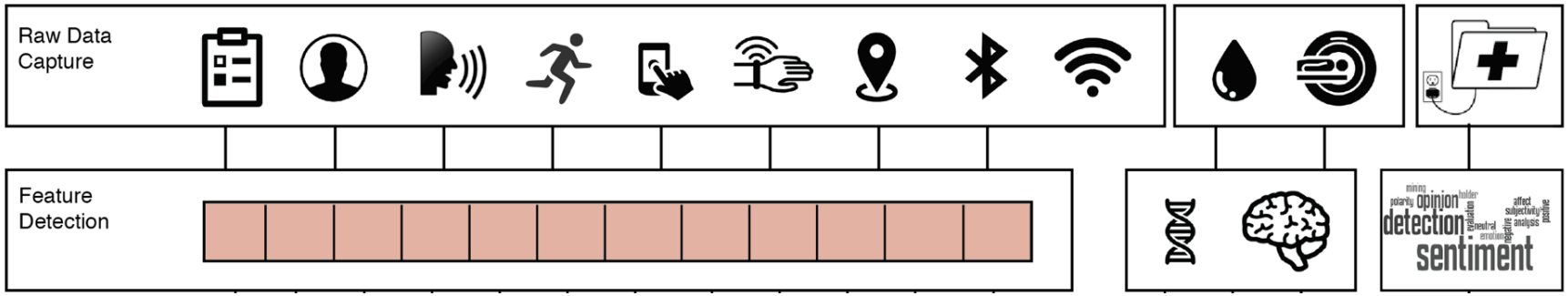
Abstract | A key goal of biology is to understand phenotypic characteristics, such as health, disease and evolutionary fitness. Phenotypic variation is produced through a complex web of interactions between genotype and environment, and such a 'genotype–phenotype' map is inaccessible without the detailed phenotypic data that allow these interactions to be studied. Despite this need, our ability to characterize phenomes — the full set of phenotypes of an individual — lags behind our ability to characterize genomes. Phenomics should be recognized and pursued as an independent discipline to enable the development and adoption of high-throughput and high-dimensional phenotyping.

Our illnesses have huge heterogeneity in presentation, which could obscure differences in biology based on group comparisons.

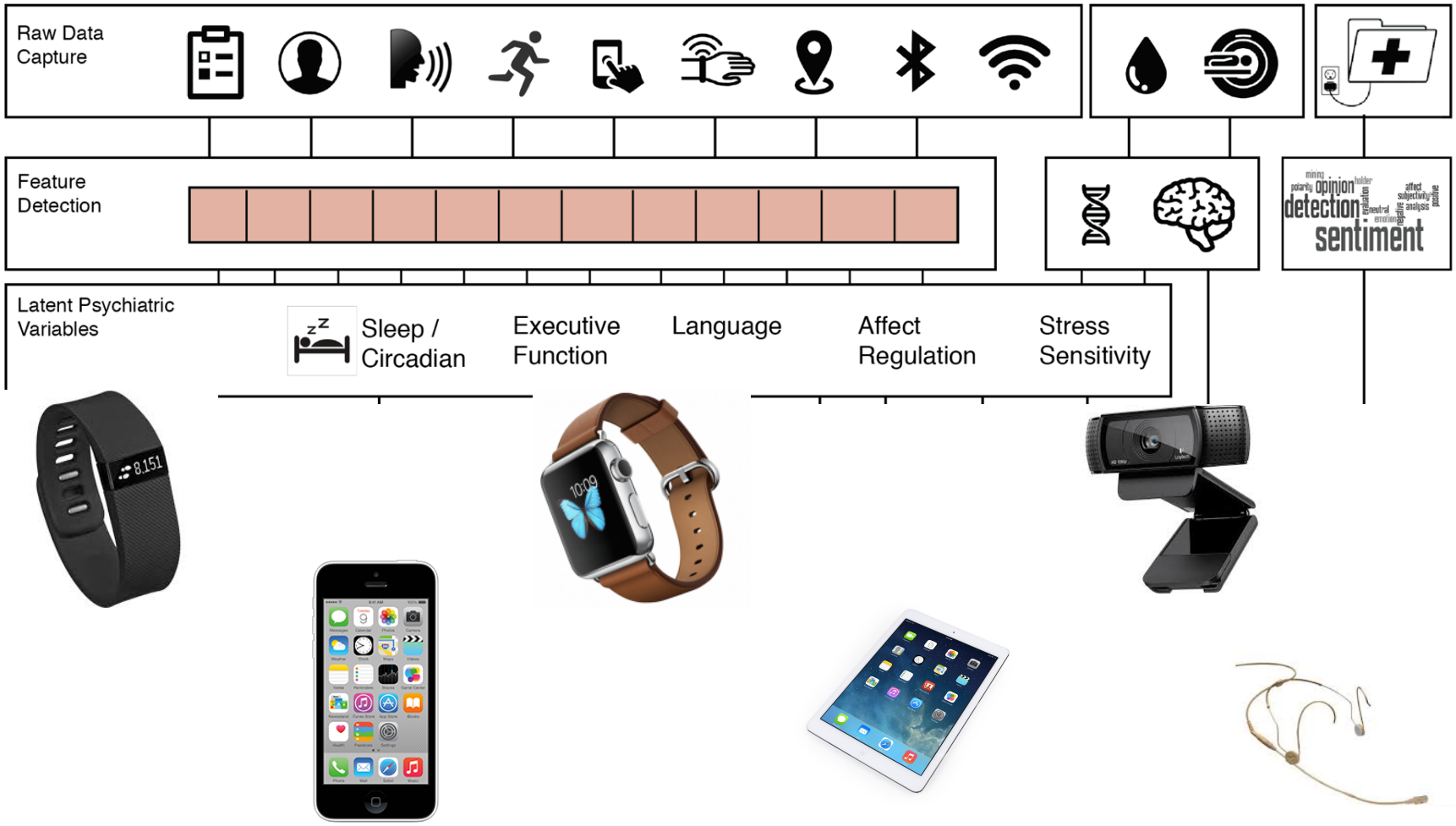
Unless we are capturing this heterogeneity accurately, scale will not help.

# Latent Variable Approach to Psychiatric Construct Definition

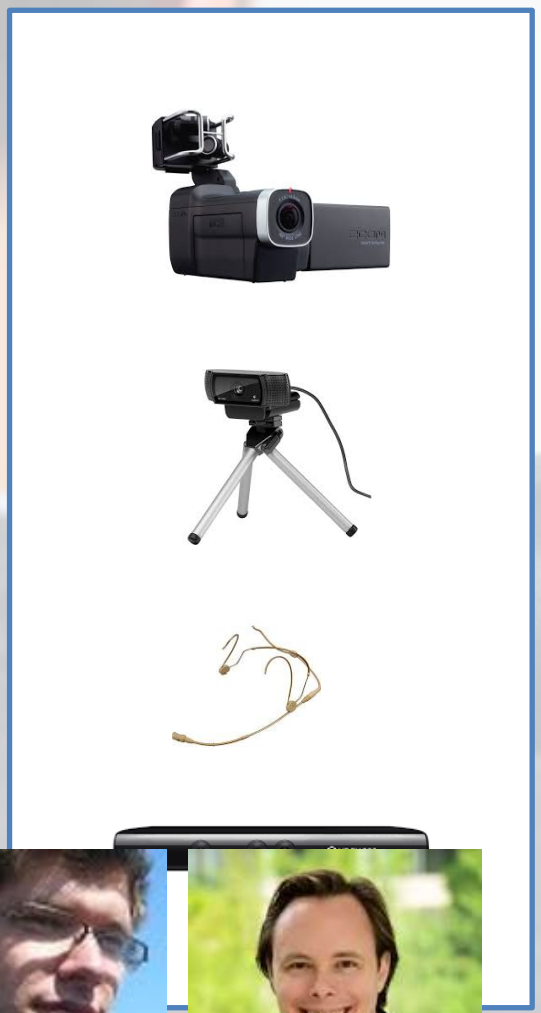
# Latent Variable Approach to Psychiatric Construct Definition

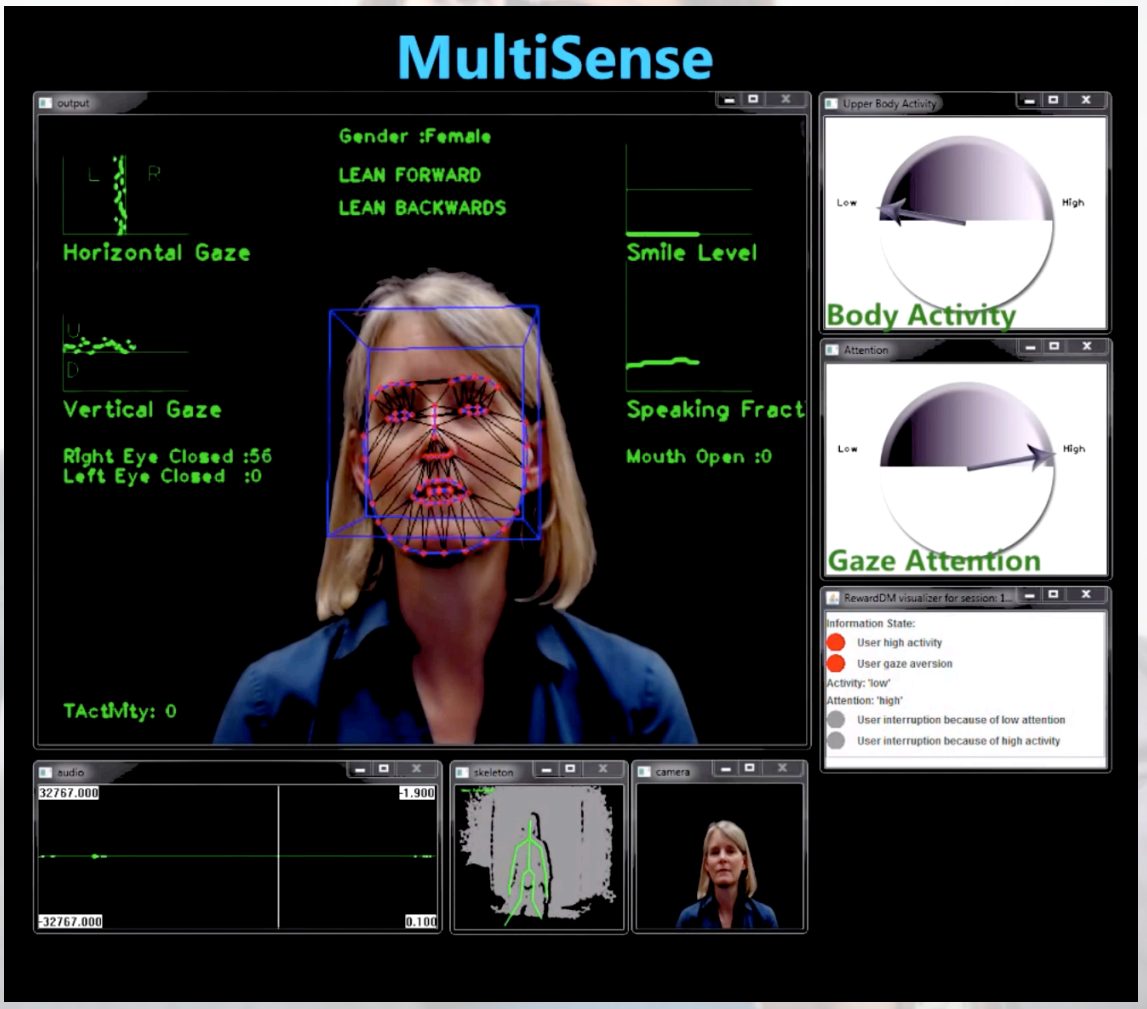


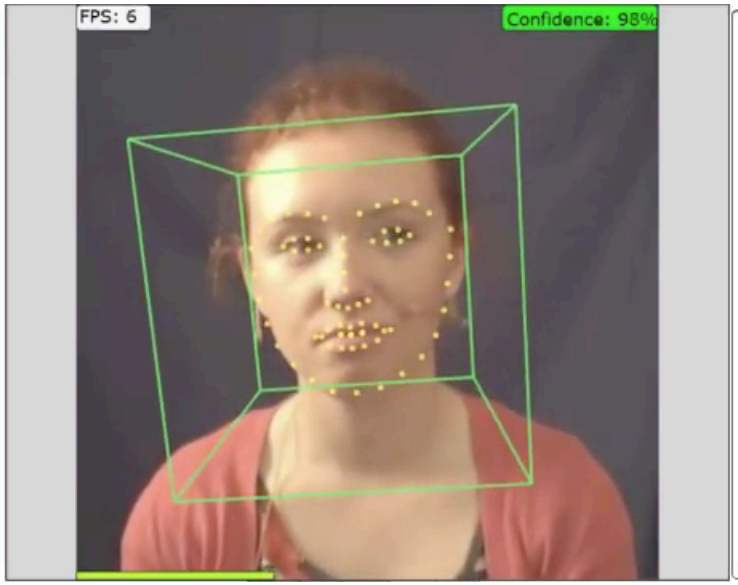
# Latent Variable Approach to Psychiatric Construct Definition

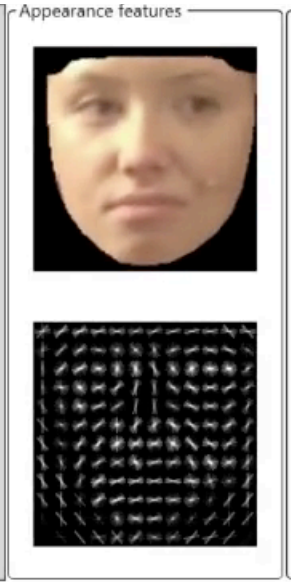


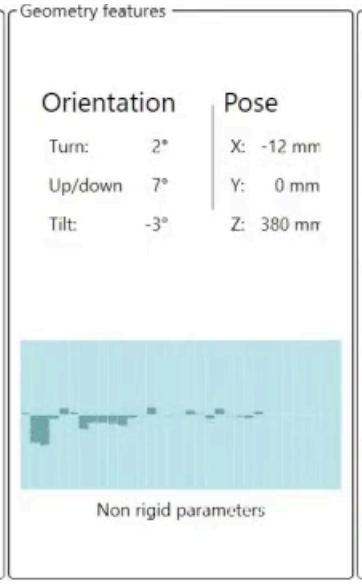
XBOX 360

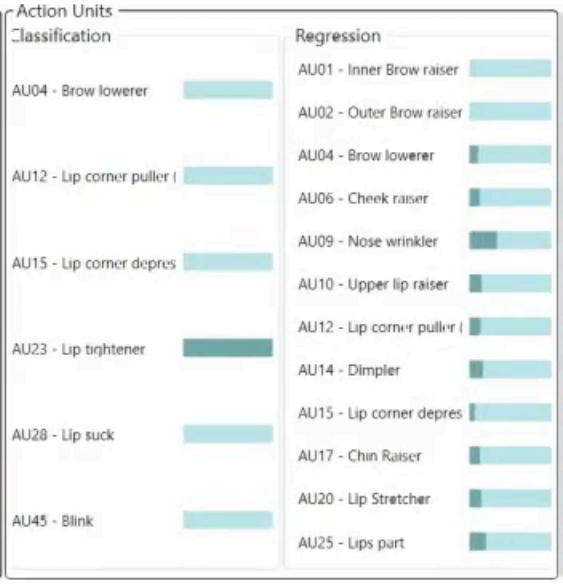


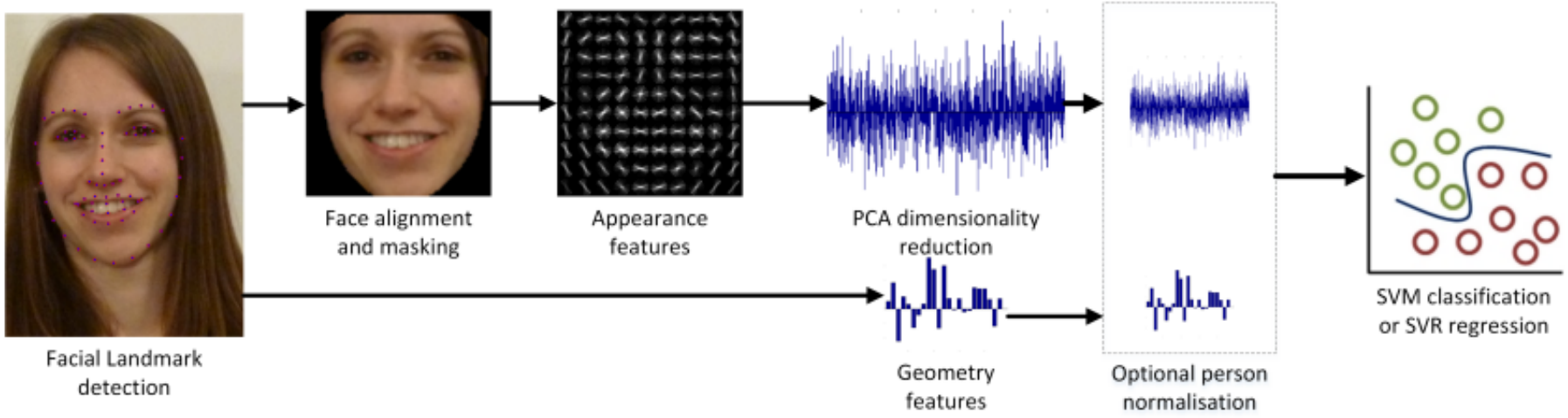

MultiSense
output
Gender :Female
LEAN FORWARD
LEAN BACKWARDS
Horizontal Gaze
Vertical Gaze
Right Eye Closed :56
Left Eye Closed :0
Smile Level
Speaking Fract
Mouth Open :0
TActMty: 0
Upper Body Activity
Low
High
Body Activity
Attention
Low
High
Gaze Attention
RewardDM visualizer for session: 1...
Information State:
User high activity
User gaze aversion
Activity: 'low'
Attention: 'high'
User interruption because of low attention
User interruption because of high activity
audio
32767.000
-1.900
-32767.000
0.100
skeleton
camera

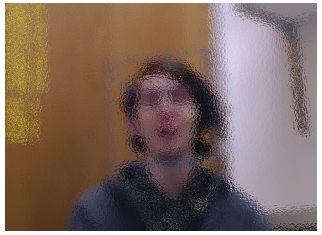

FPS: 6
Confidence: 98%


Appearance features

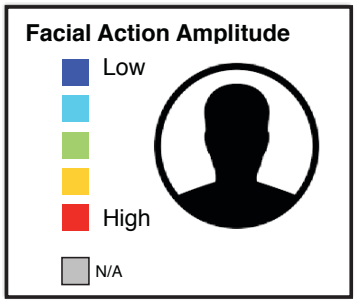

Geometry features
Orientation
Turn: 2°
Up/down 7°
Tilt: -3°
Pose
X: -12 mm
Y: 0 mm
Z: 380 mm
Non rigid parameters

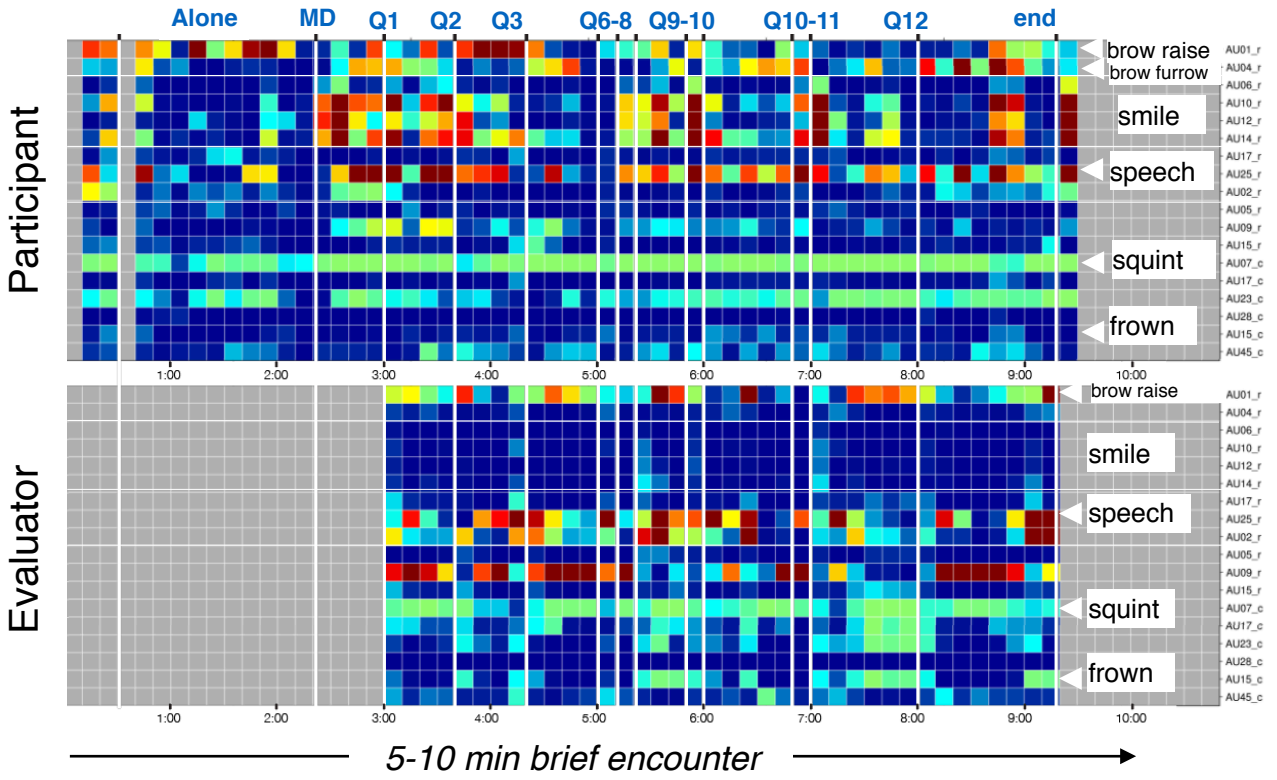

Action Units
Classification
AU04 - Brow lowerer
AU12 - Lip corner puller
AU15 - Lip corner depres
AU23 - Lip tightener
AU28 - Lip suck
AU45 - Blink
Regression
AU01 - Inner Brow raiser
AU02 - Outer Brow raiser
AU04 - Brow lowerer
AU06 - Cheek raiser
AU09 - Nose wrinkler
AU10 - Upper lip raiser
AU12 - Lip corner puller
AU14 - Dimpler
AU15 - Lip corner depres
AU17 - Chin Raiser
AU20 - Lip Stretcher
AU25 - Lips part


Facial Landmark detection
Face alignment and masking
Appearance features
PCA dimensionality reduction
Geometry features
Optional person normalisation
SVM classification or SVR regression



**Q1** What brought you into the hospital?
**Q2** Has anything in particular been on your mind recently?
**Q5** What are you 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?



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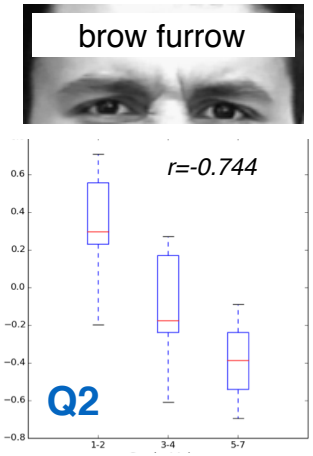
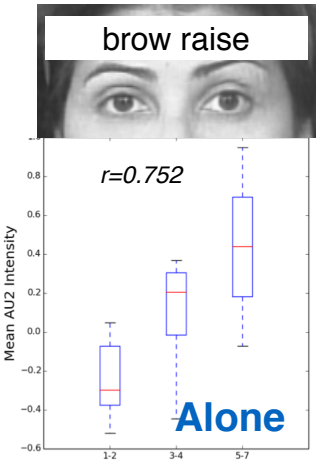
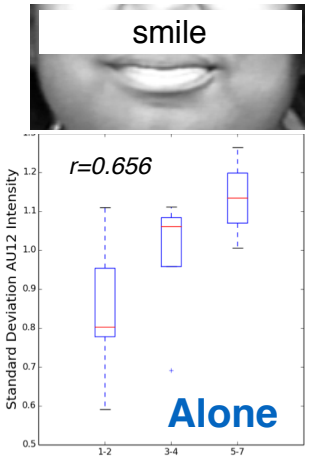
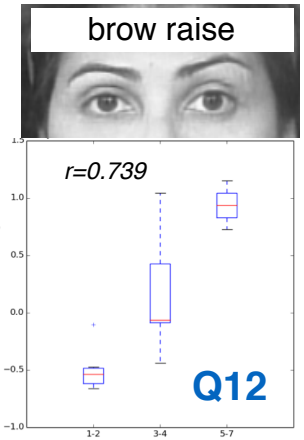



Depression (BPRS)

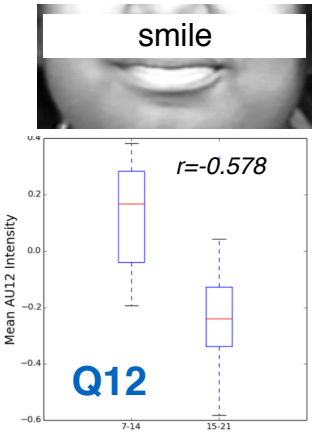


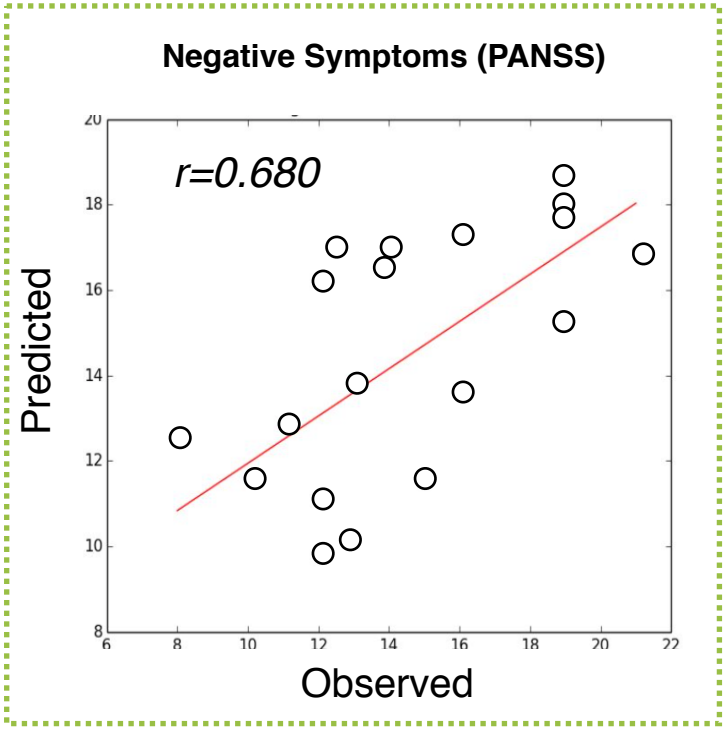

Unusual Thought Content (PANSS)



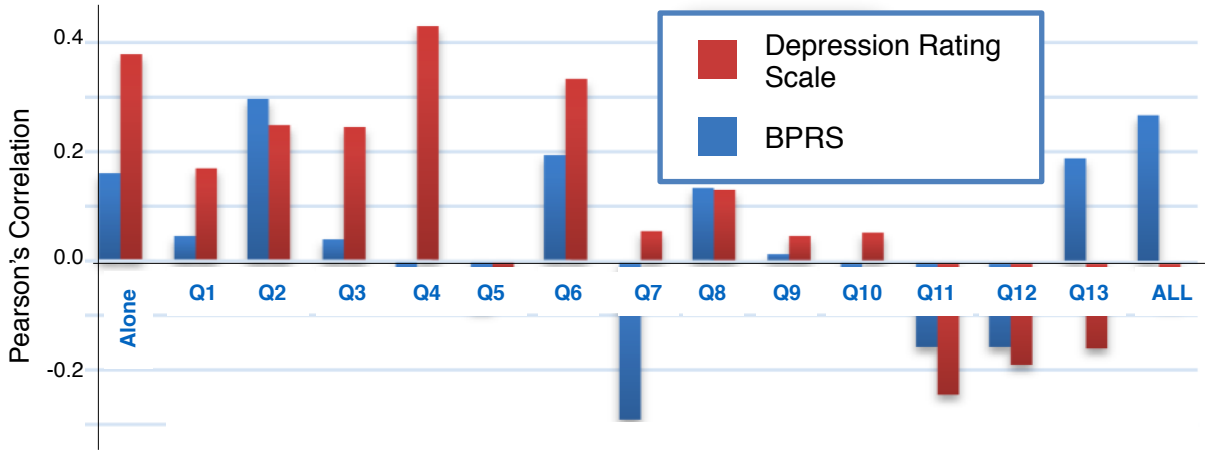

Delusions (PANSS)

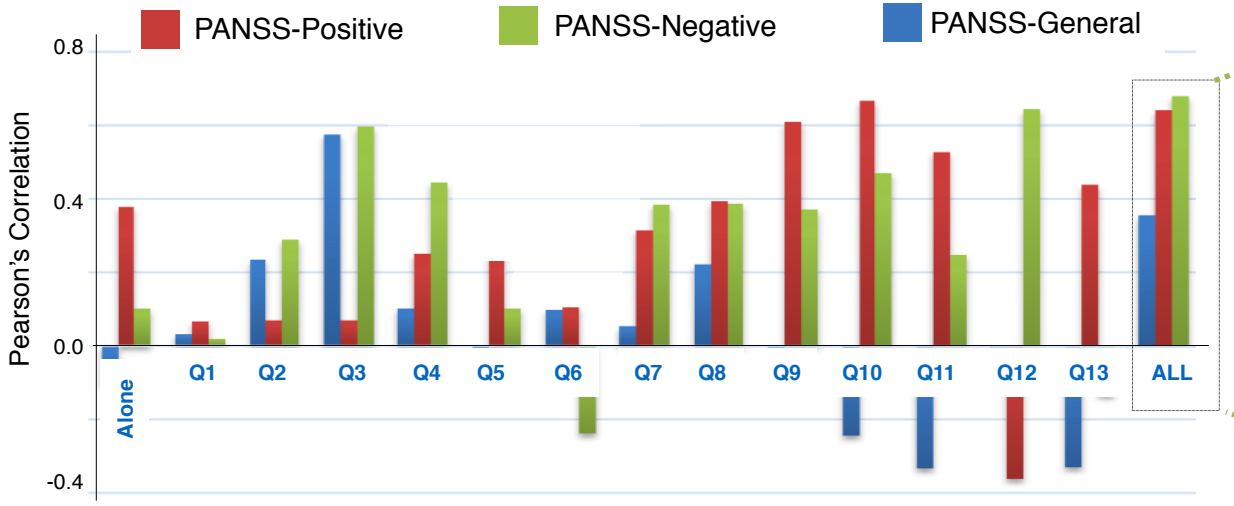


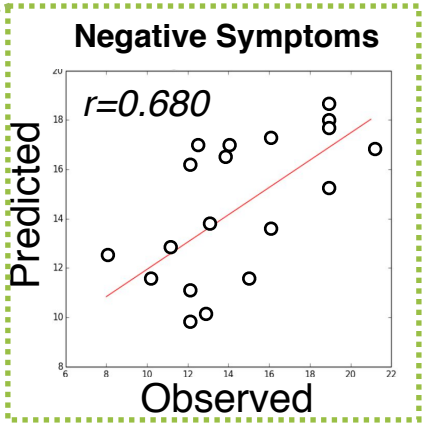

Negative Sxs (PANSS)



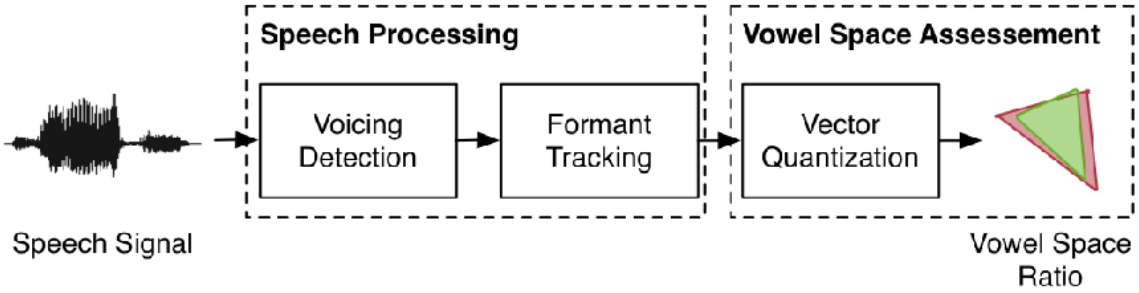
Q1 What brought you into the hospital?
Q2 Has anything in particular been on your mind recently?
Q5 What are you goals for this hospitalization?
Q6 How are people treating you here?
Q7 How's the food been?
Q8 How's your mood?
Q9 How's your thinking?
Q10 How's your energy?
Q11 How many hours have you slept?
Q12 How's your self-confidence now compared to usual for you?

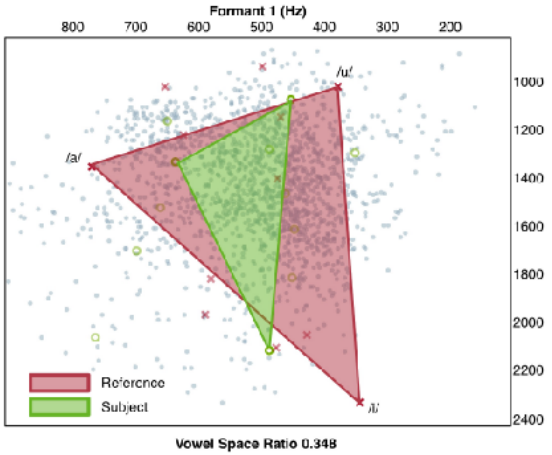


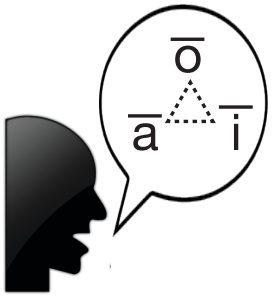



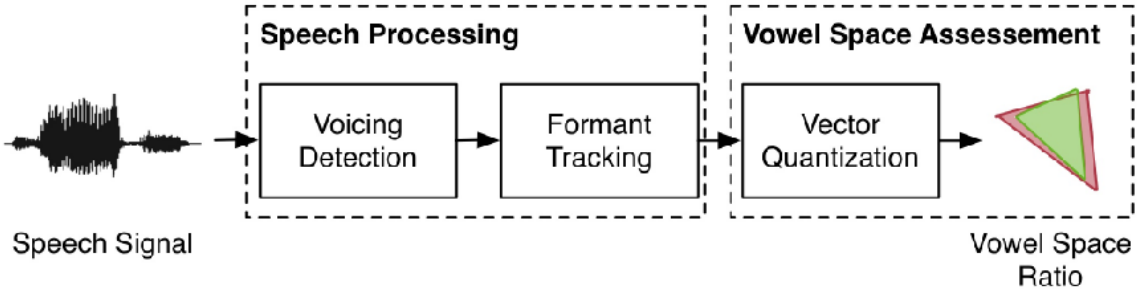
# Voice as a psychiatric VS?

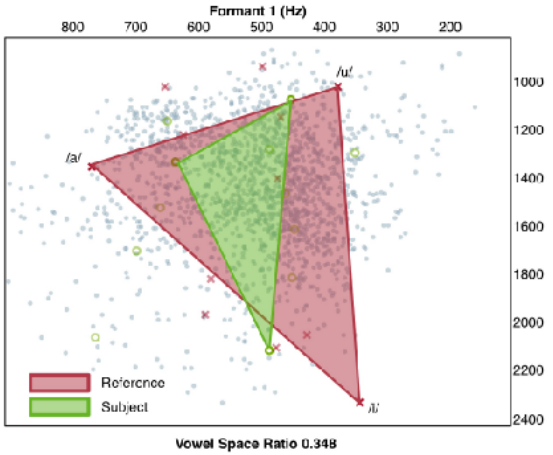


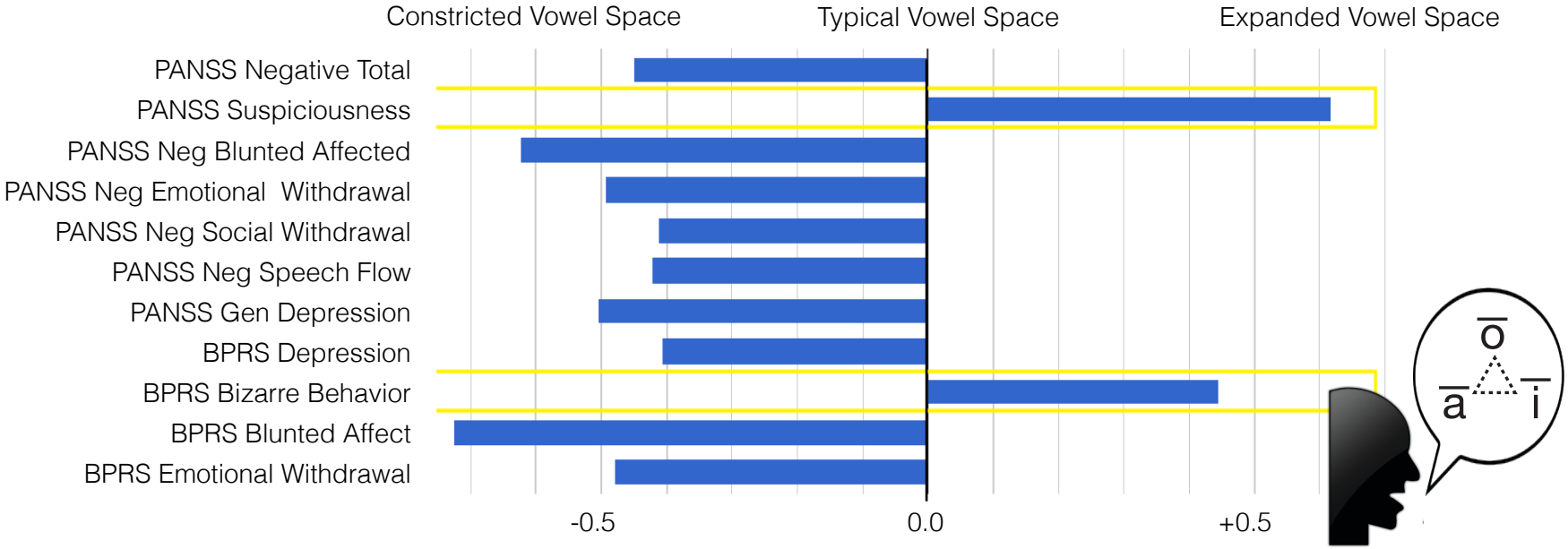



# Voice as a psychiatric VS?

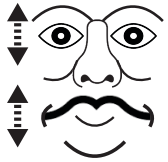


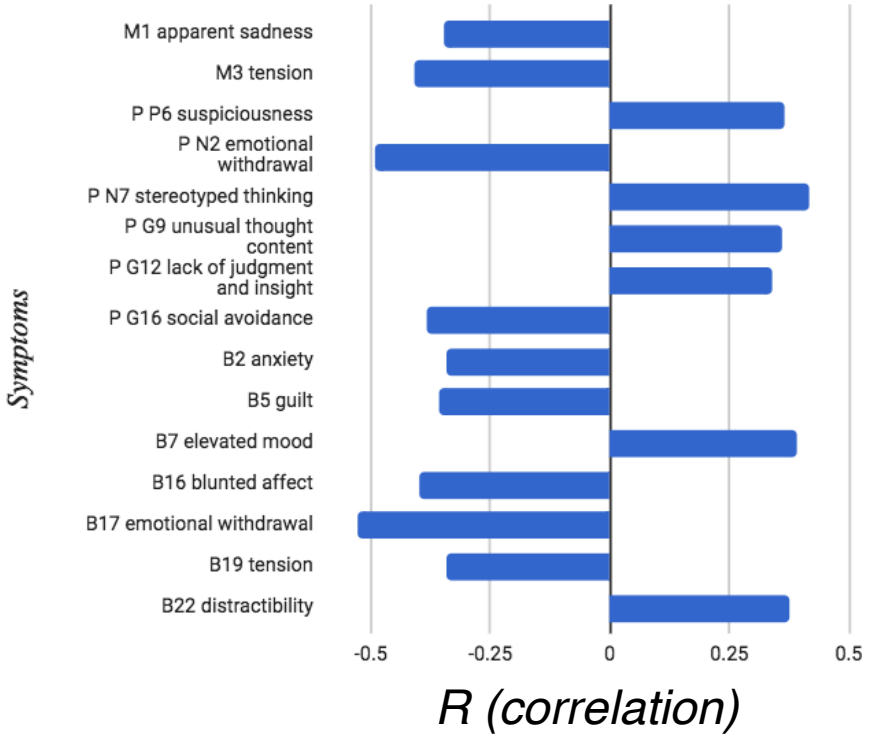



# Expressivity as a psychiatric VS?

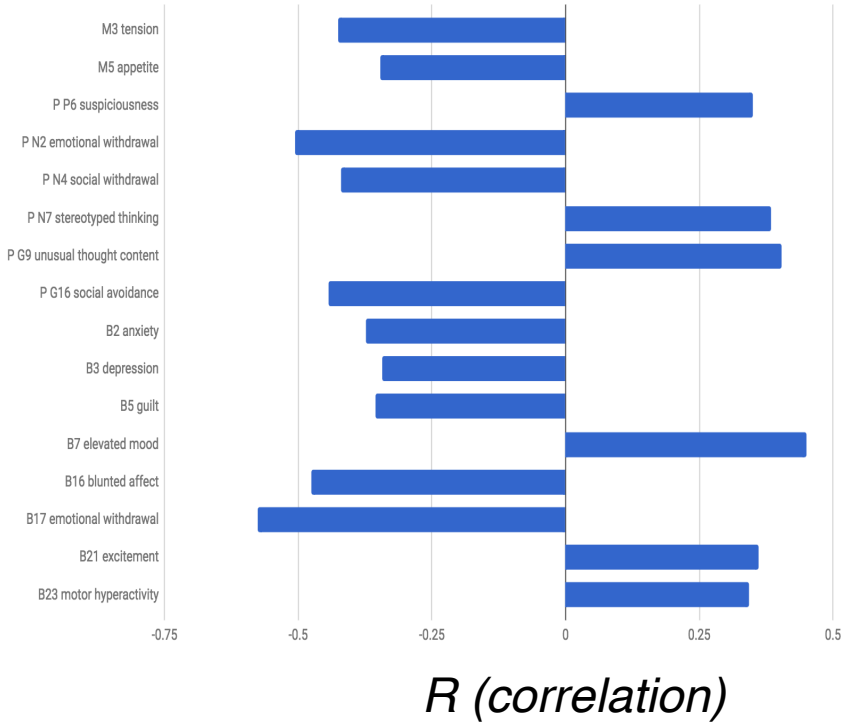
Item-level Symptom Severity with Facial Expressivity



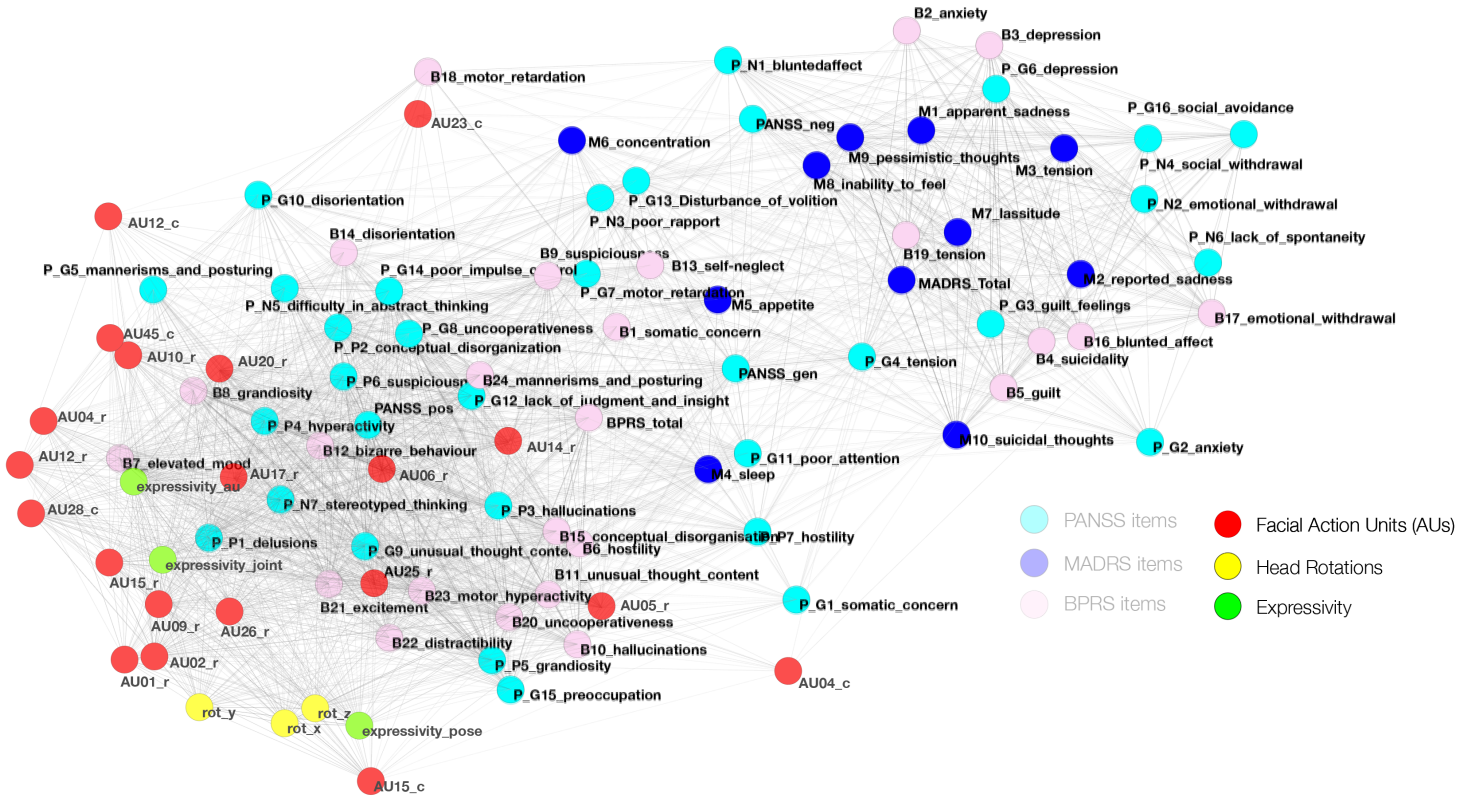
## Alone Time



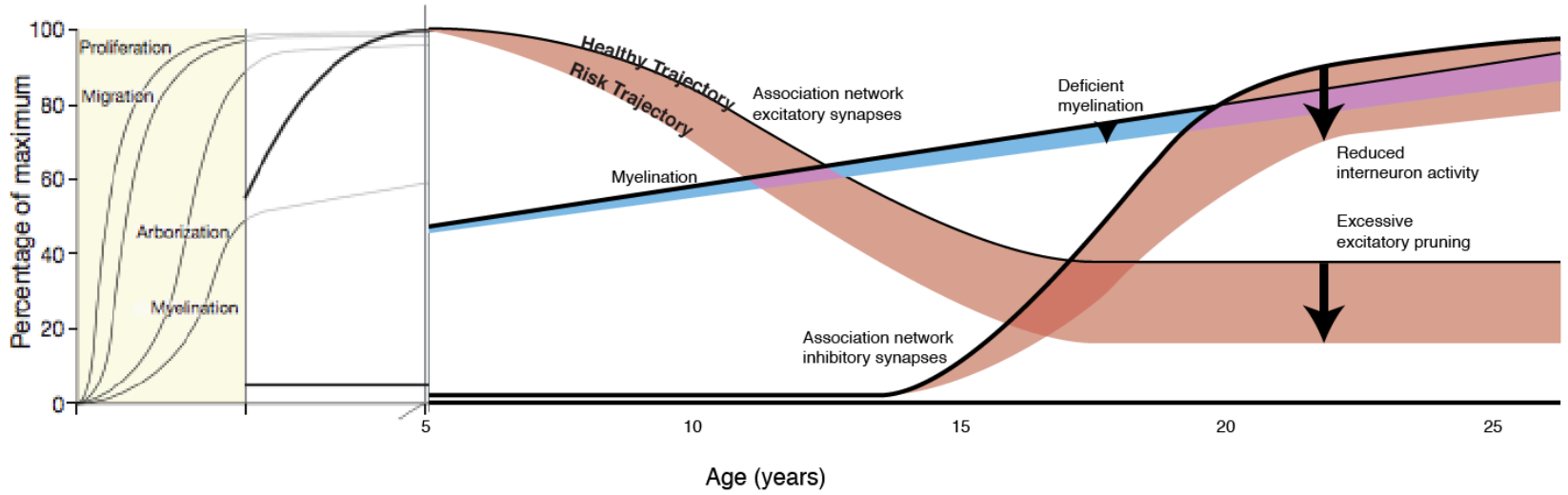

## Entire Interview

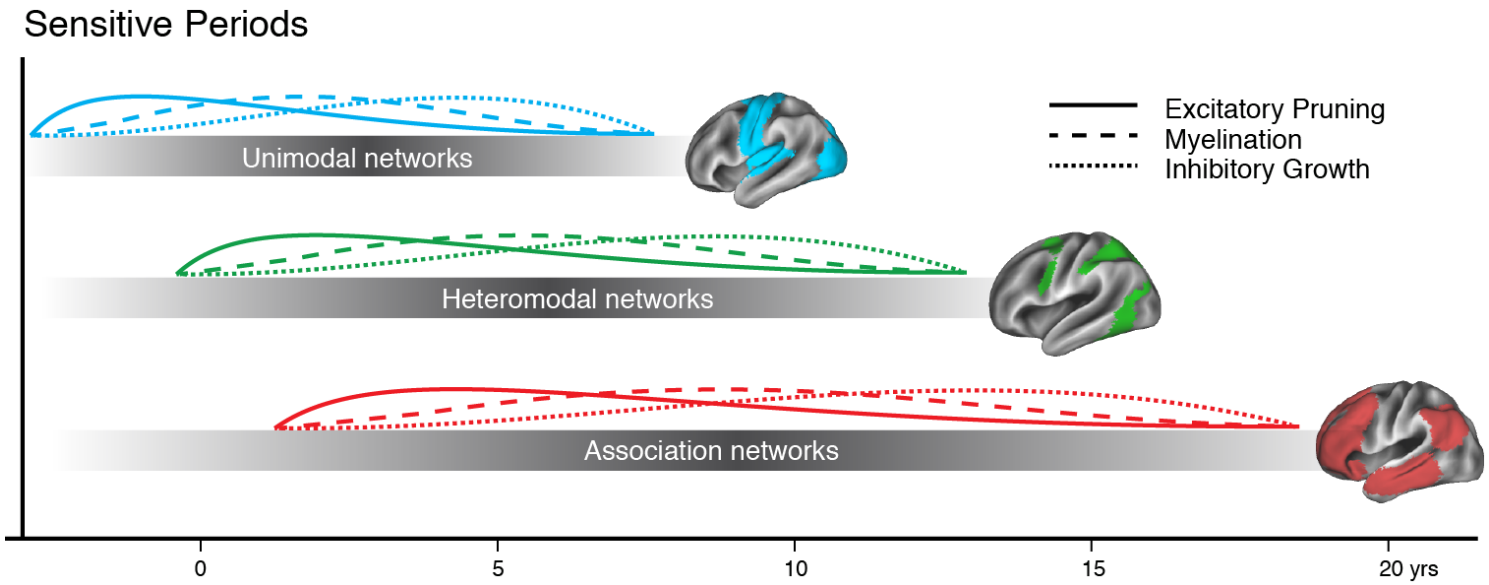


# Relationship of Automatic and Conventionally Acquired Measures



# Syndromes change over time



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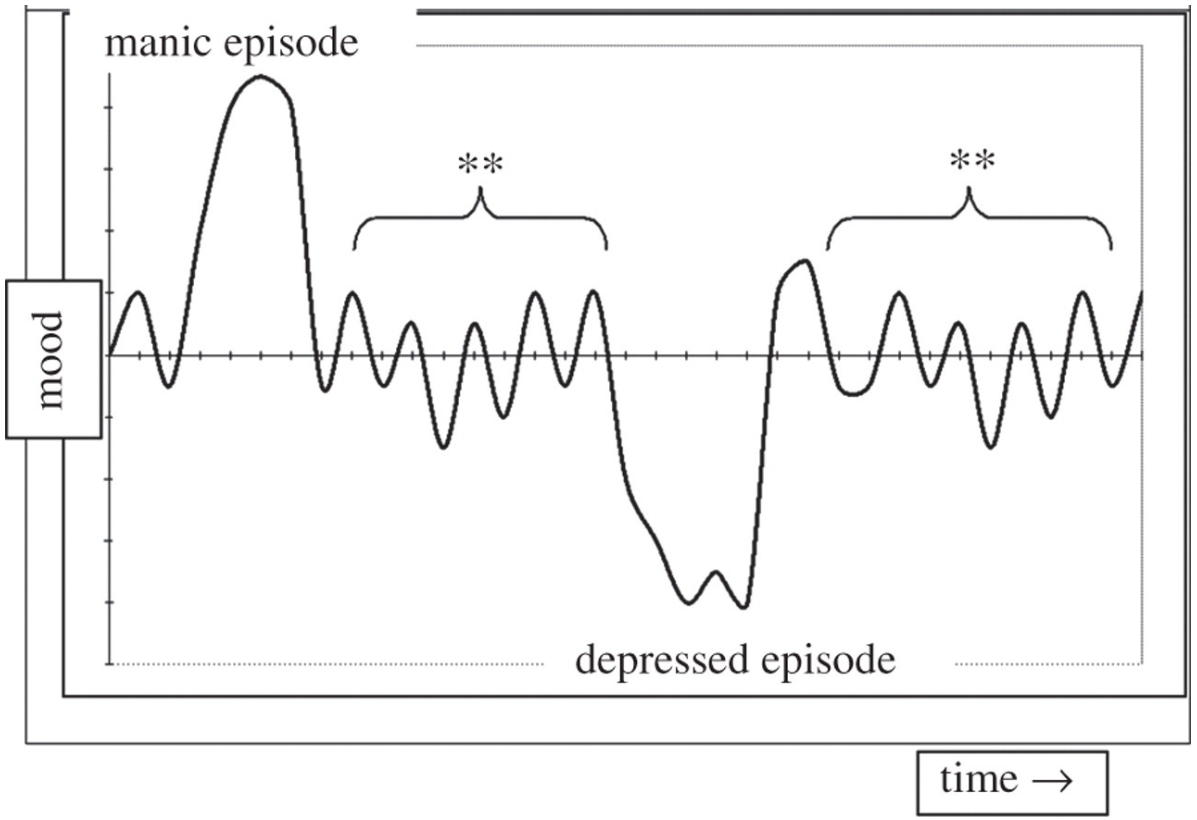
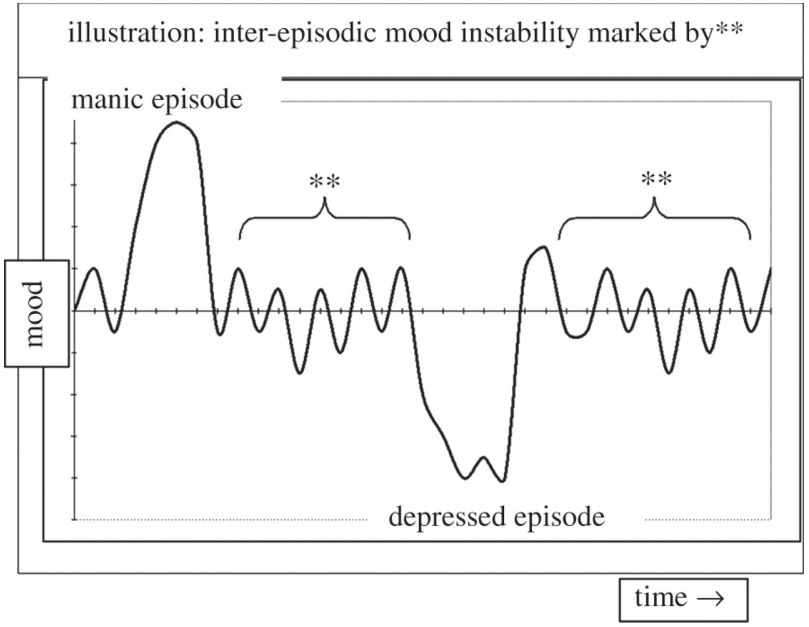


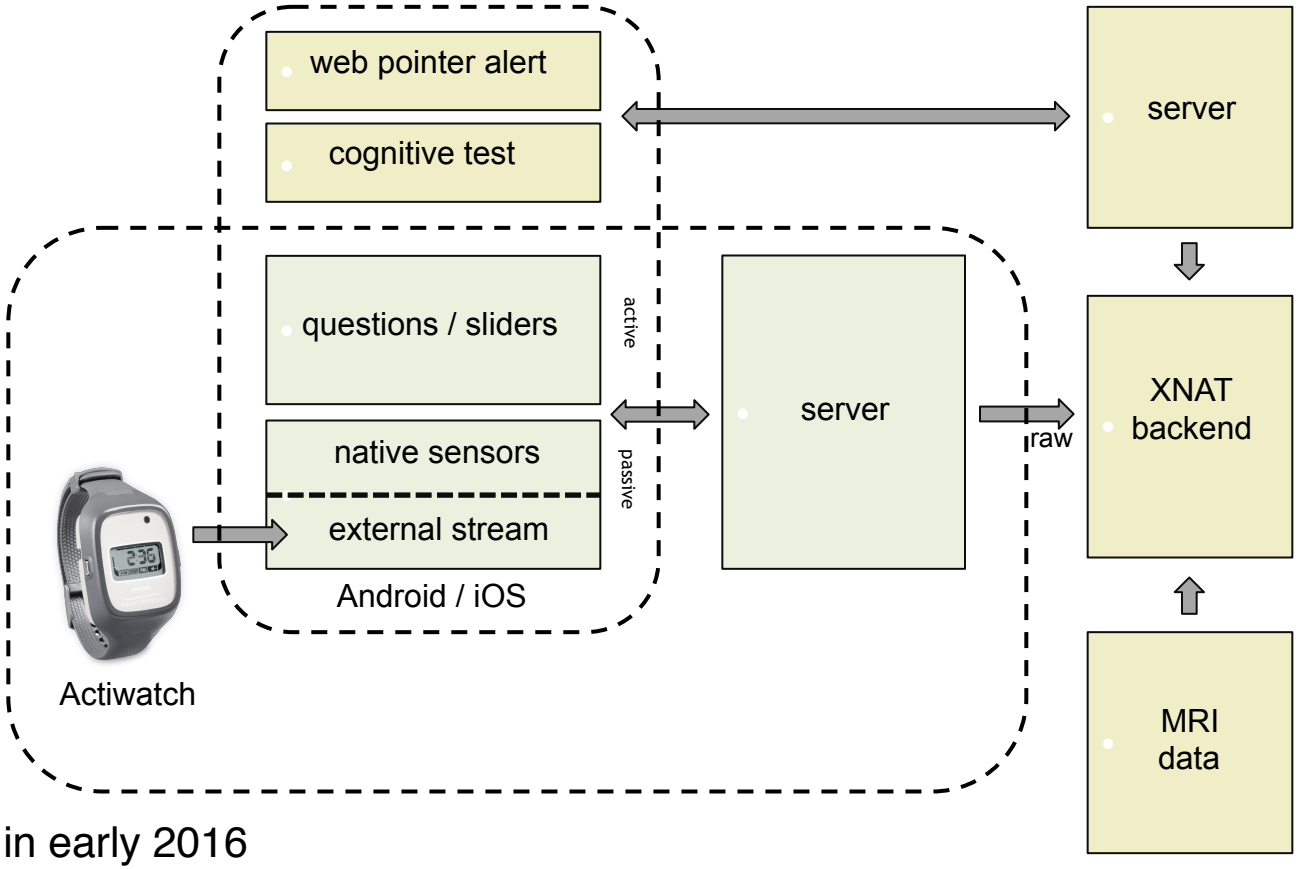
# Intensive Longitudinal Case Series in Bipolar Disorder



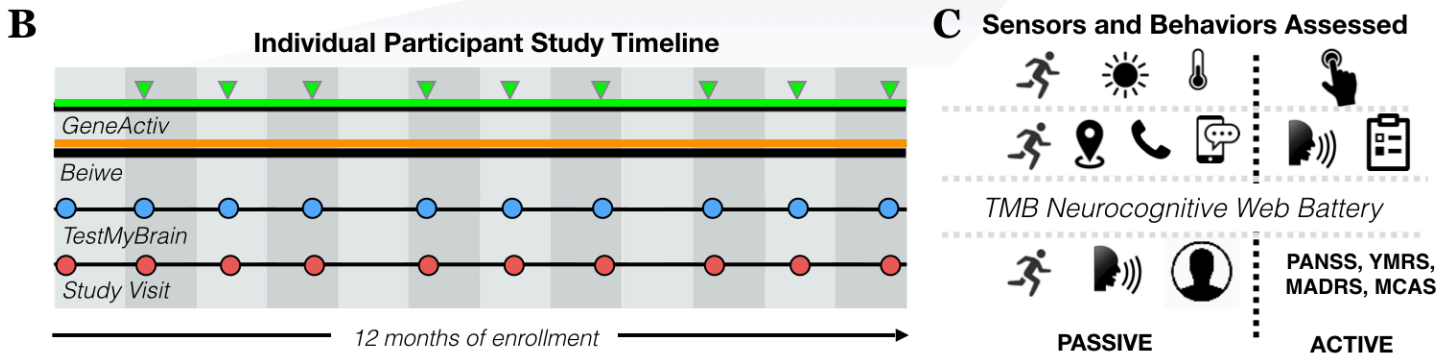
# “Deep Phenotyping”

- Multimodal, multi-time scale behavioral recordings robust to changes in exposome, development, and illness fluctuations.

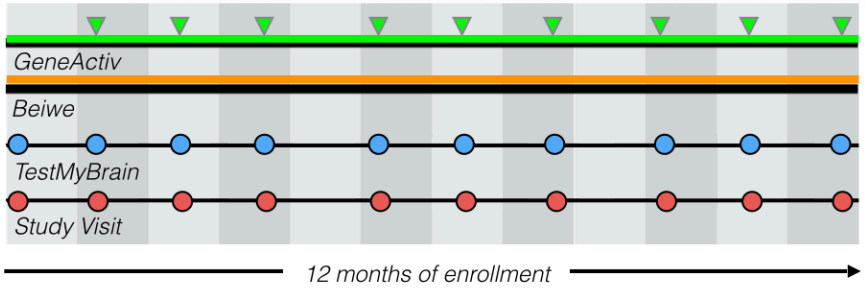
# Deep Phenotyping in Severe Mental Illness



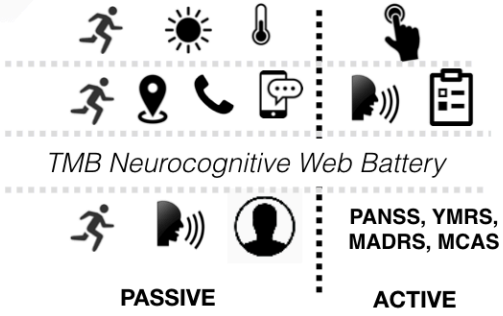

- Started in early 2016
- Continuous monitoring of 15 individuals with chronic forms of bipolar disorder and schizophrenia in real-world settings and serial study visits.
- Randy Buckner (Harvard), JP Onnela (HSPH)


B
Individual Participant Study Timeline
GeneActiv
Beiwe
TestMyBrain
Study Visit
12 months of enrollment
C
Sensors and Behaviors Assessed
TMB Neurocognitive Web Battery
PANSS, YMRS,
MADRS, MCAS
PASSIVE
ACTIVE

**B**



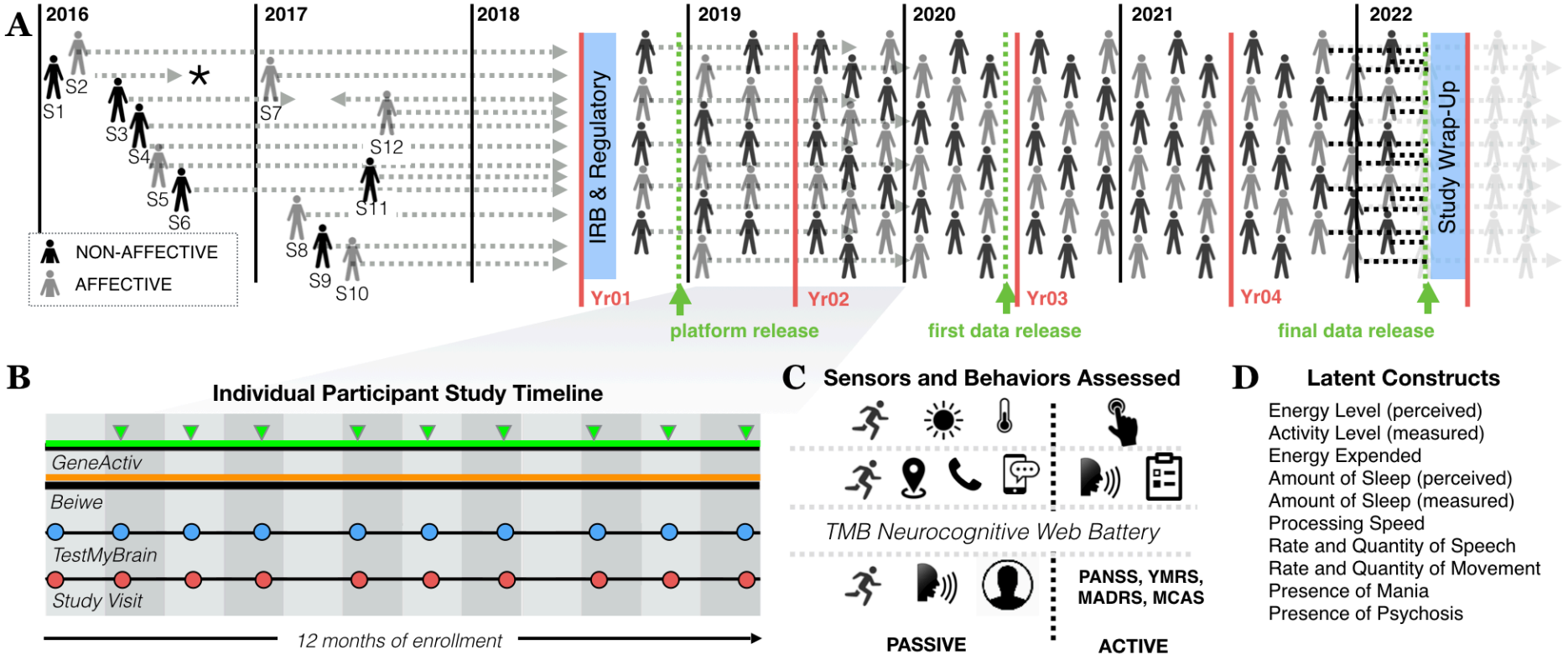

**C**




**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


A
2016
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2019
2020
2021
2022
S1
S2
S3
S4
S5
S6
S7
S8
S9
S10
S11
S12
NON-AFFECTIVE
AFFECTIVE
IRB & Regulatory
Study Wrap-Up
Yr01
Yr02
Yr03
Yr04
platform release
first data release
final data release
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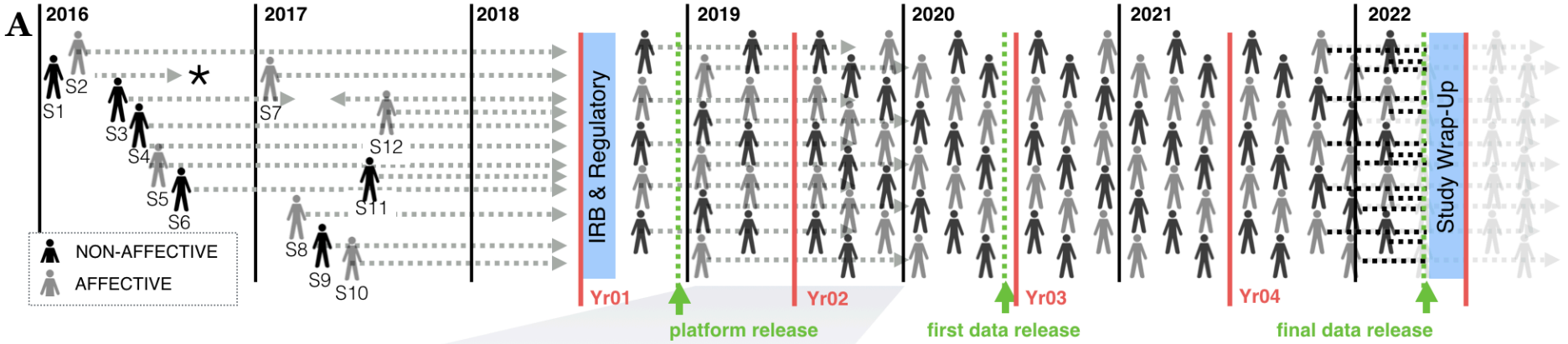
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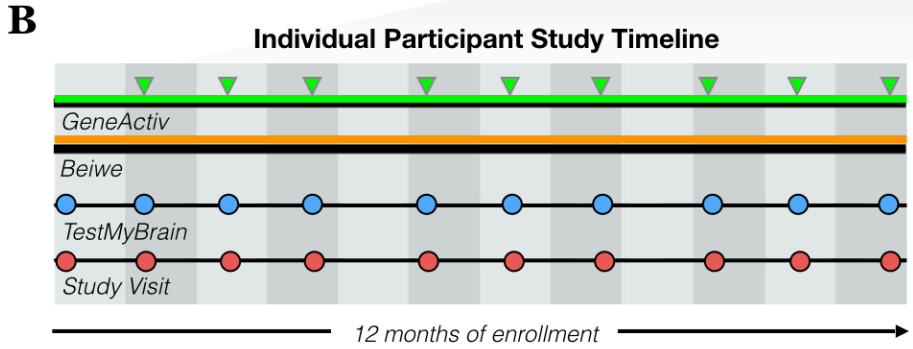
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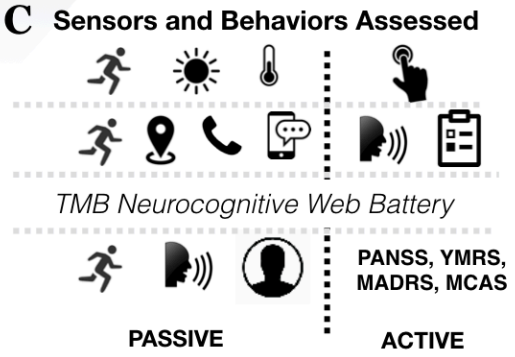
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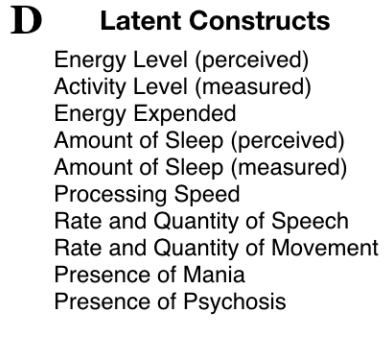
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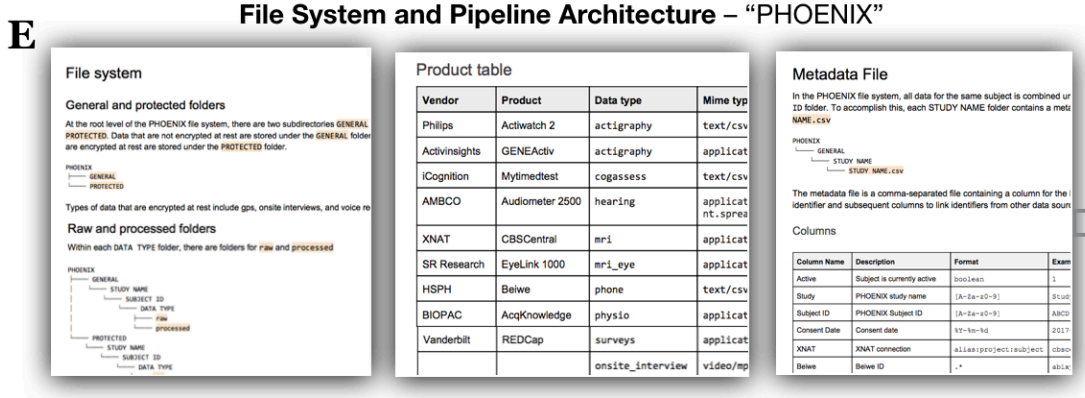
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File System and Pipeline Architecture – "PHOENIX"
File system
General and protected folders
Raw and processed folders
Product table
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Product
Data type
Philips
Actiwatch 2
actigraphy
Activinsights
GENEActiv
Mytimedtest
iCognition
cogassess
AMBCO
Audiometer 2500
hearing
XNAT
CBSCentral
mri
SR Research
EyeLink 1000
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HSPH
Beiwe
phone
BIOPAC
AcqKnowledge
physio
Vanderbilt
REDCap
surveys
onsite_interview
Metadata File
Columns
Column Name
Description
Format
Active
Subject is currently active
boolean
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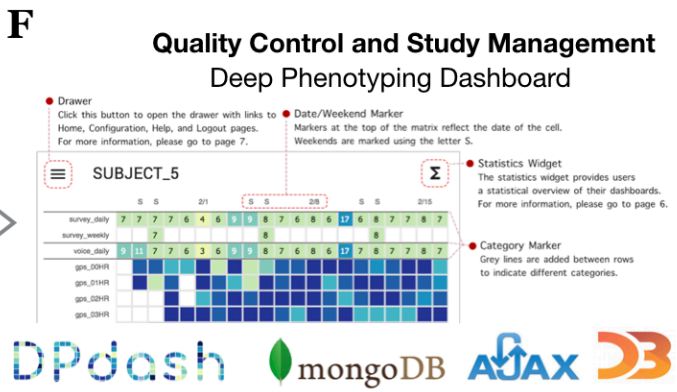
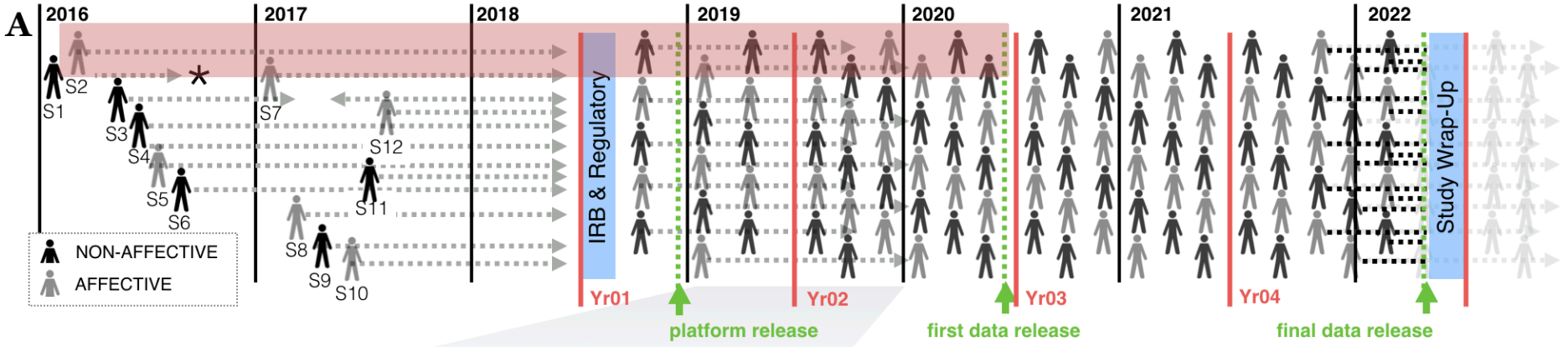
PHOENIX study name
Subject ID
PHOENIX Subject ID
Consent Date
Consent date
XNAT
XNAT connection
Beiwe
Beiwe ID


F
Quality Control and Study Management
Deep Phenotyping Dashboard
Drawer
Click this button to open the drawer with links to Home, Configuration, Help, and Logout pages.
For more information, please go to page 7.
Date/Weekend Marker
Markers at the top of the matrix reflect the date of the cell.
Weekends are marked using the letter S.
SUBJECT_5
Statistics Widget
The statistics widget provides users a statistical overview of their dashboards.
For more information, please go to page 6.
Category Marker
Grey lines are added between rows to indicate different categories.
DPdash
mongoDB
AJAX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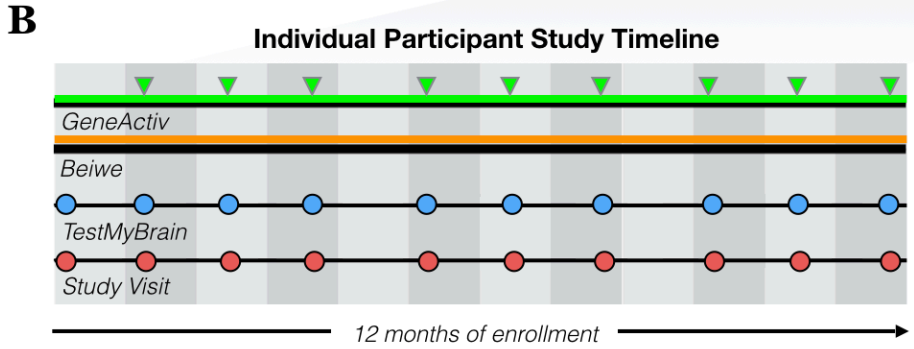
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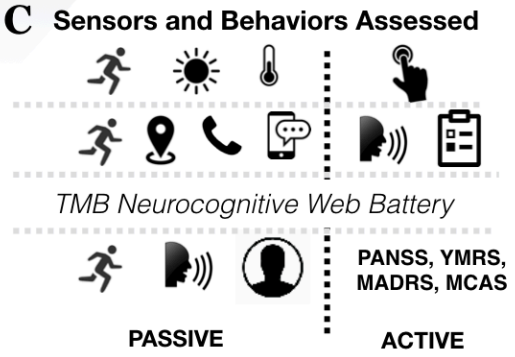
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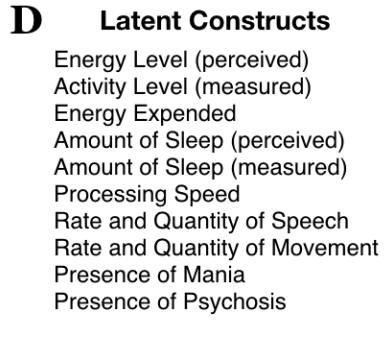
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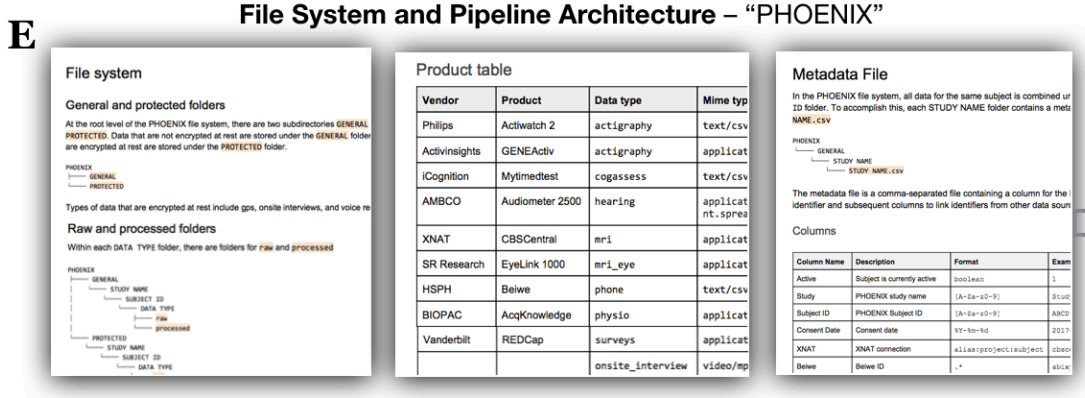
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Raw and processed folders
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Data type
Mime typ
Philips
Actiwatch 2
actigraphy
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GENEActiv
actigraphy
applicat
iCognition
Mytimedtest
cogassess
text/csv
AMBCO
Audiometer 2500
hearing
applicat nt.sprea
XNAT
CBSCentral
mri
applicat
SR Research
EyeLink 1000
mri_eye
applicat
HSPH
Beiwe
phone
text/csv
BIOPAC
AcqKnowledge
physio
applicat
Vanderbilt
REDCap
surveys
applicat
onsite_interview
video/mp
Metadata File
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Column Name
Description
Format
Exam
Active
Subject is currently active
boolean
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Study
PHOENIX study name
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XNAT
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Beiwe
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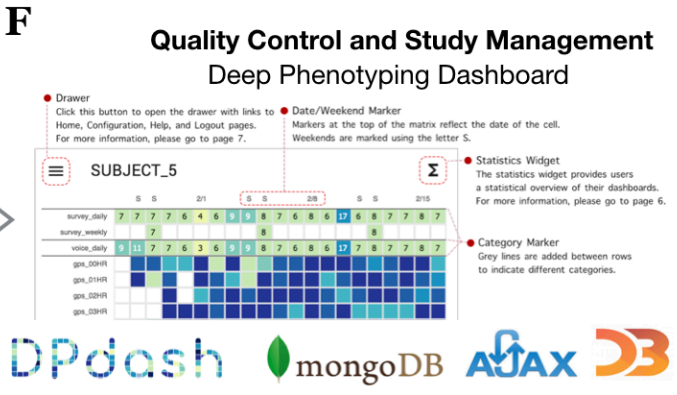
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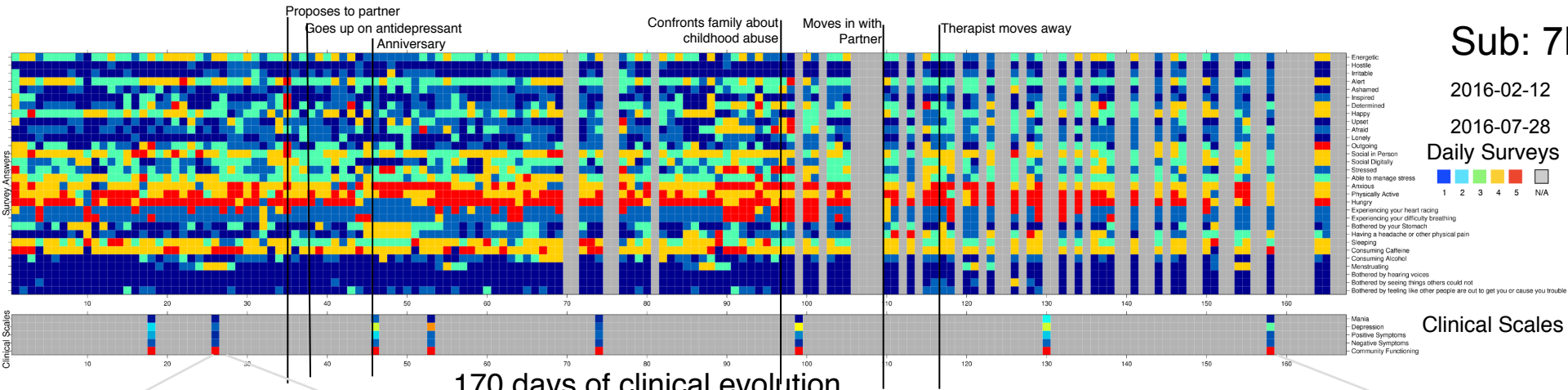
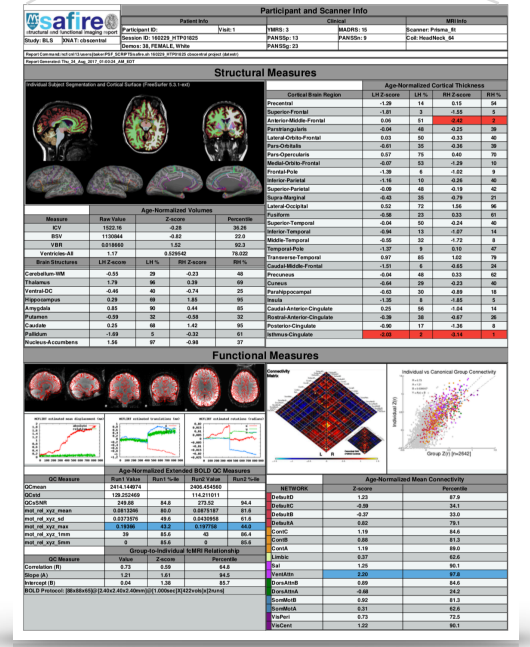
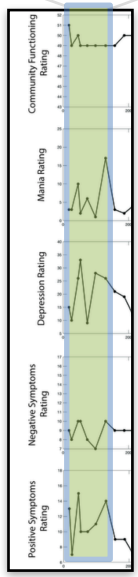
# 37yo F with schizoaffective / bipolar disorder over 165 days of continuous monitoring and serial MRI

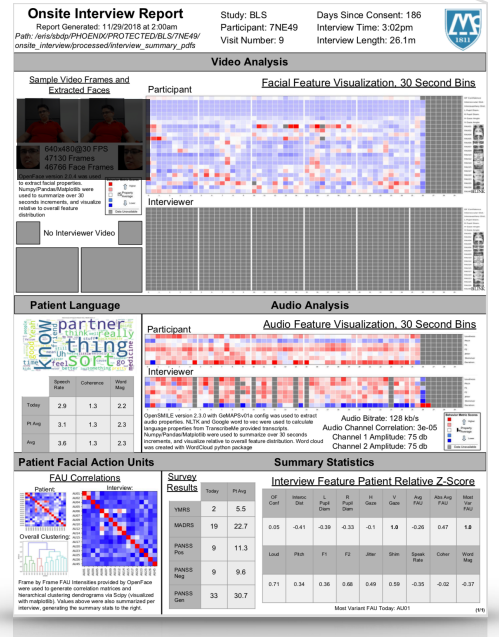



170 days of clinical evolution

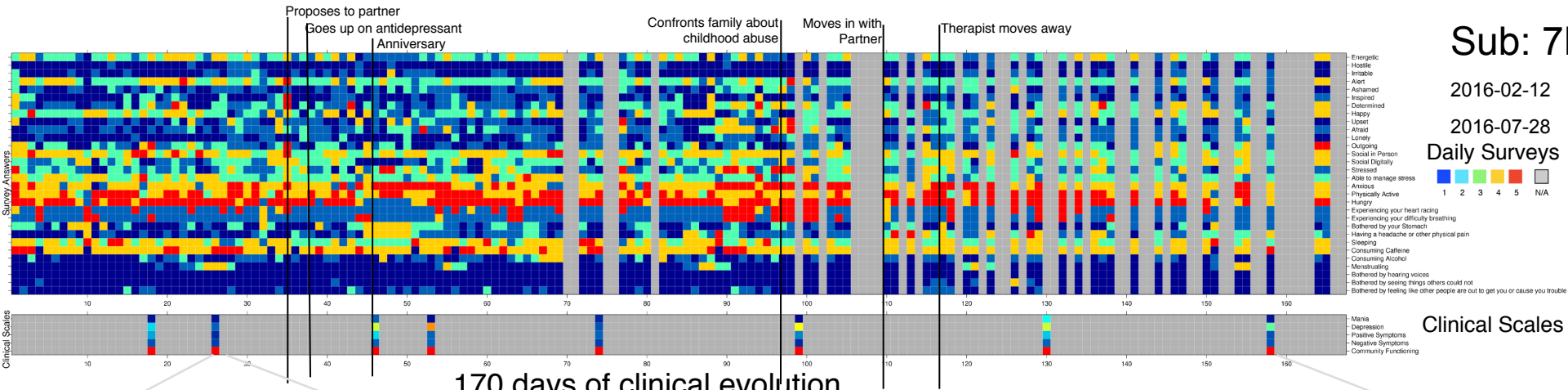


170 days of clinical evolution



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

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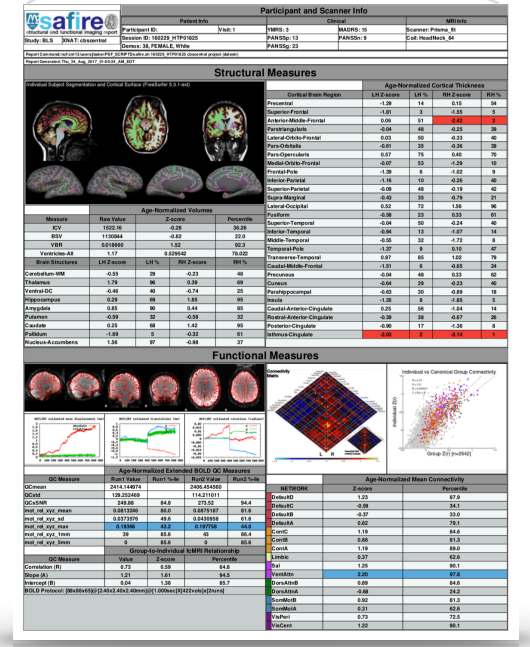
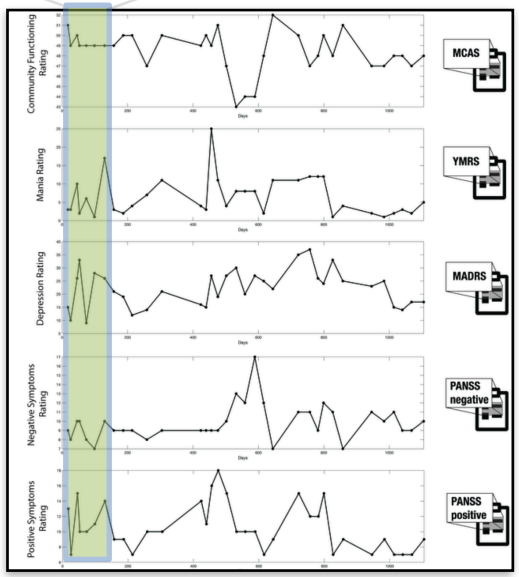
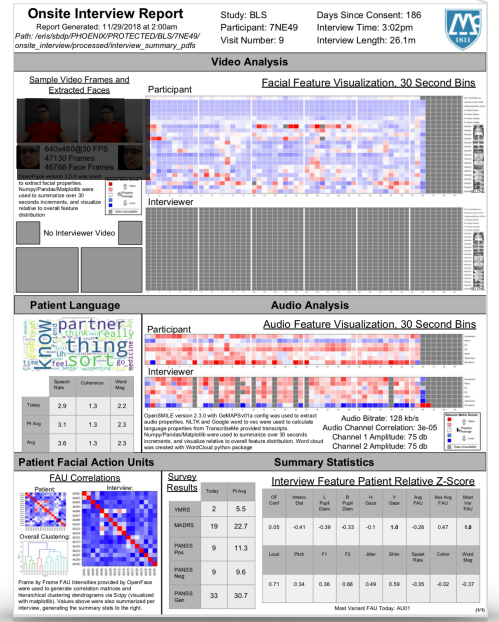



1000 days of clinical evolution



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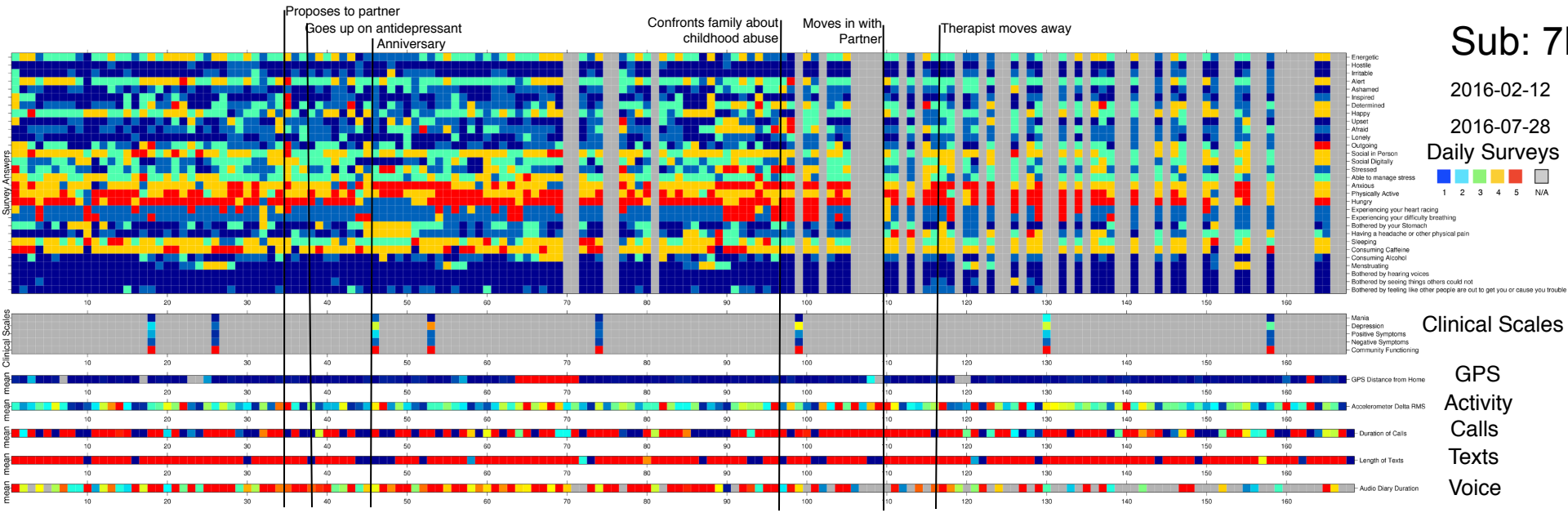



Sub: 7

2016-02-12

2016-07-28

Daily Surveys

1 2 3 4 5 N/A

Clinical Scales

GPS

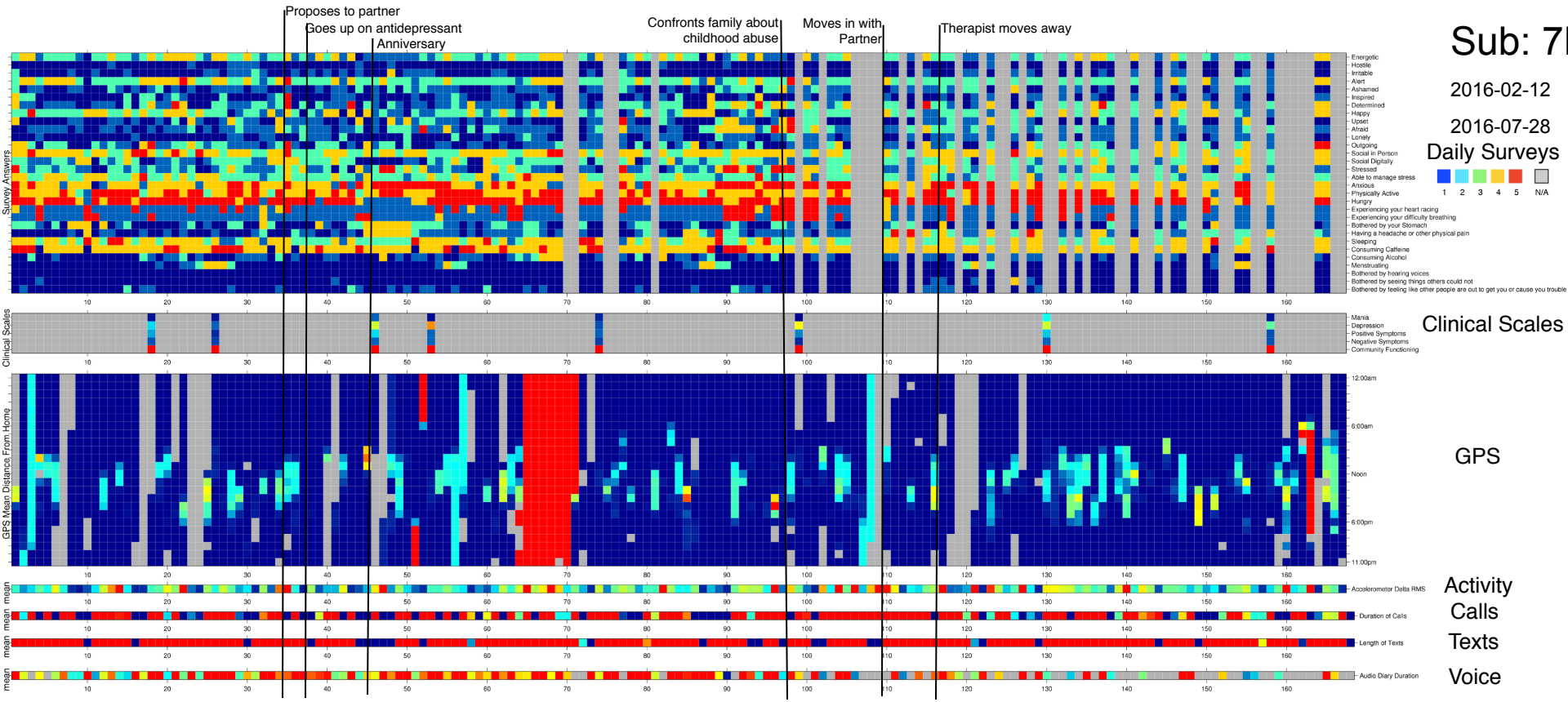
Activity

Calls

Texts

Voice

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



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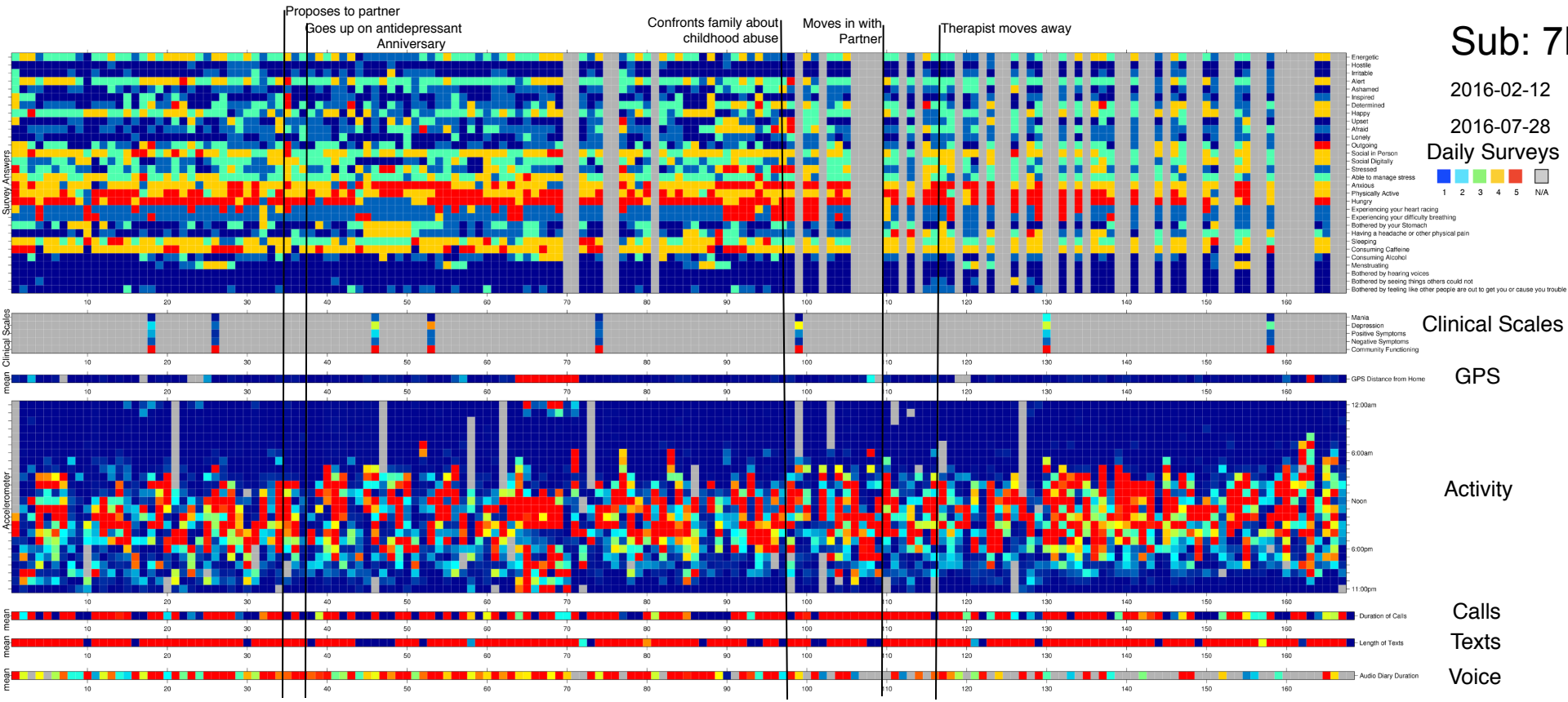


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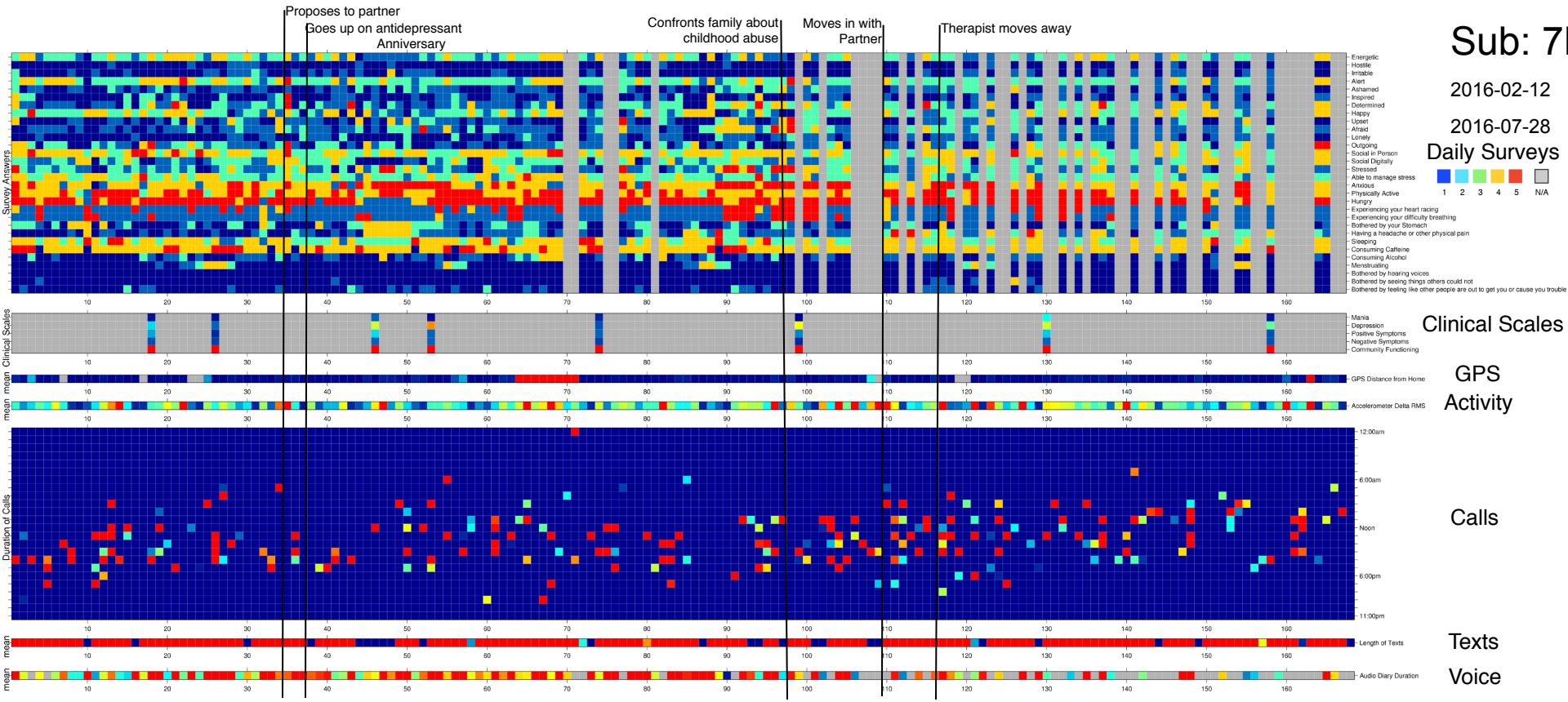


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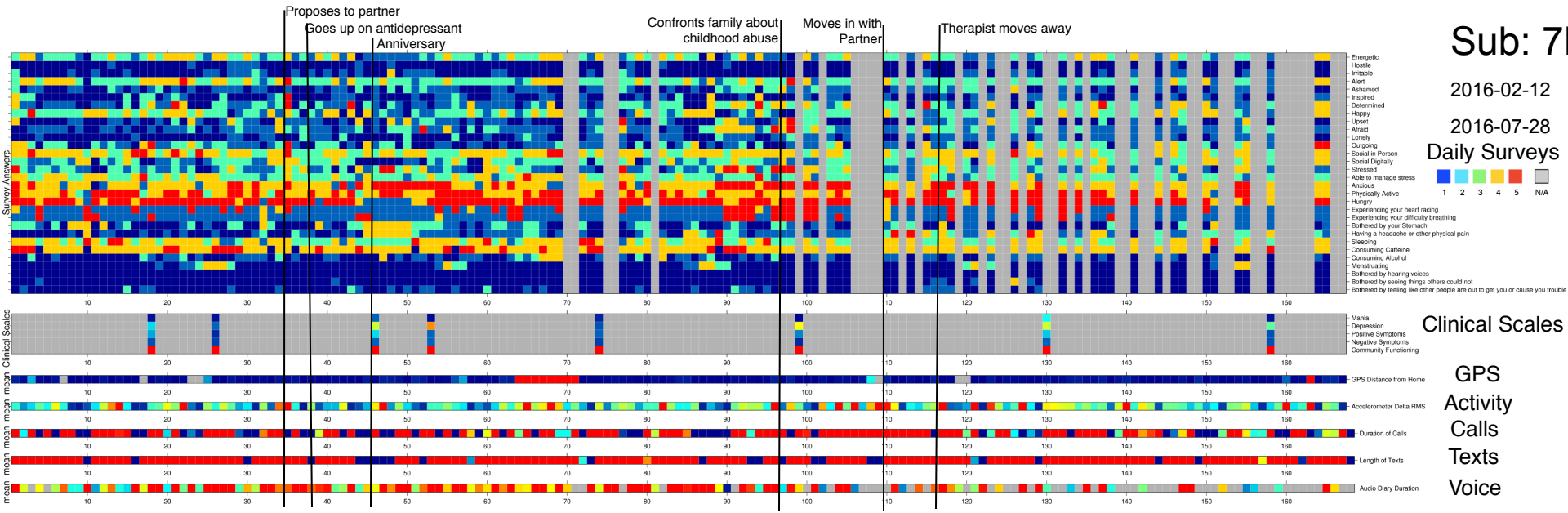


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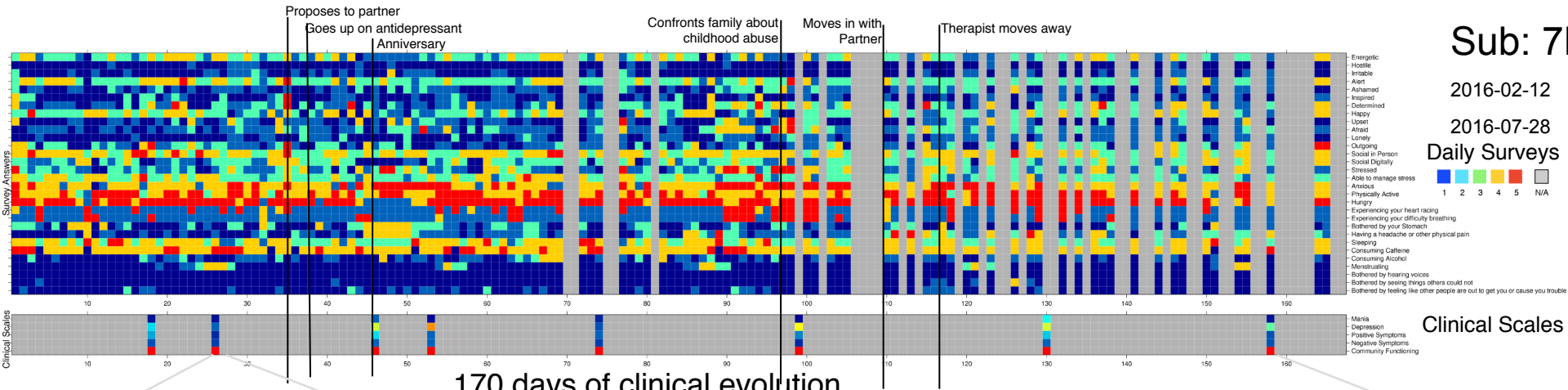


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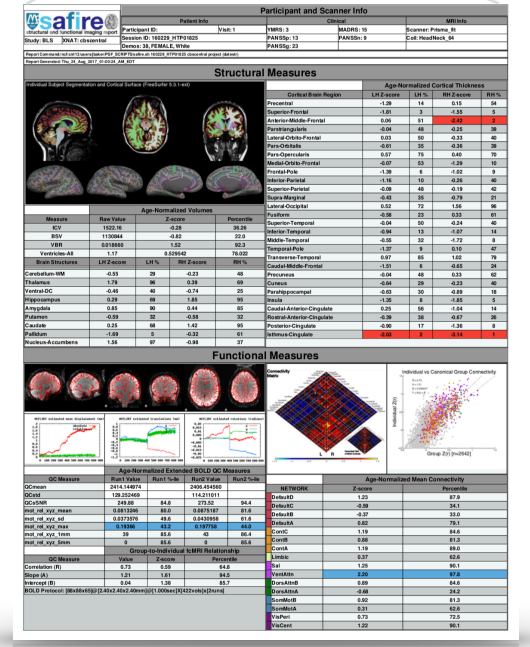


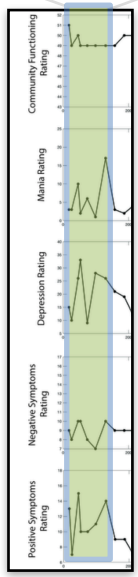

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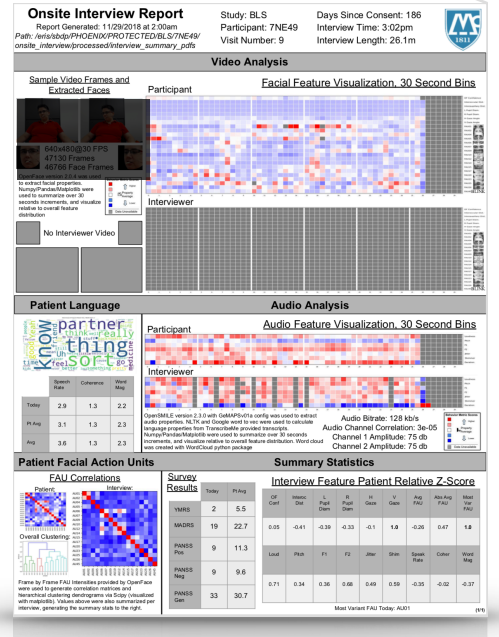

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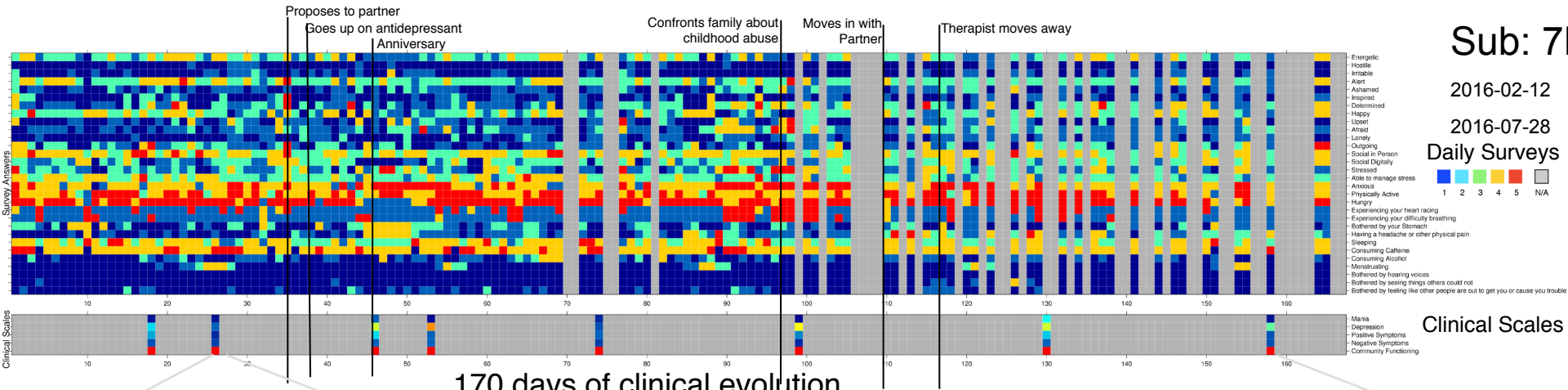


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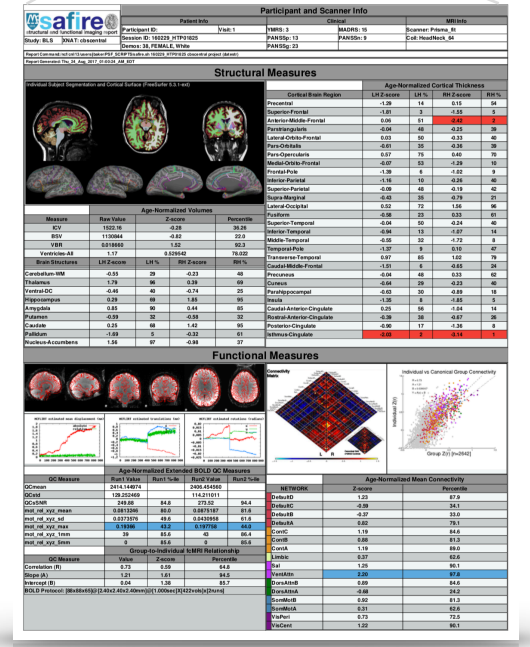
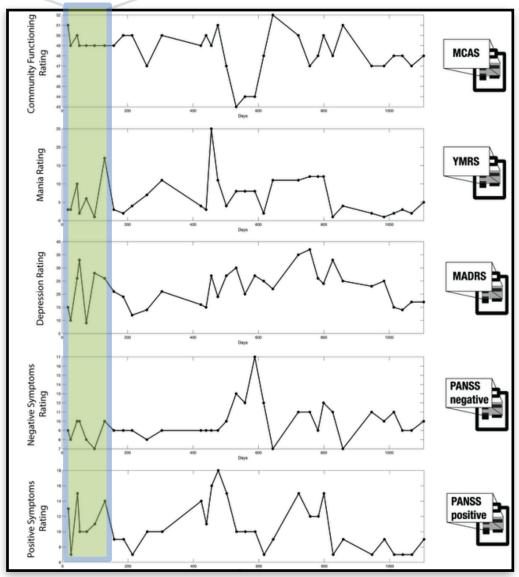
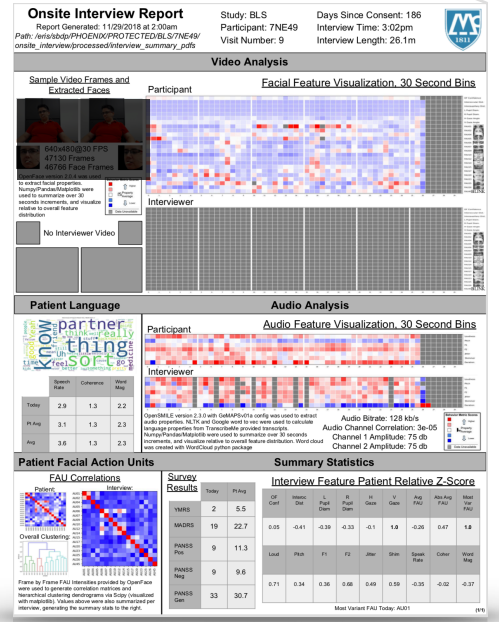
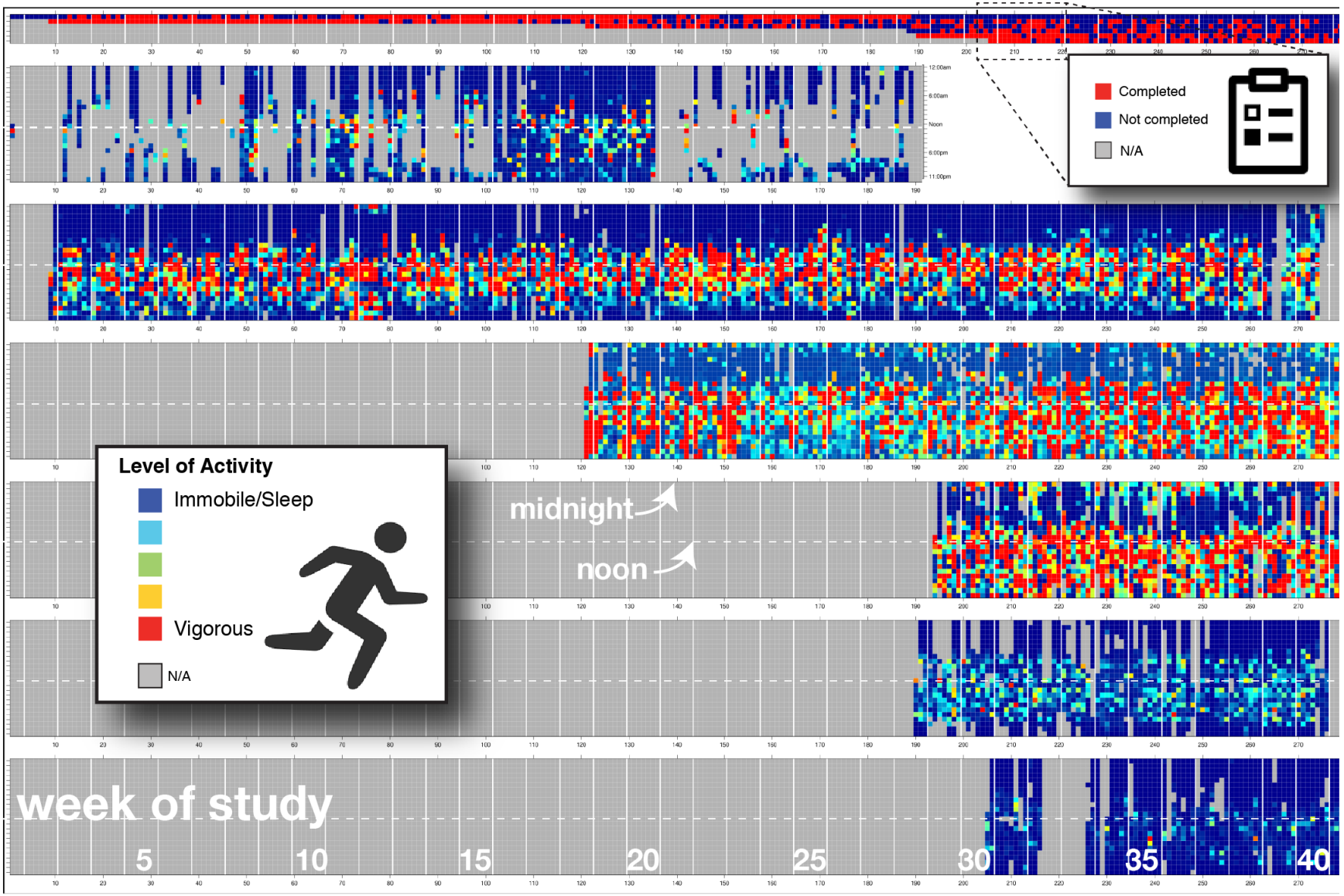


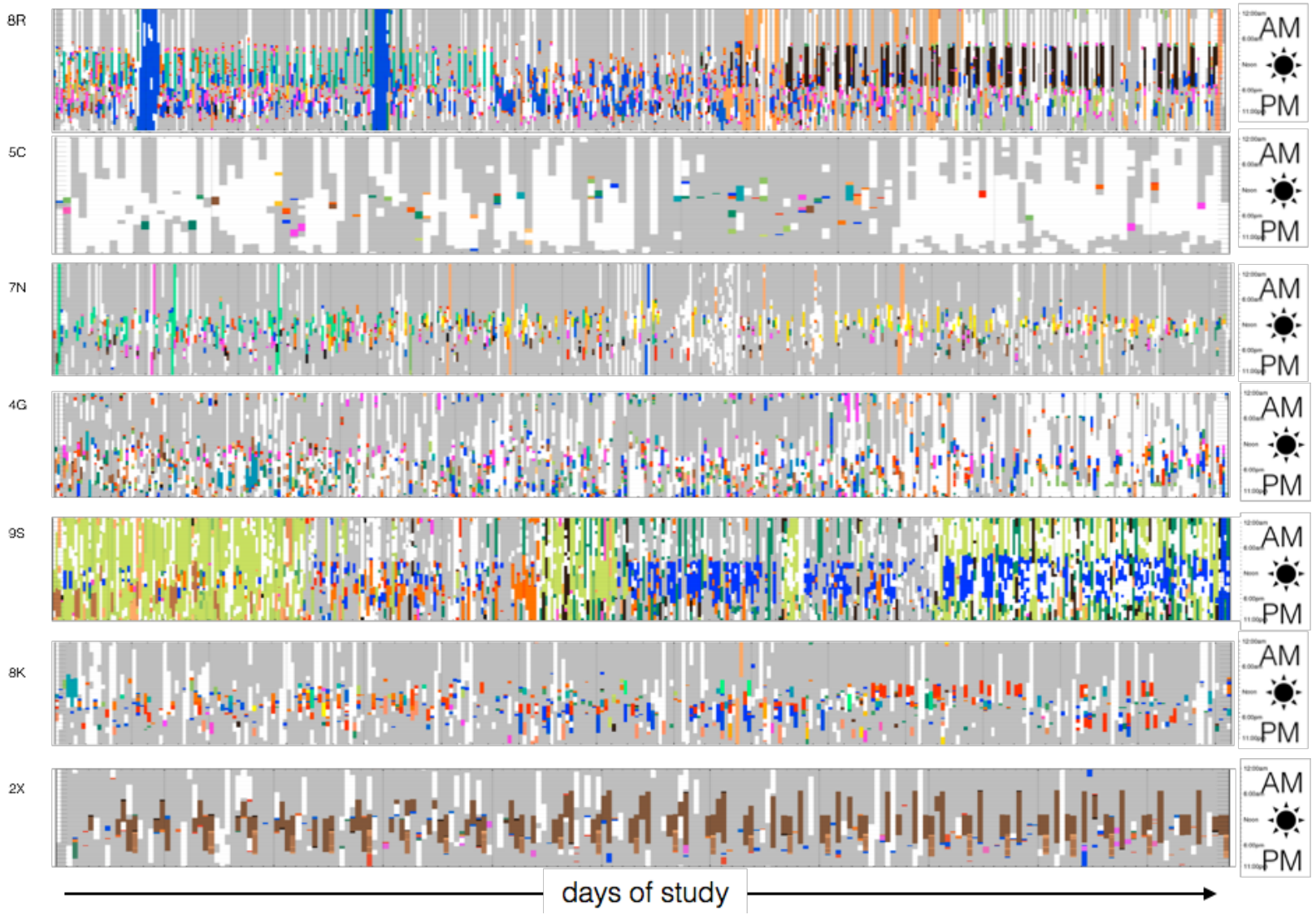

1000 days of clinical evolution



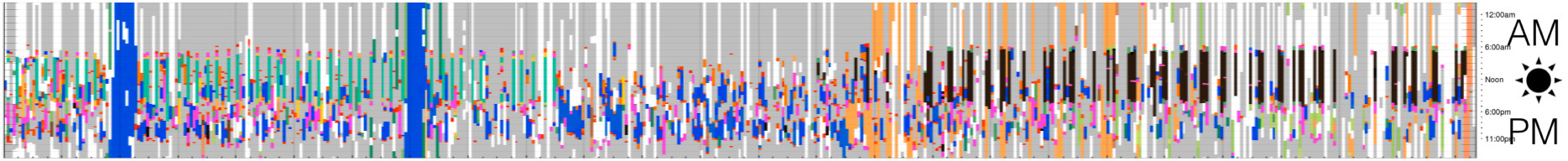
# Six Individuals with Mental Illness



Automated, minimal-burden, continuous assessment of community and social functioning in individuals with severe mental illness

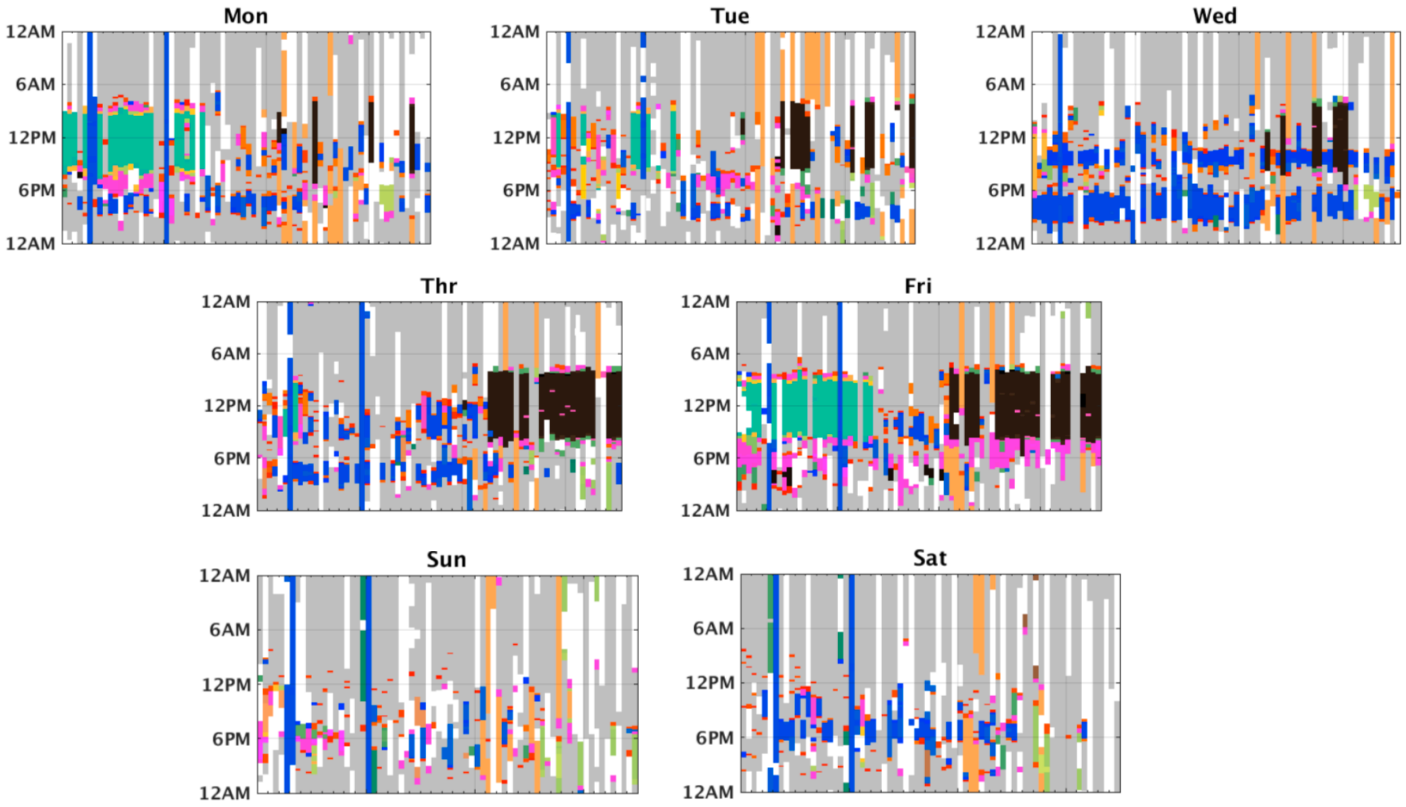


# Significant Locations
# Two years of Geospatial Recording



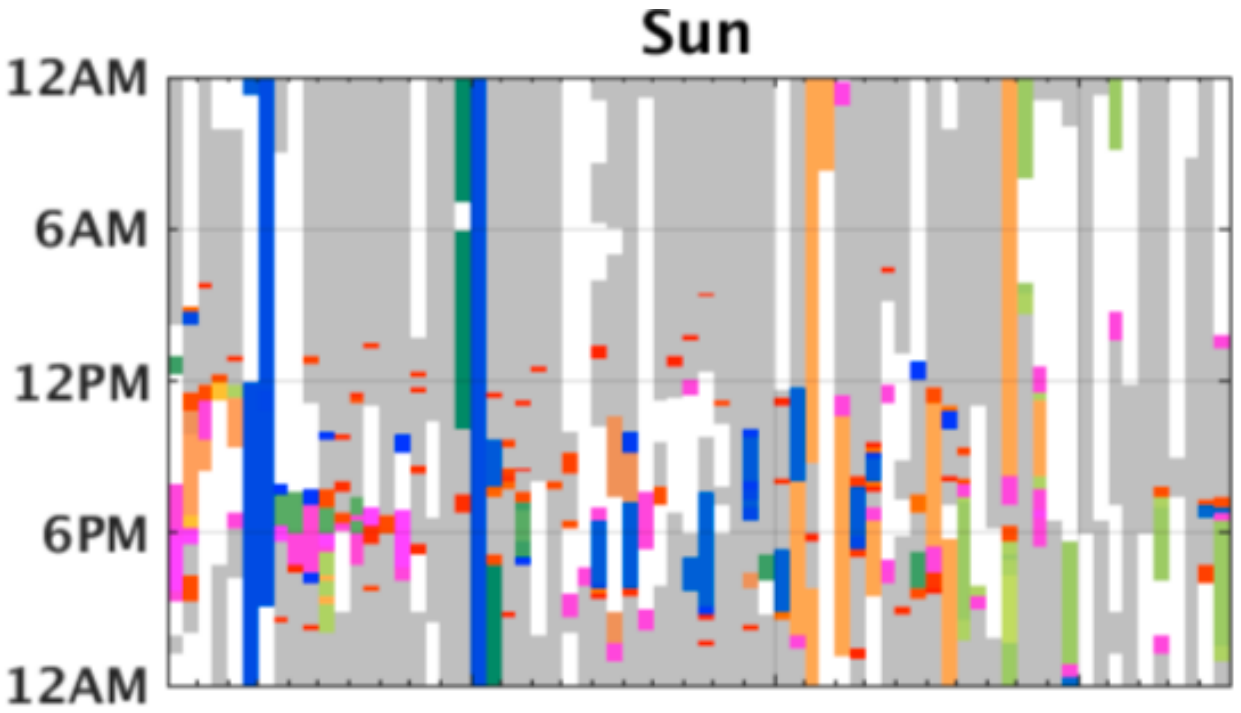

**Location classes** (most to least common)

# 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)

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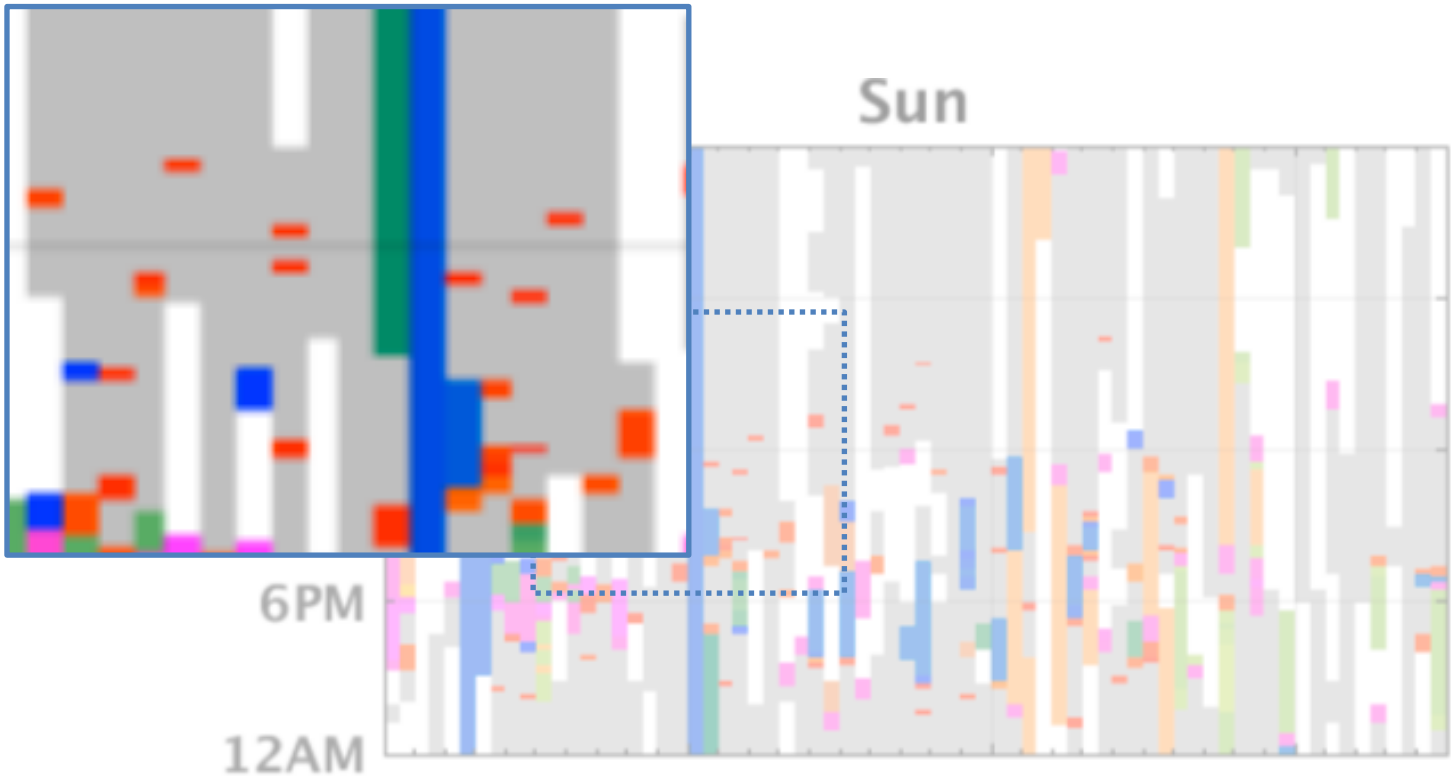


**Location classes** (most to least common)

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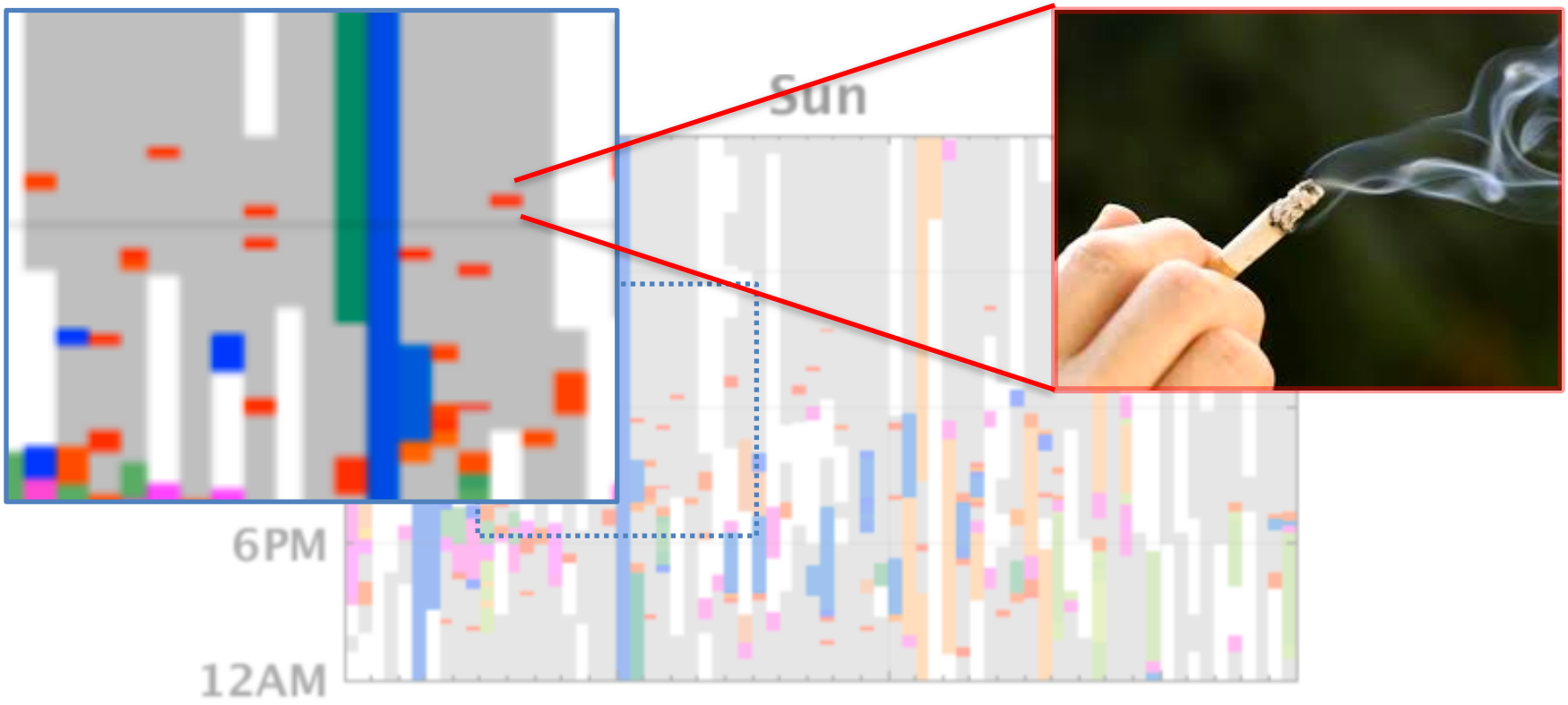
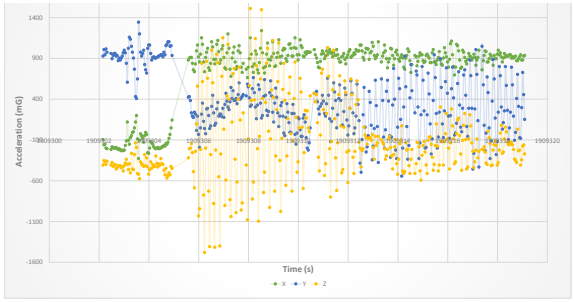


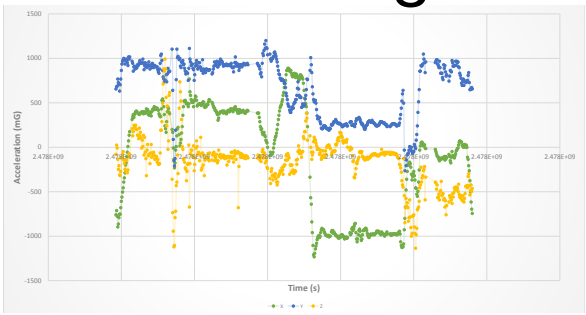

**Location classes** (most to least common)

# Activity classification with wearable sensors

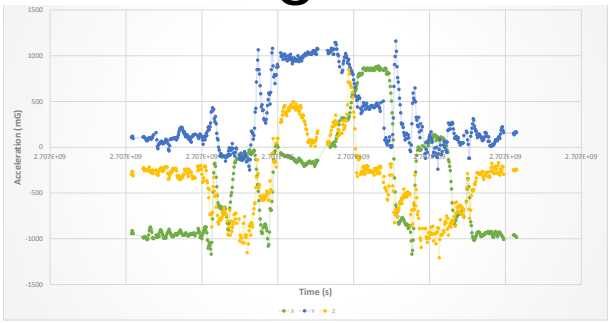
## Brushing teeth



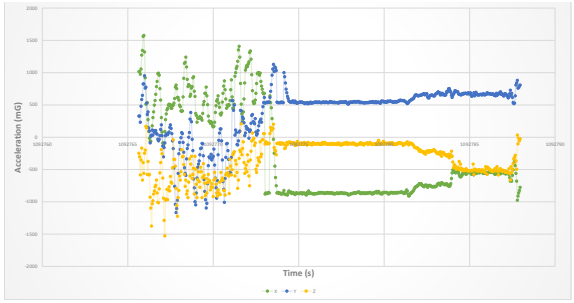

## Smoking



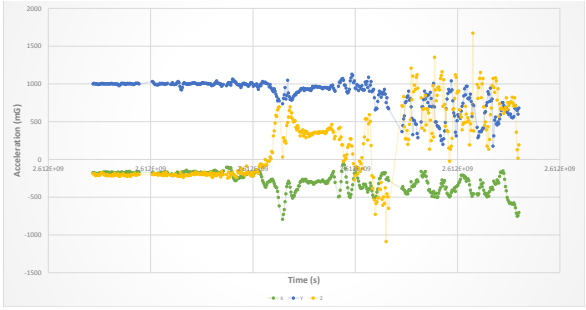

## Taking Meds



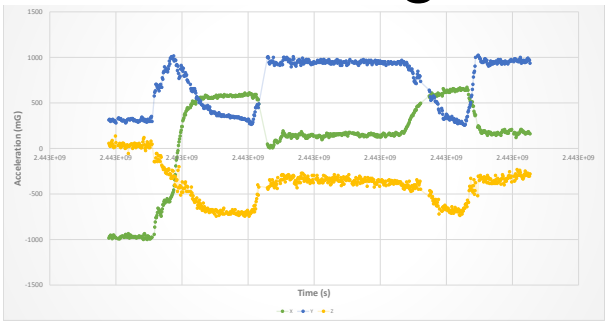

## Combing Hair




## Washing Hands

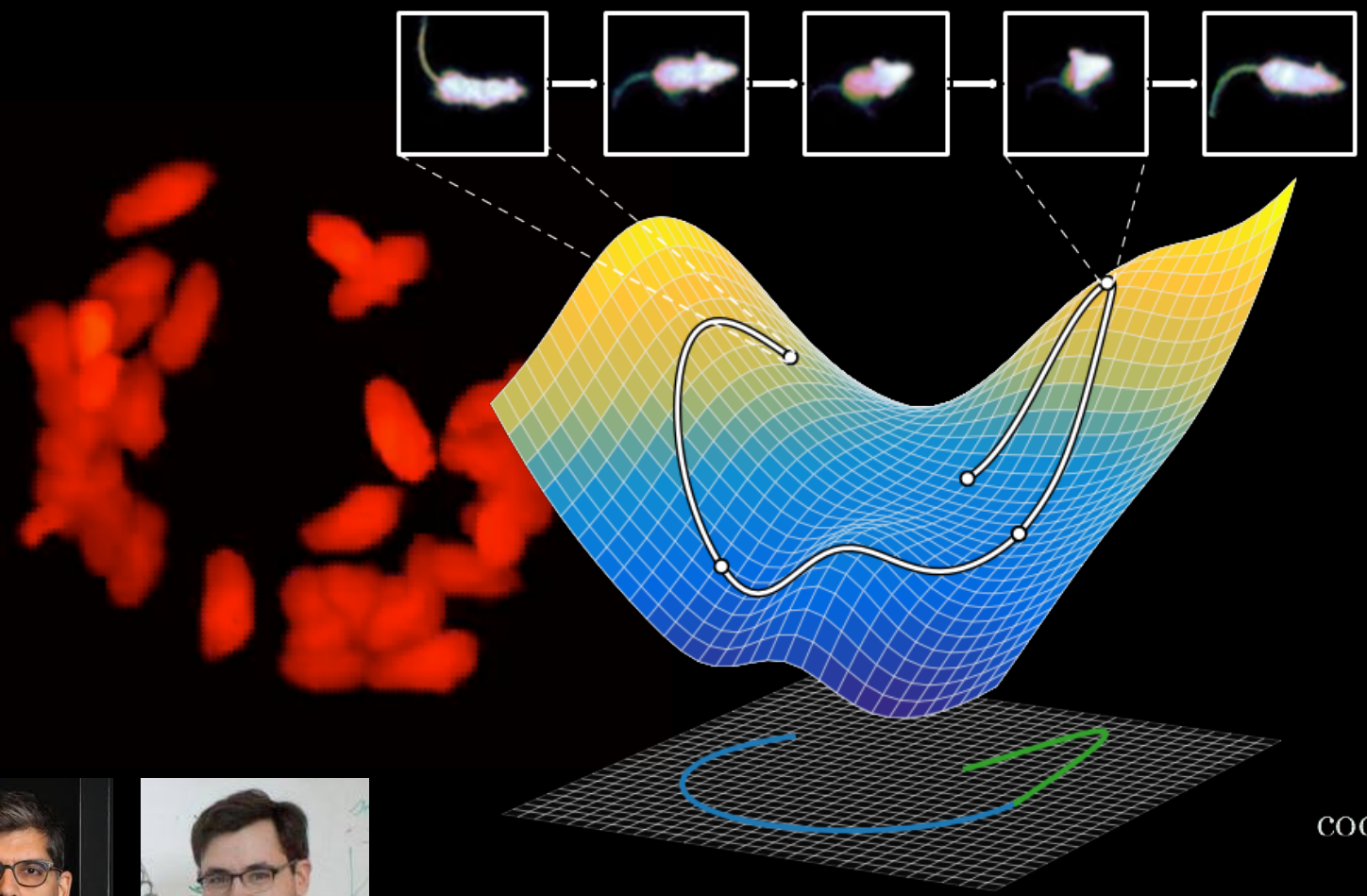



## Drinking



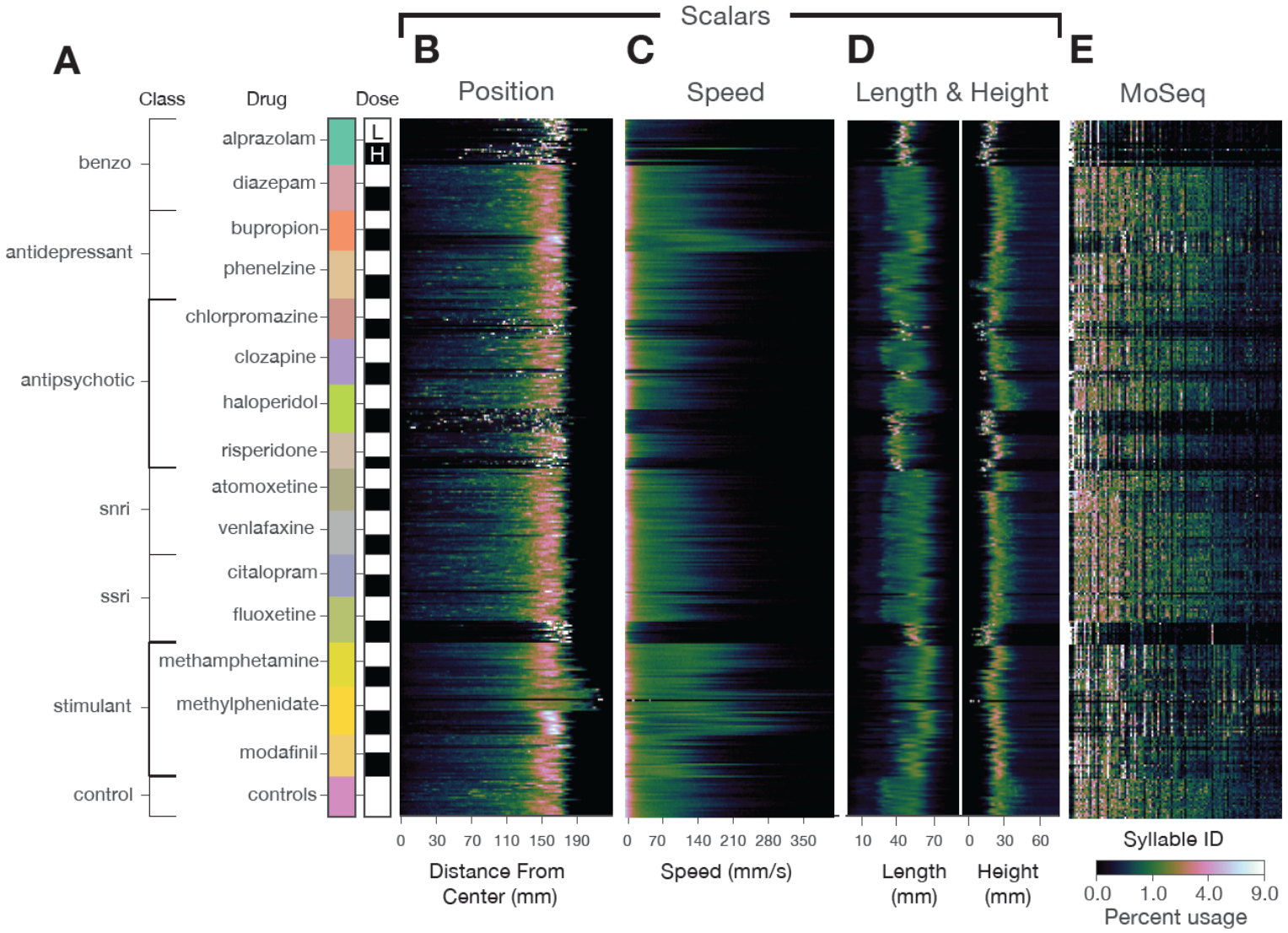

*Cherian et al.* *Pervasive Health'17,* May 23–26, 2017, Barcelona, Spain

# Learning a Behavioral State Space



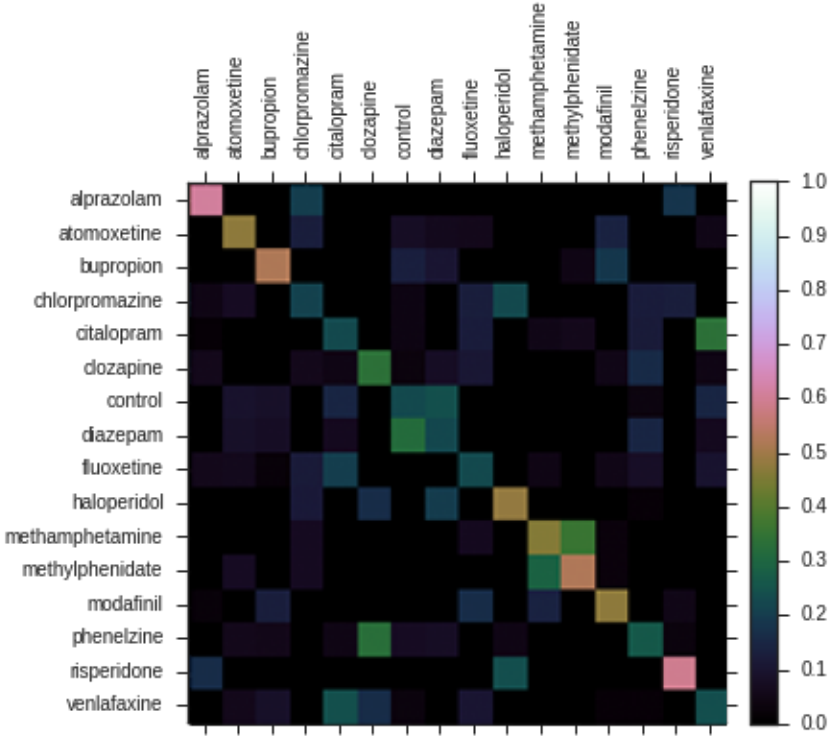
Johnson et al, 2016

# Building Behavioral Fingerprints

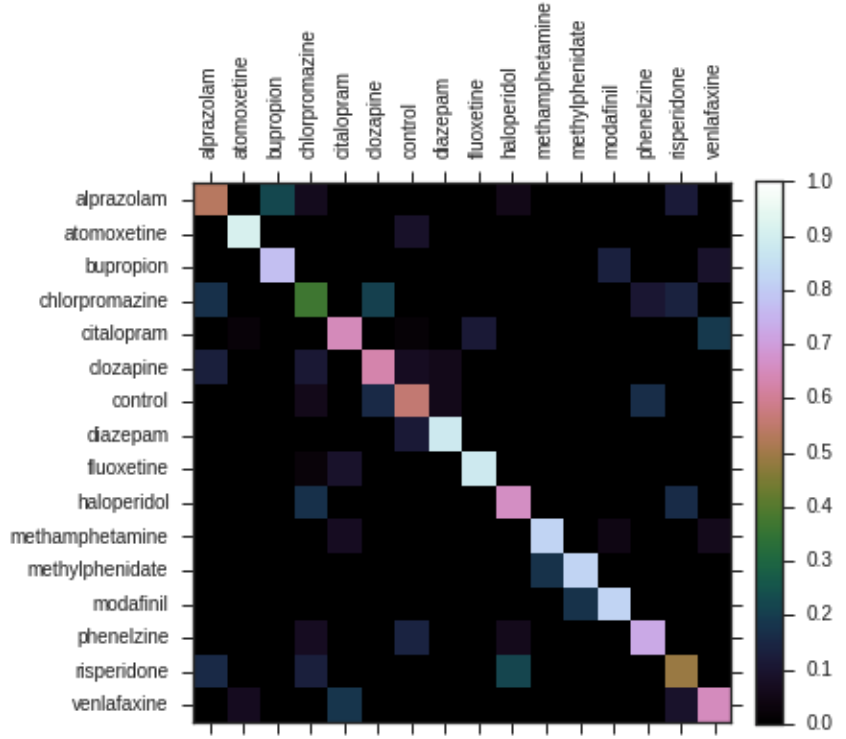


# Predicting Drug Identity

## K-Means, Scalars

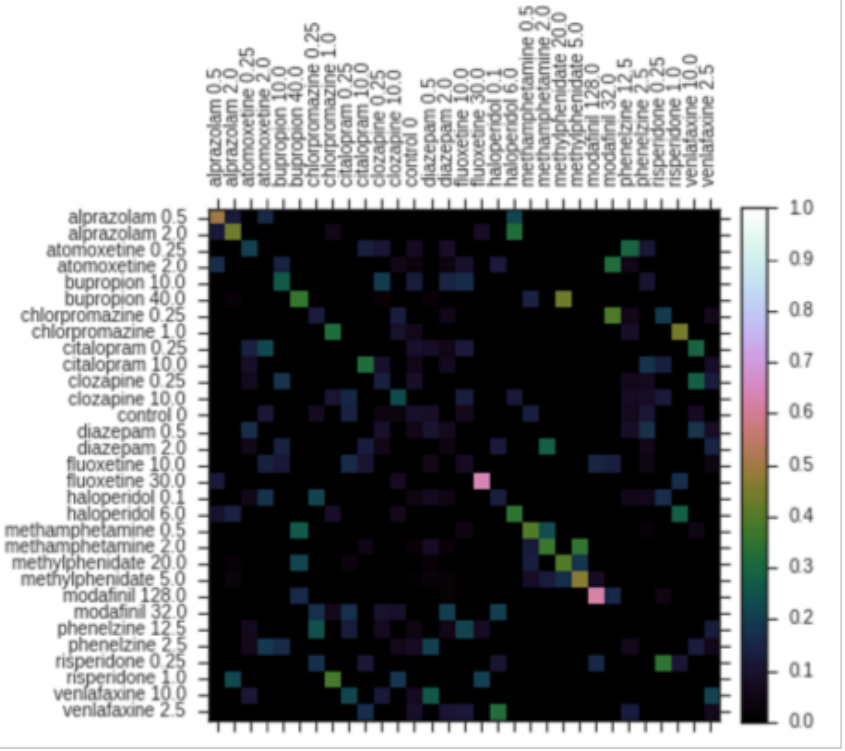



## AR-HMM

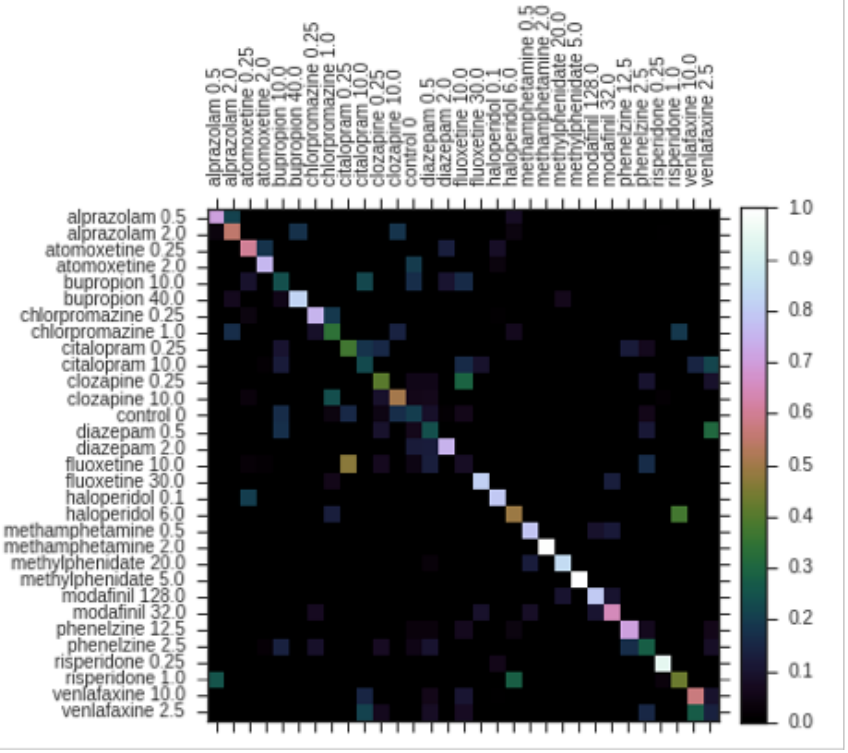


# Predicting Drug Identity and Dose

## Scalars



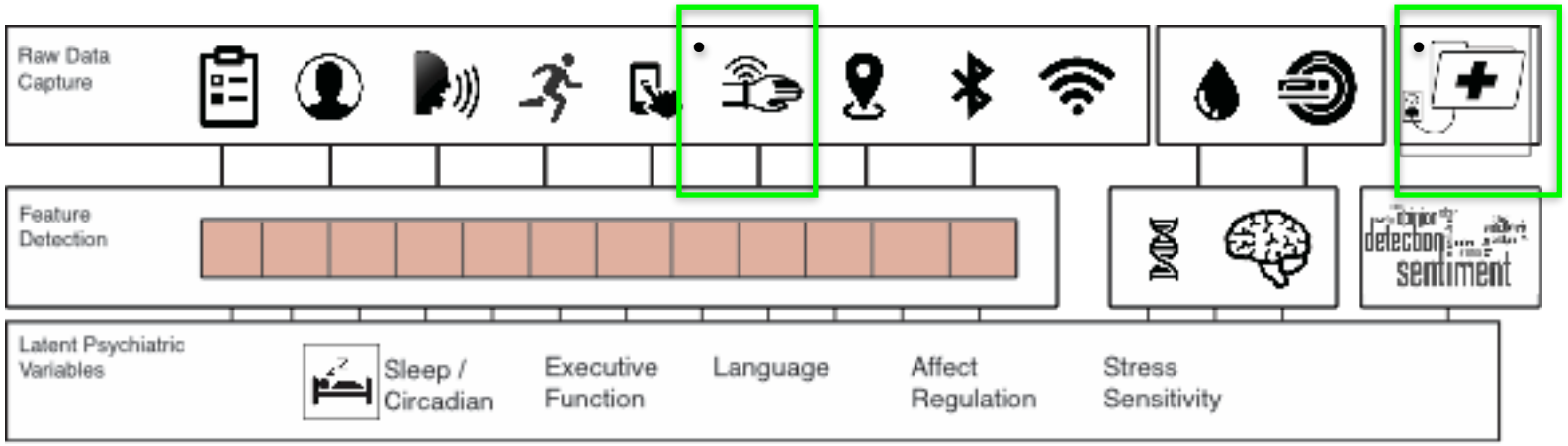

## AR-HMM



# Device

# EHR

| | Last | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|---|
| **Stats & One Times (1)** | | | | | | | | | | |
| **Metoprolol (Lopresor)** 100 mg PO now | | ✔ | | | | | | | | |
| **Meds (3)** | | | | | | | | | | |
| **Captopril (Capoten)** 12.5 mg Q8 hrs | ✔ | | | | | | ● | | | |
| **Digoxin (Lanoxin)** 0.125 mg = 1 tablet PO QD | ✔ | ✔ | | | | | | | | |
| **Furosemide (Lasix)** 40 mg PO Q6 hrs | ✔ | ✔ | | | | | | ✖ | | |
| **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 | ✔ | | | ✔ | ✔ | | | ✔ | | |



# Device

# EHR

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|---|---|---|---|---|---|---|---|---|---|---|
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| **Meds (3)** | | | | | | | | | | |
| **Captopril (Capoten)** 12.5 mg Q8 hrs | ✔ | | | | | | ● | | | |
| **Digoxin (Lanoxin)** 0.125 mg = 1 tablet PO QD | ✔ | ✔ | | | | | | | | |
| **Furosemide (Lasix)** 40 mg PO Q6 hrs | ✔ | ✔ | | | | | | ✖ | | |
| **PRNs (4)** | | | | | | | | | | |
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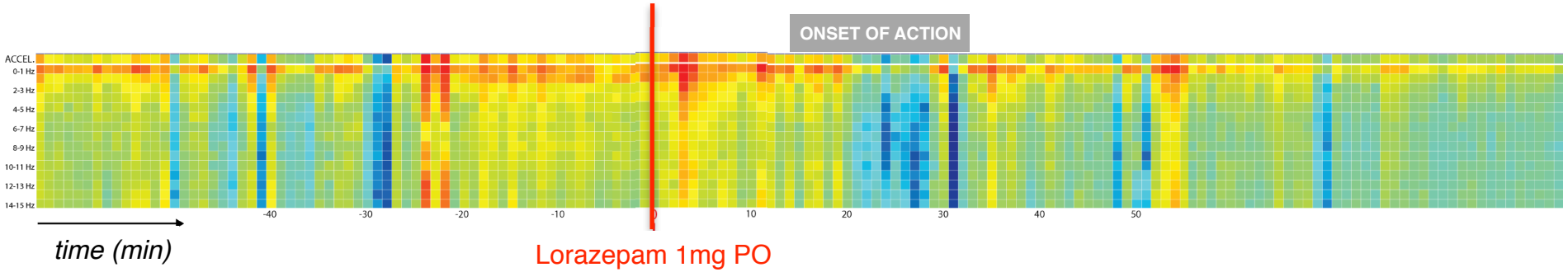
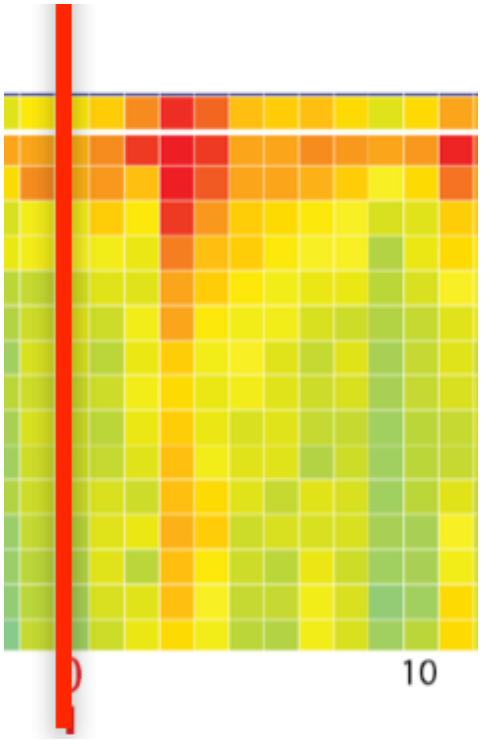
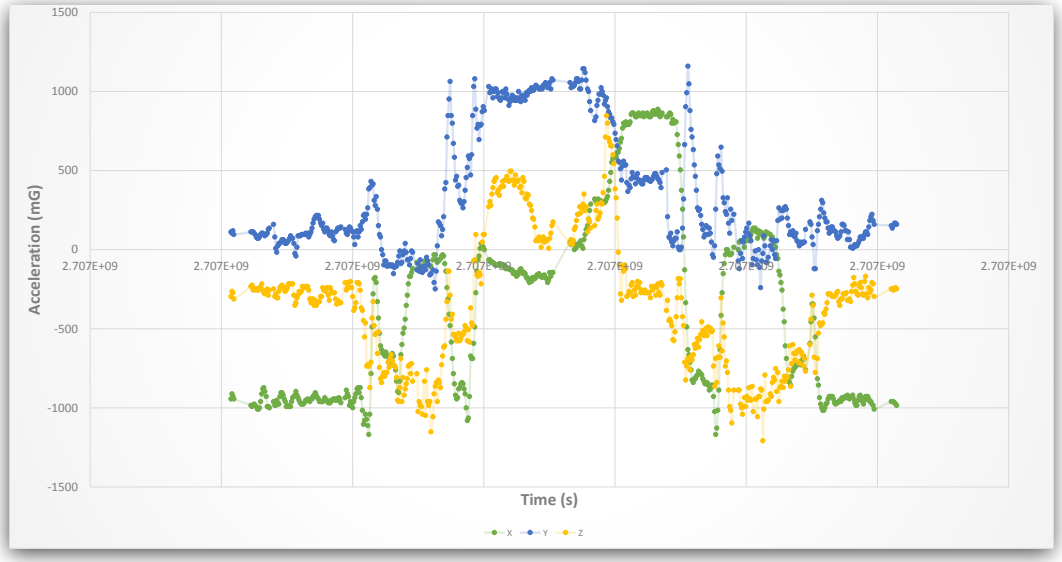



- Real time recordings of wrist actigraphy and medication administration times reflected in the electronic health record

# Taking Meds

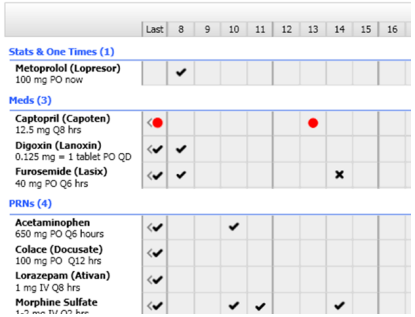


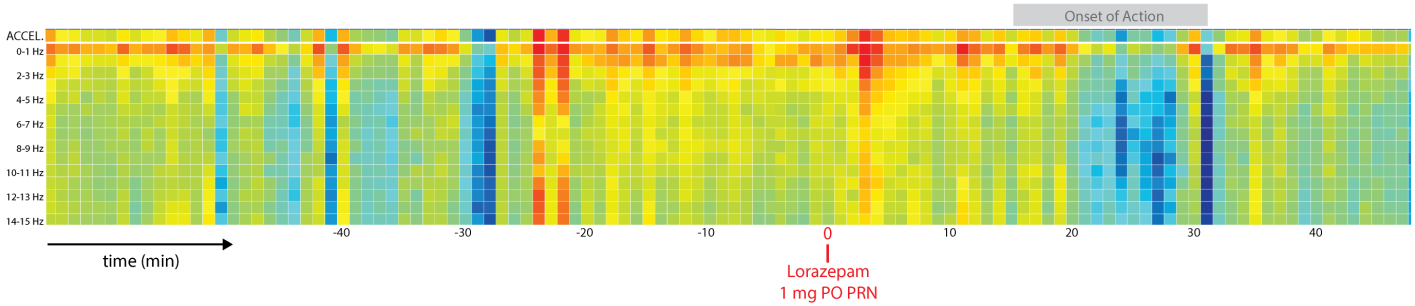

Lorazepam 1mg PO

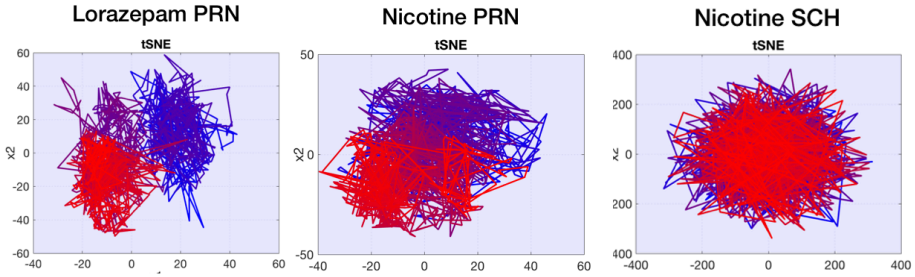


## Device

## EMR

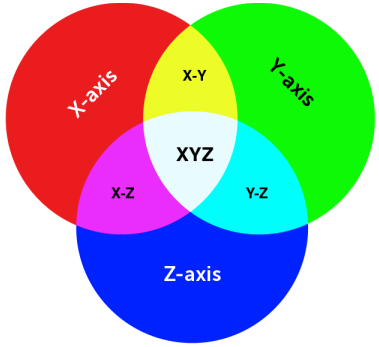


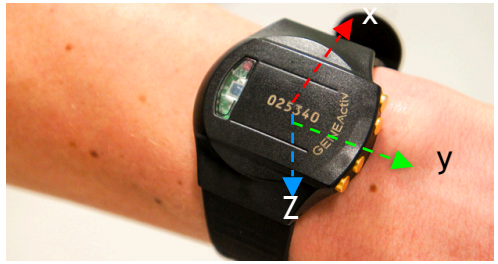



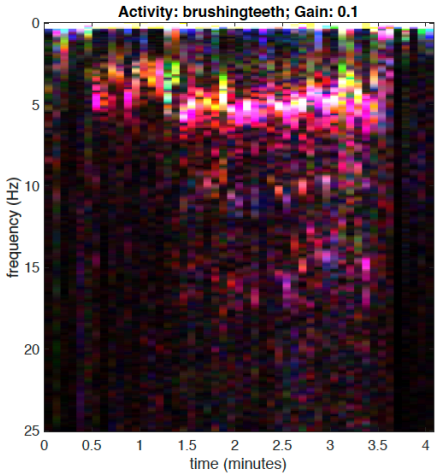



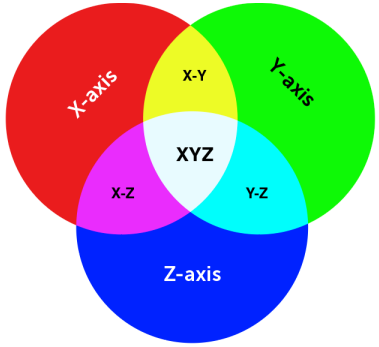

Before

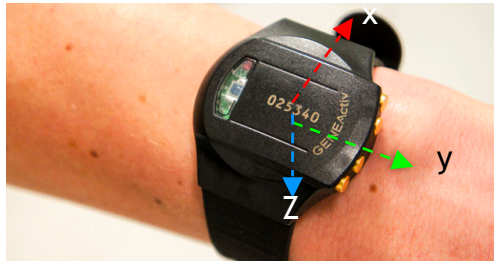
After

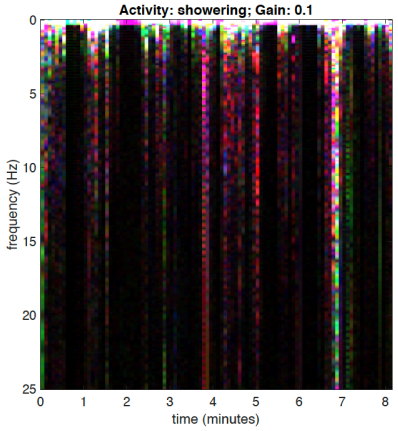

X-axis
Y-axis
Z-axis
X-Y
X-Z
Y-Z
XYZ

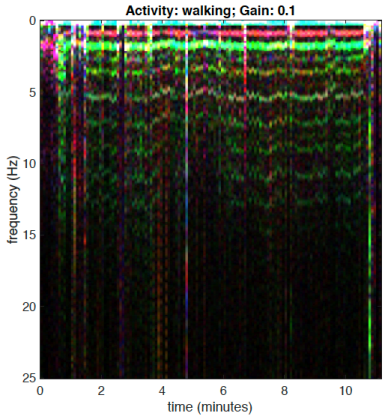

x
y
z
025340
GENEActiv

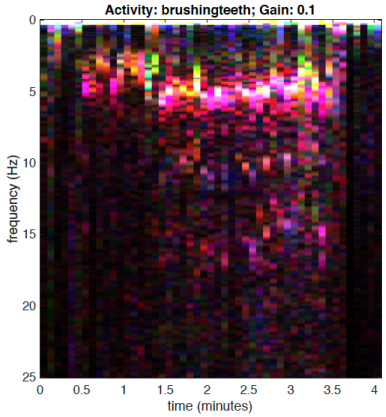

Activity: brushingteeth; Gain: 0.1
frequency (Hz)
time (minutes)
0
5
10
15
20
25
0
0.5
1
1.5
2
2.5
3
3.5
4

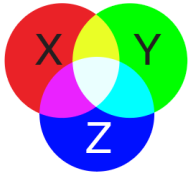

X-axis
Y-axis
Z-axis
X-Y
X-Z
Y-Z
XYZ


x
y
z
025340
GENEActiv


Activity: showering; Gain: 0.1
frequency (Hz)
time (minutes)

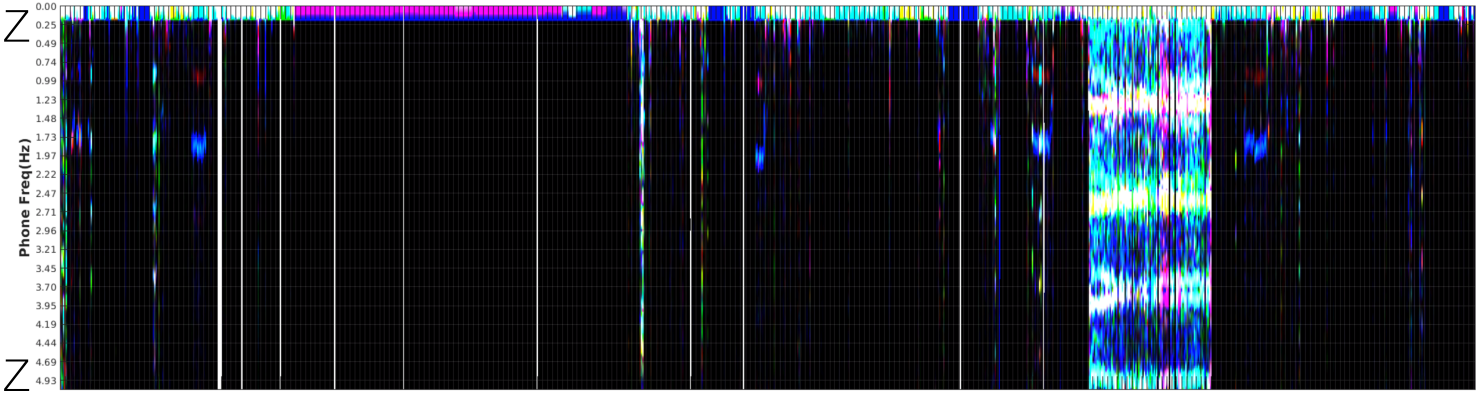

Activity: walking; Gain: 0.1
frequency (Hz)
time (minutes)


Activity: brushingteeth; Gain: 0.1
frequency (Hz)
time (minutes)

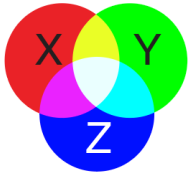



# Power Spectral Density of Human Movement over 24 hours

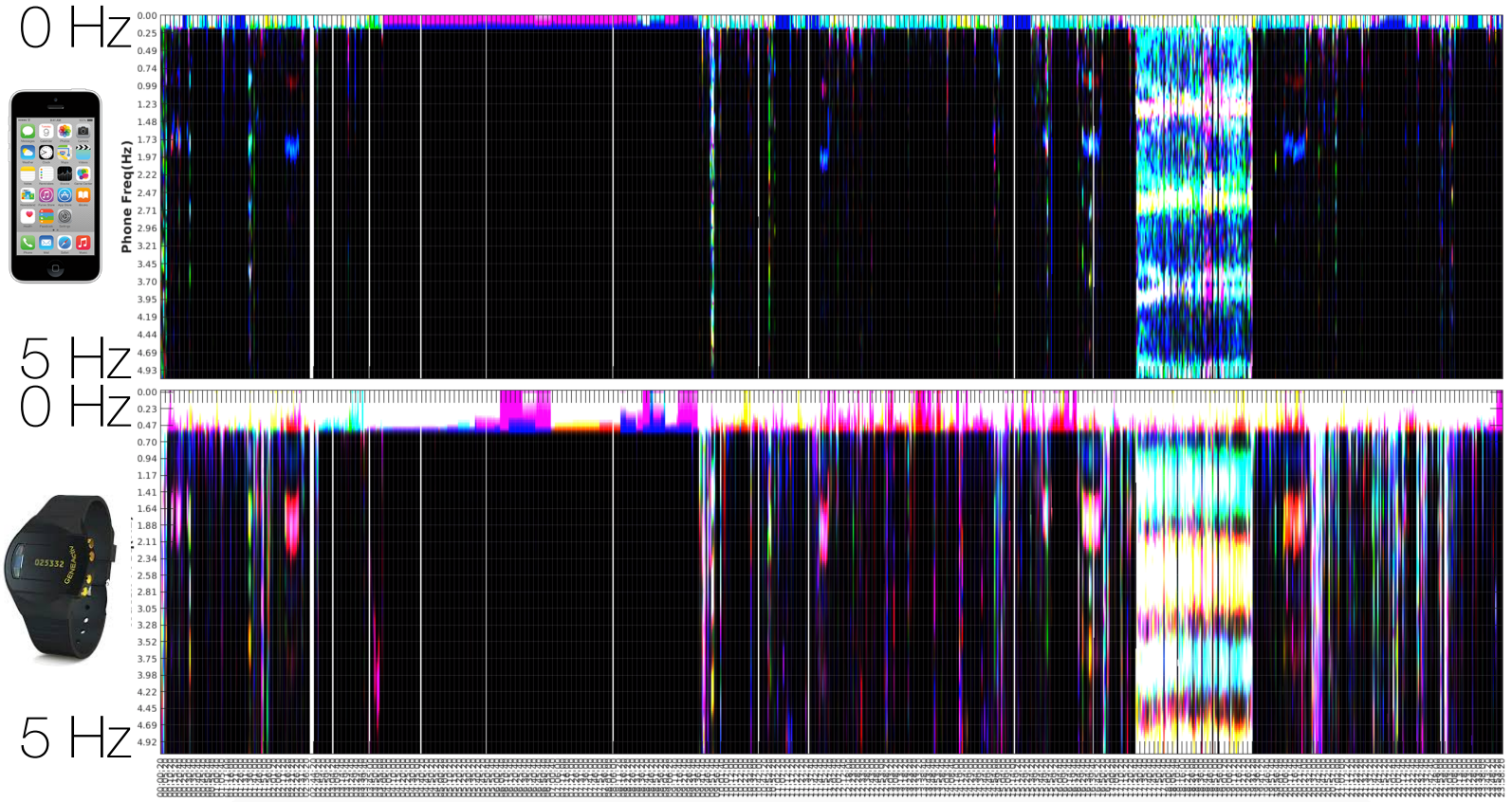
0 Hz

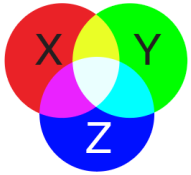



5 Hz




# Power Spectral Density of Human Movement over 24 hours



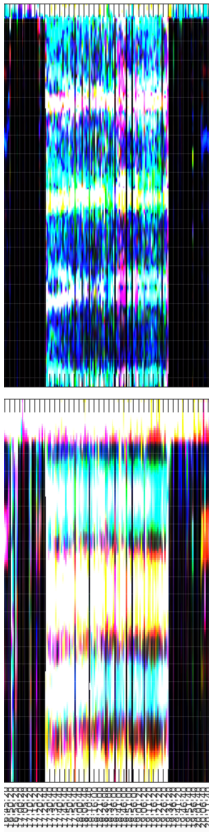


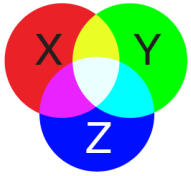

# Power Spectral Density of Human Movement over 24 hours

0 Hz

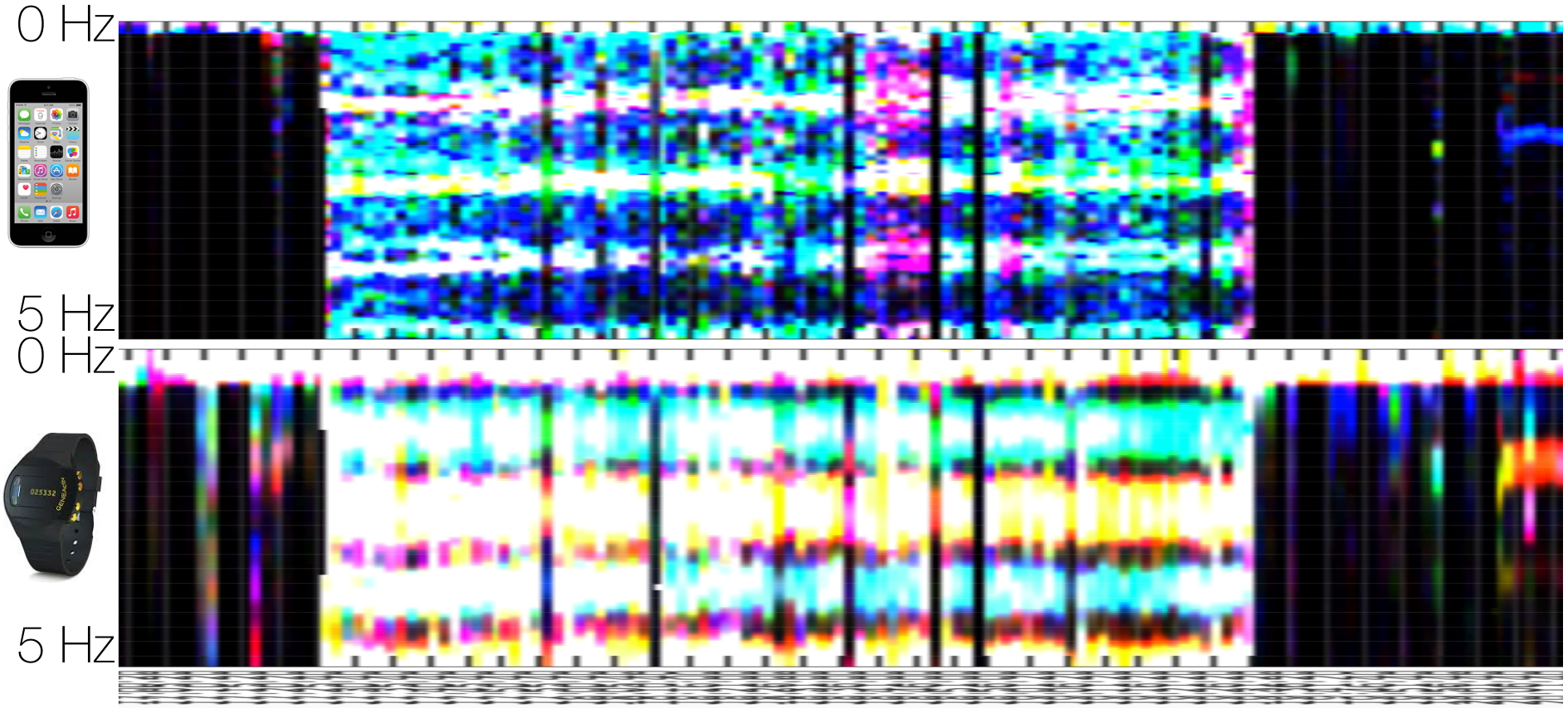
5 Hz
0 Hz

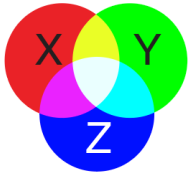
5 Hz






# Power Spectral Density of Human Movement over 24 Min



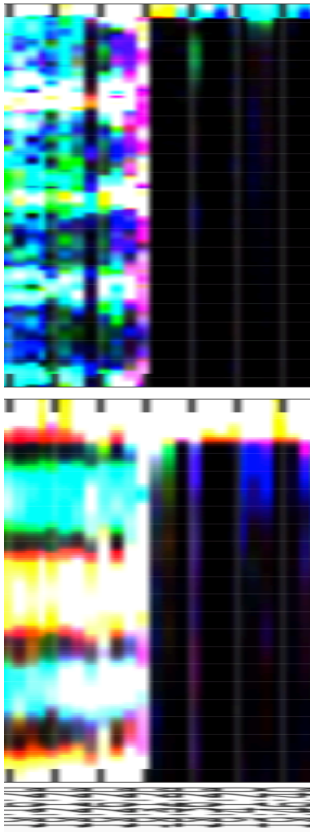


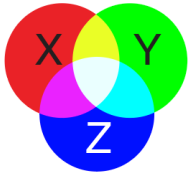

# Power Spectral Density of Human Movement over 24 Min

0 Hz

5 Hz
0 Hz

5 Hz



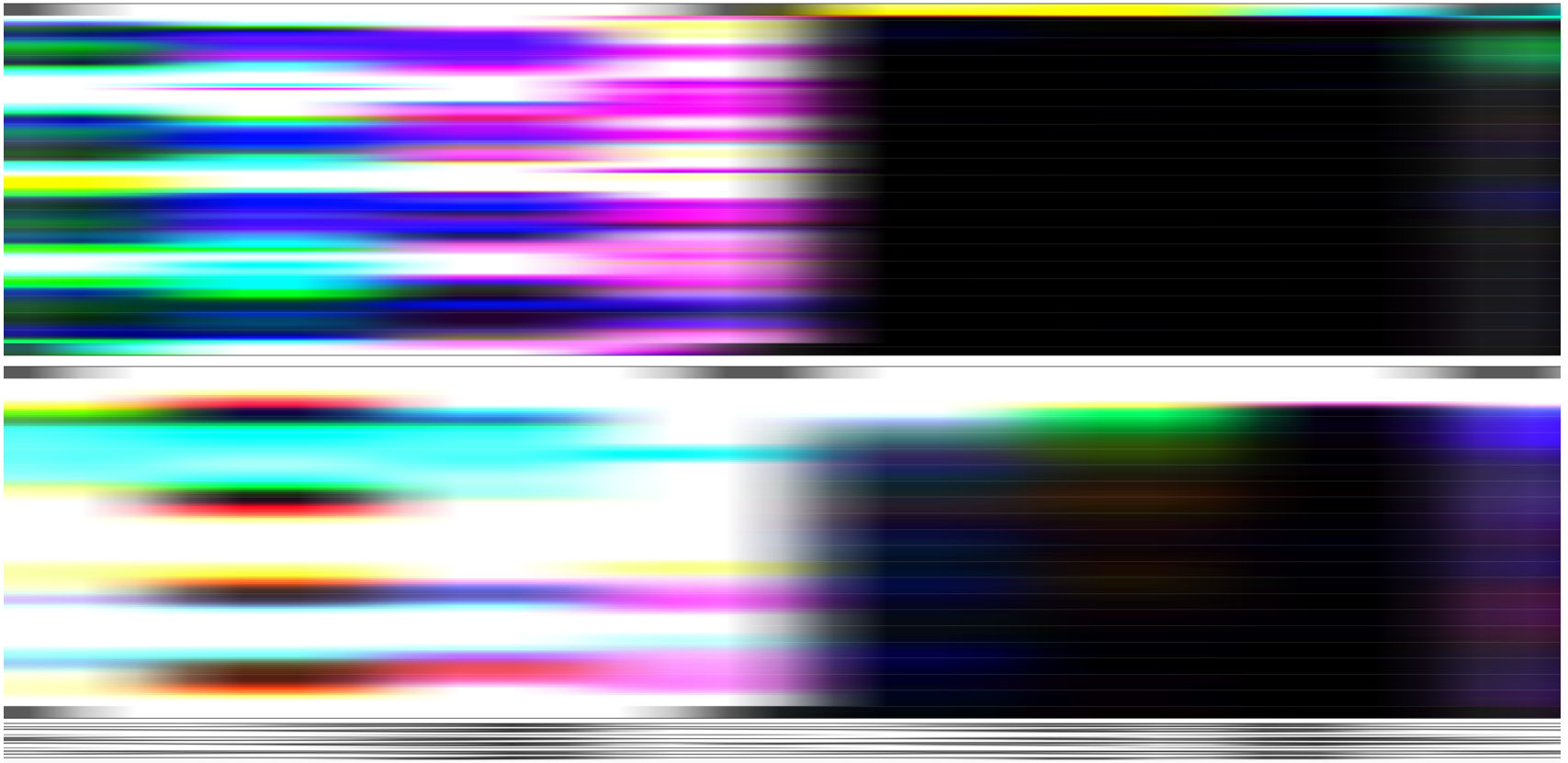


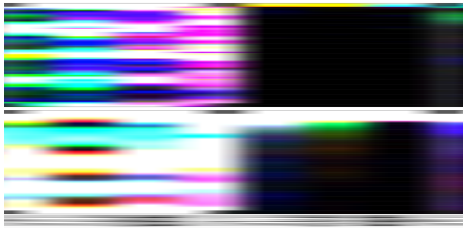

# Power Spectral Density of Human Movement over 3 min

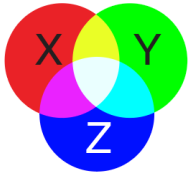
0 Hz

5 Hz
0 Hz

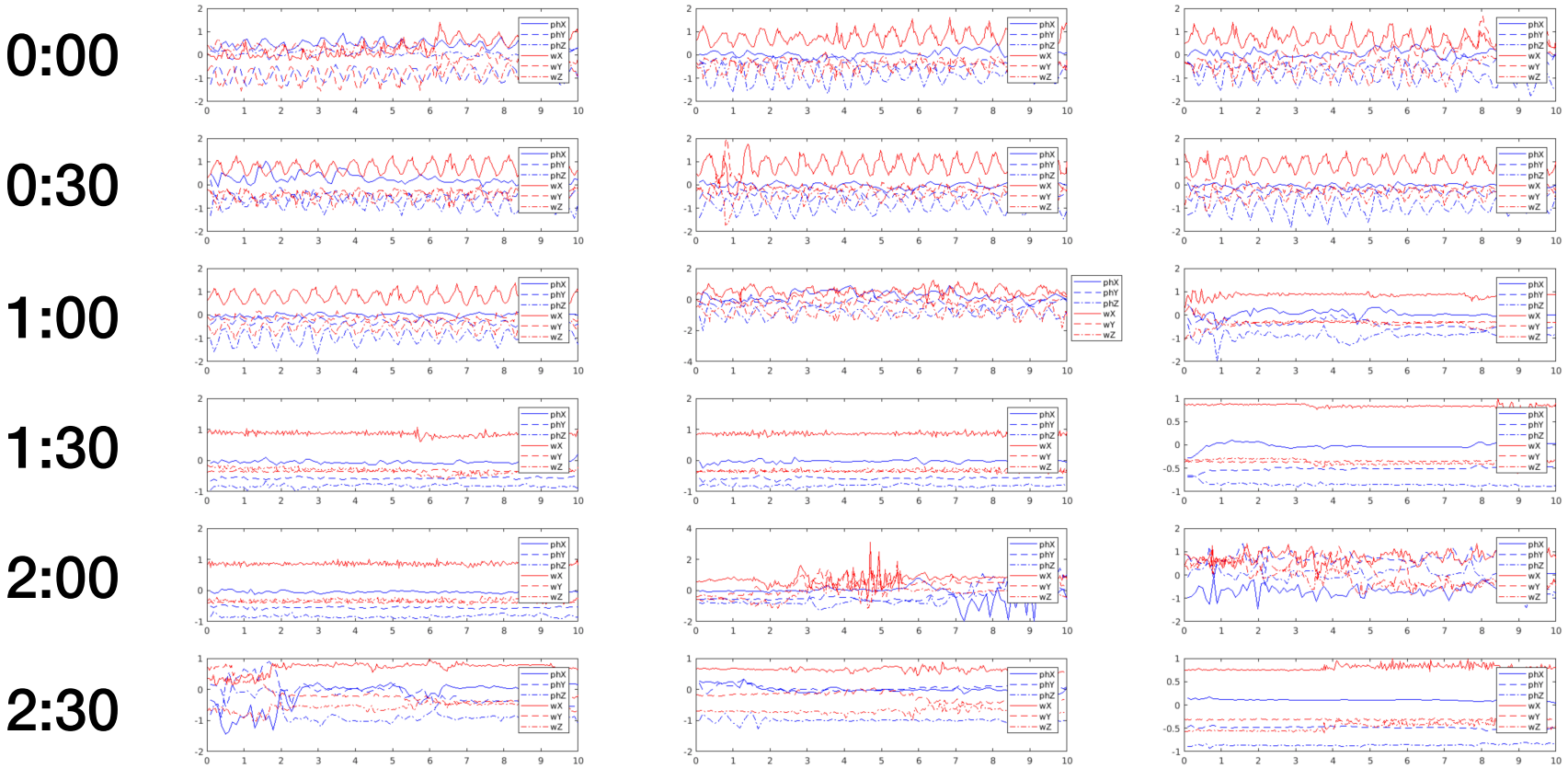
5 Hz



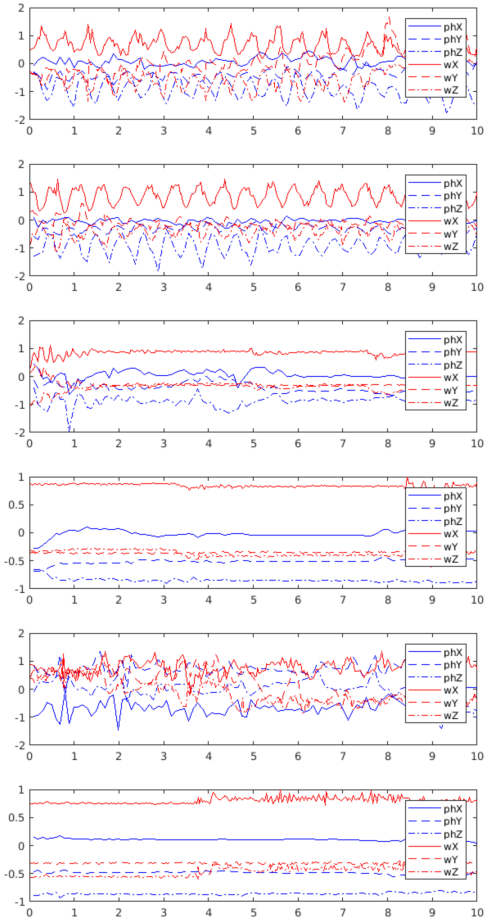




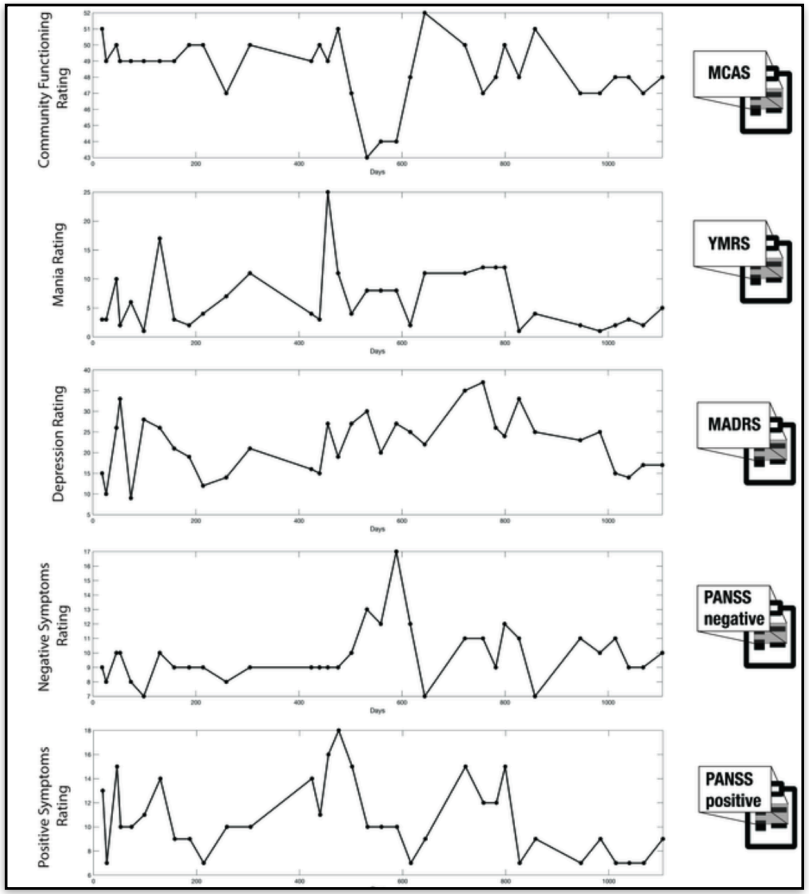

# Power Spectral Density and Raw Accelerometry over 3 minutes as Exercise Epoch is Ending



# Using **Behavioral Variation** to Understand the Brain and Disease

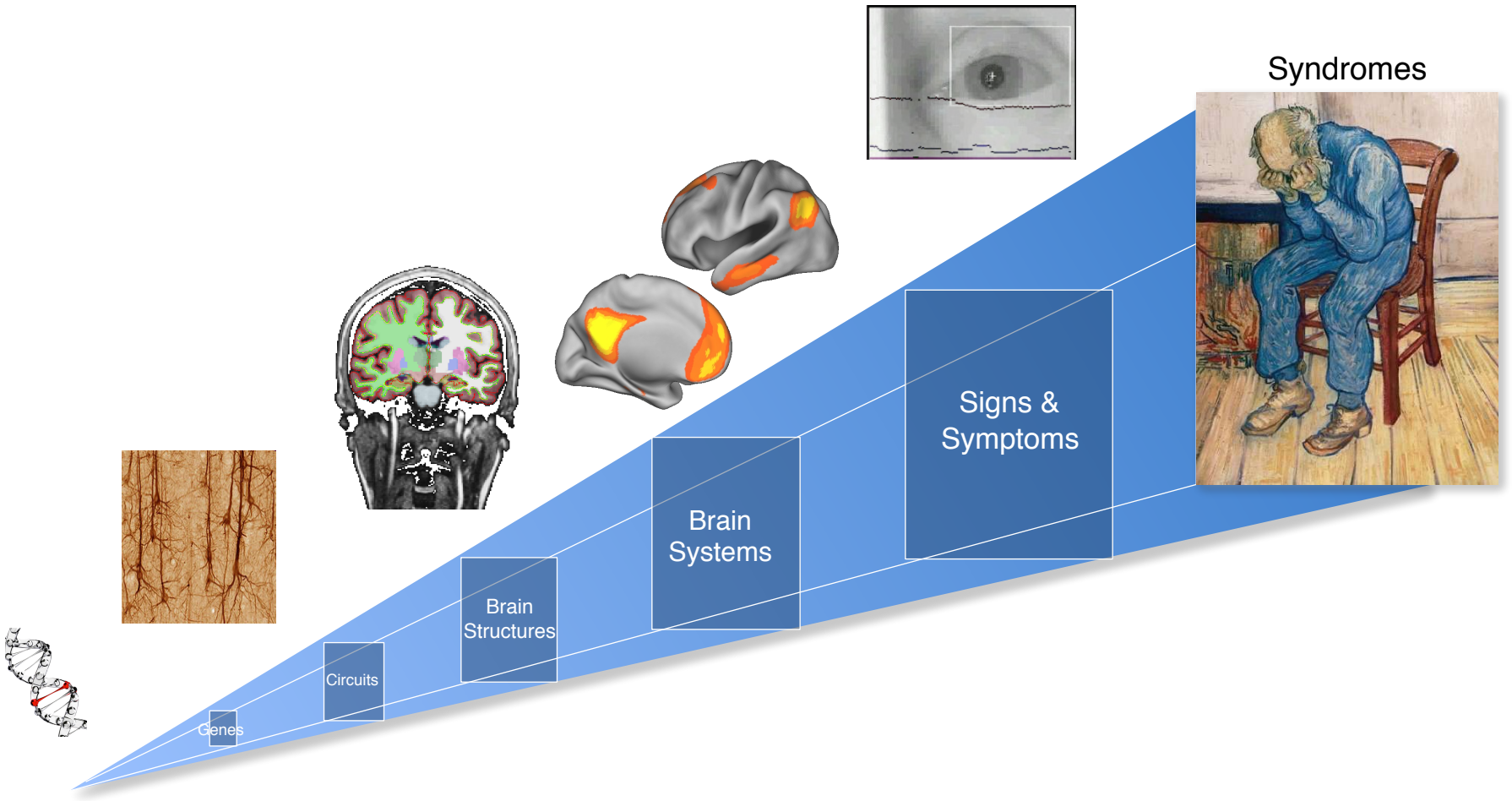



10 seconds of behavioral changes

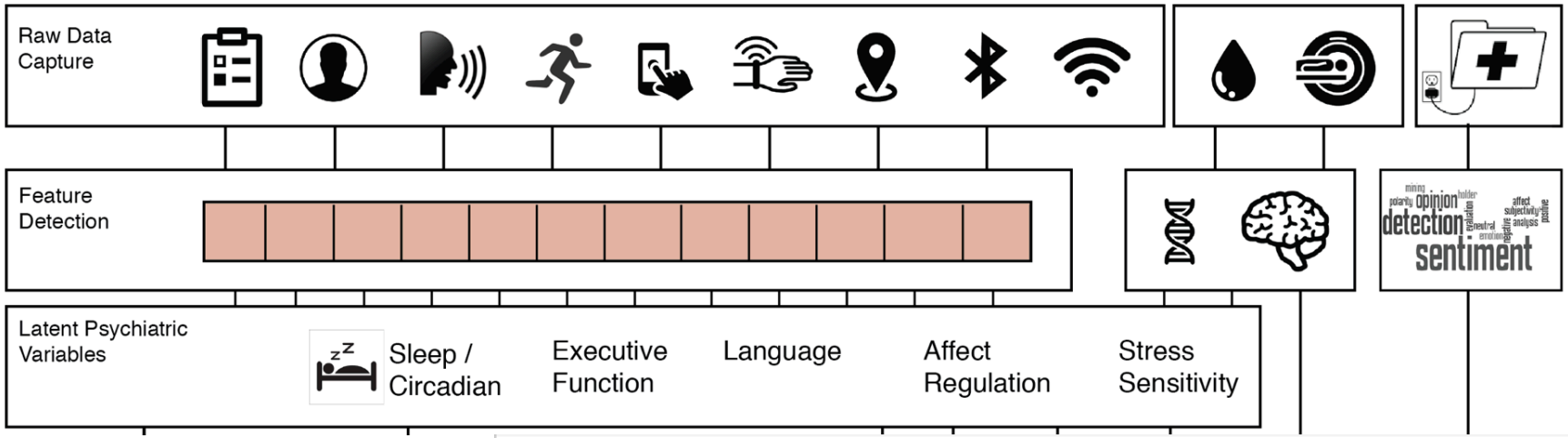


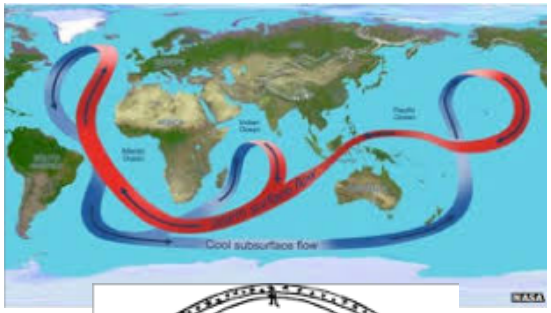

1000 days of behavioral changes

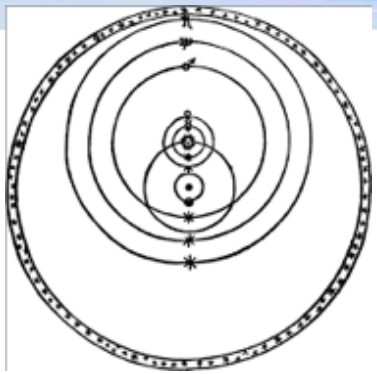
# Using **Behavioral Variation** to Understand the Brain and Disease



# Latent Variable Approach to Psychiatric Construct Definition



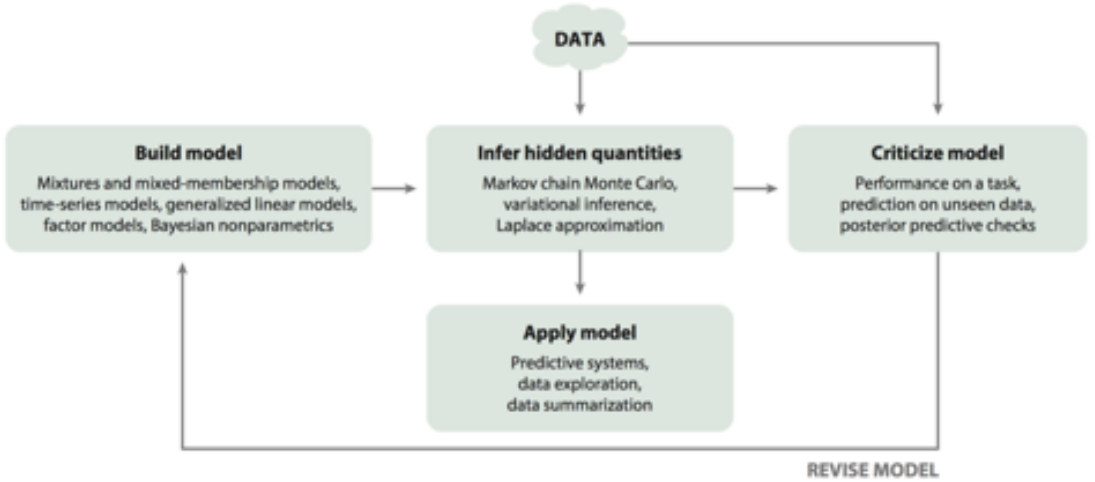



**Figure 1**

Box's loop. Building and computing with models are part of an iterative process for solving data-analysis problems. This is Box's loop, a modern interpretation of the perspective of Box (1976).

# Questions?

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