Precision Psychiatry, A Vision for the Future

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Massachusetts General Hospital

First Annual Conference on
Precision Psychiatry

October 1, 2021

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National Institute of Mental Health

Agenda

- Re-examining Our Frameworks
- A Framework for the Future
- How Can We Get There?

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- Re-examining Our Frameworks
  - Theory-Driven vs Data-Driven
  - Diagnoses → Symptoms
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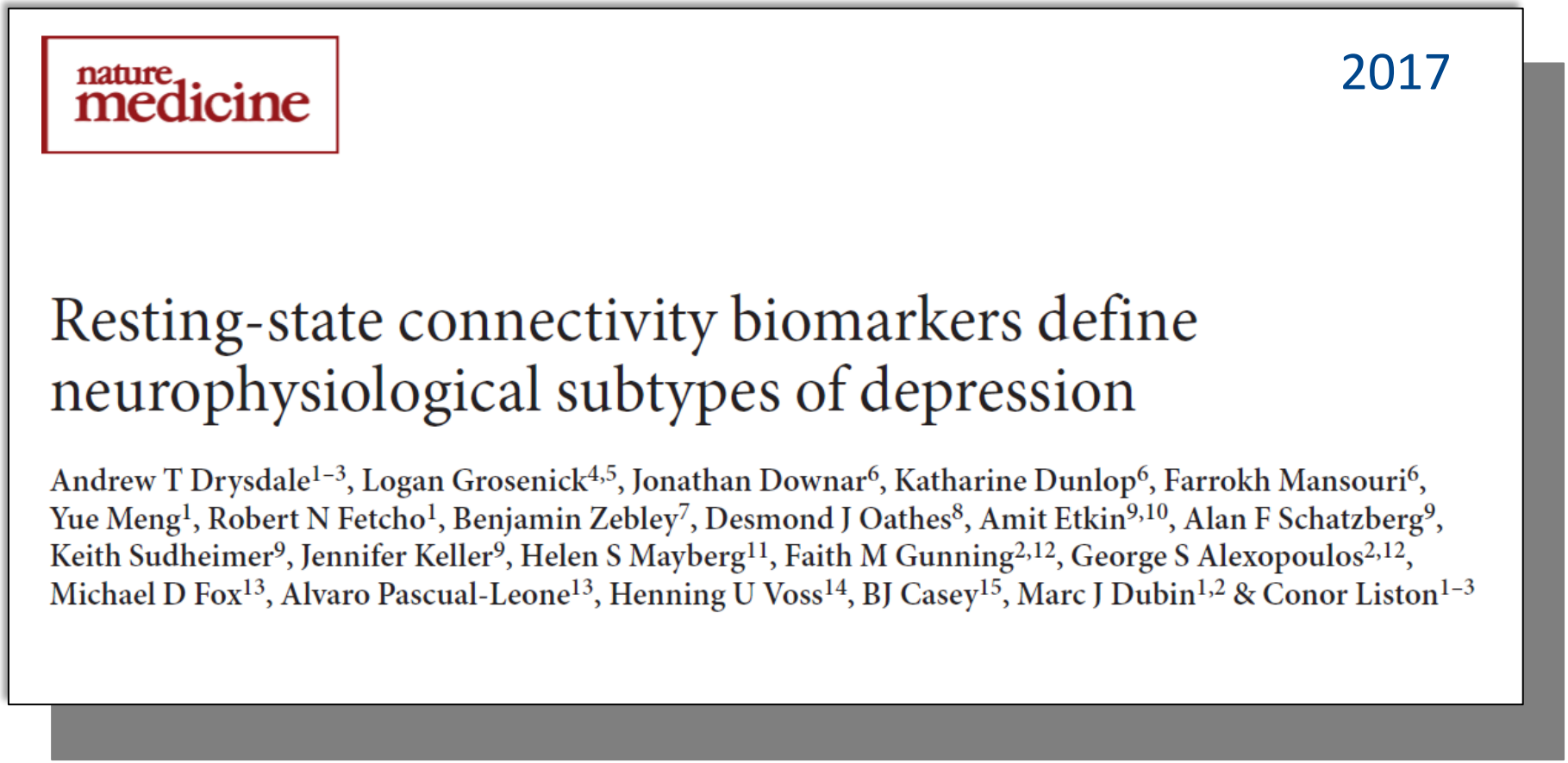
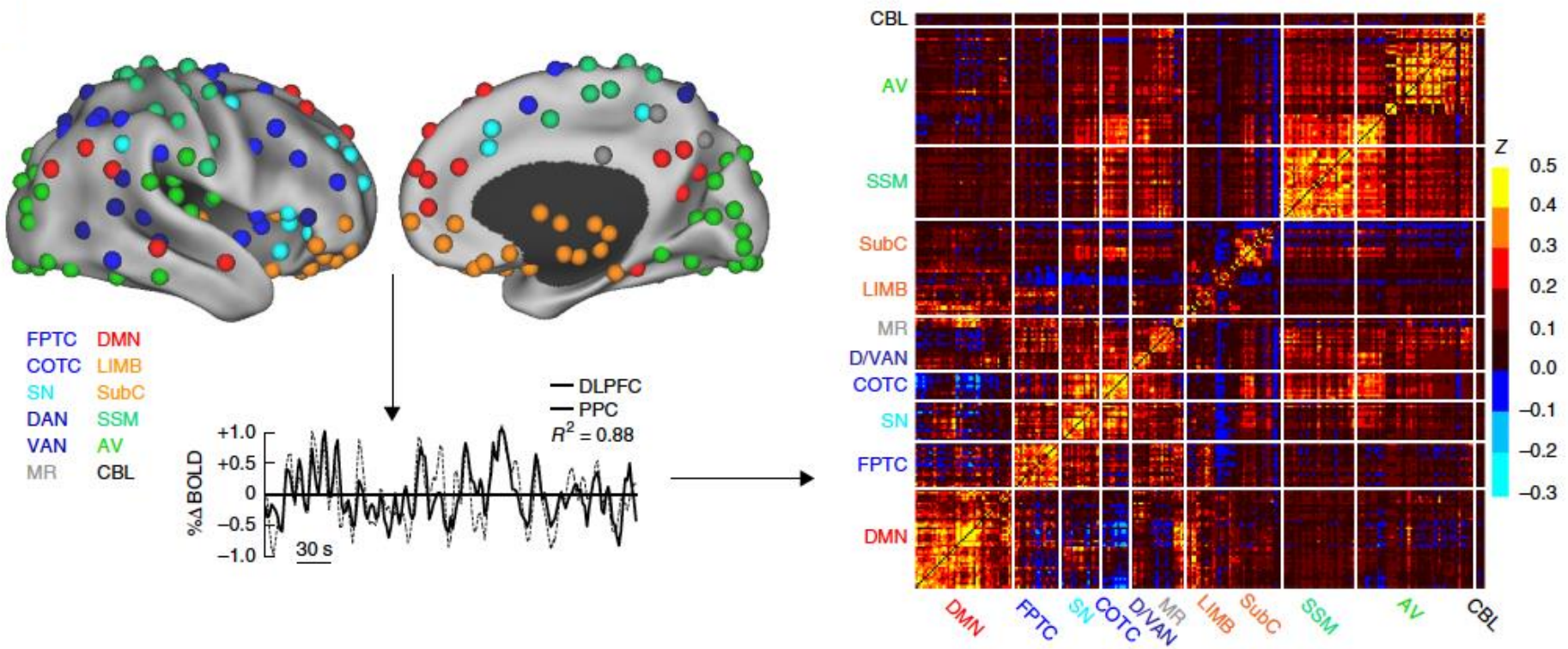
Data-Driven Approaches to Precision Psychiatry

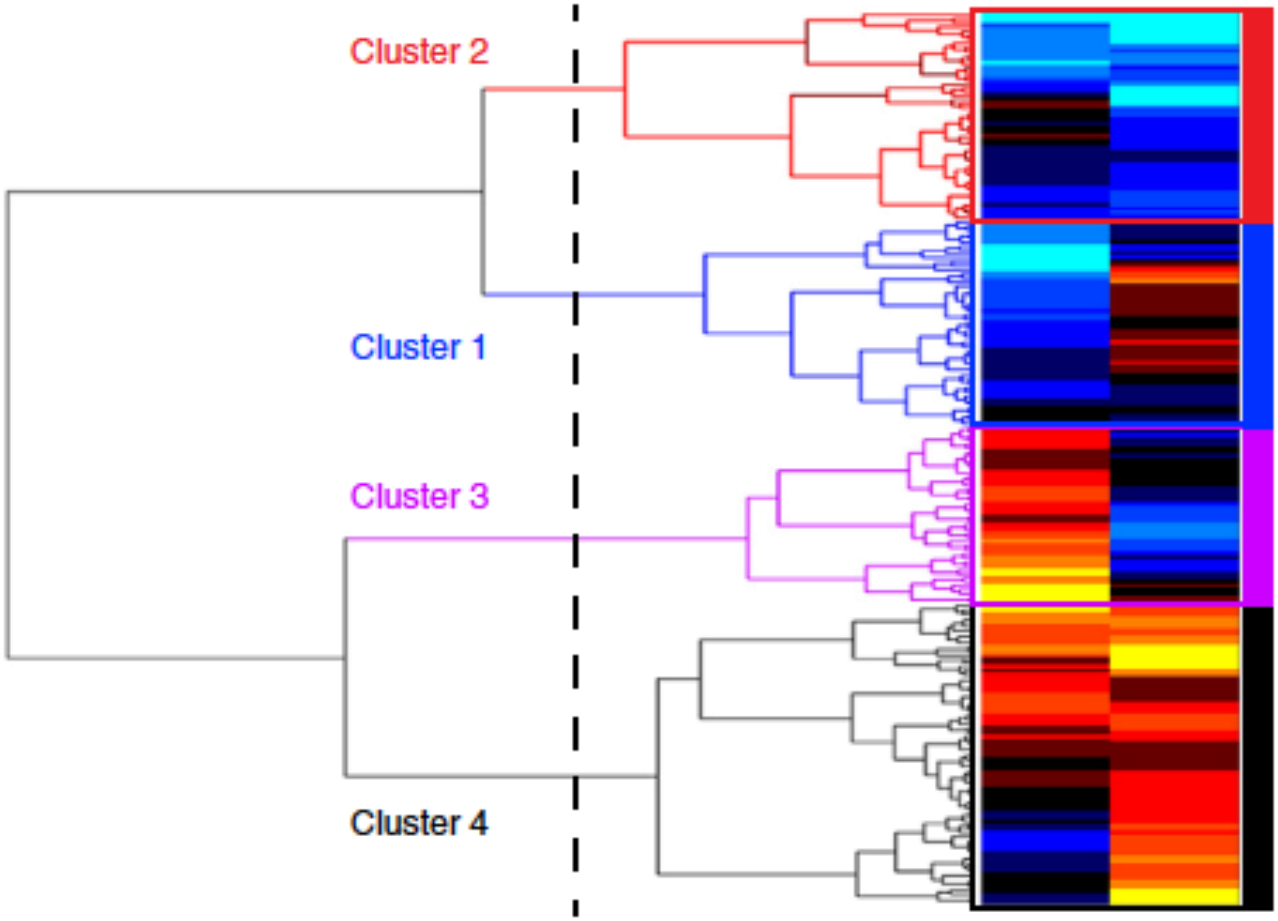


Patterns of Resting State Connectivity



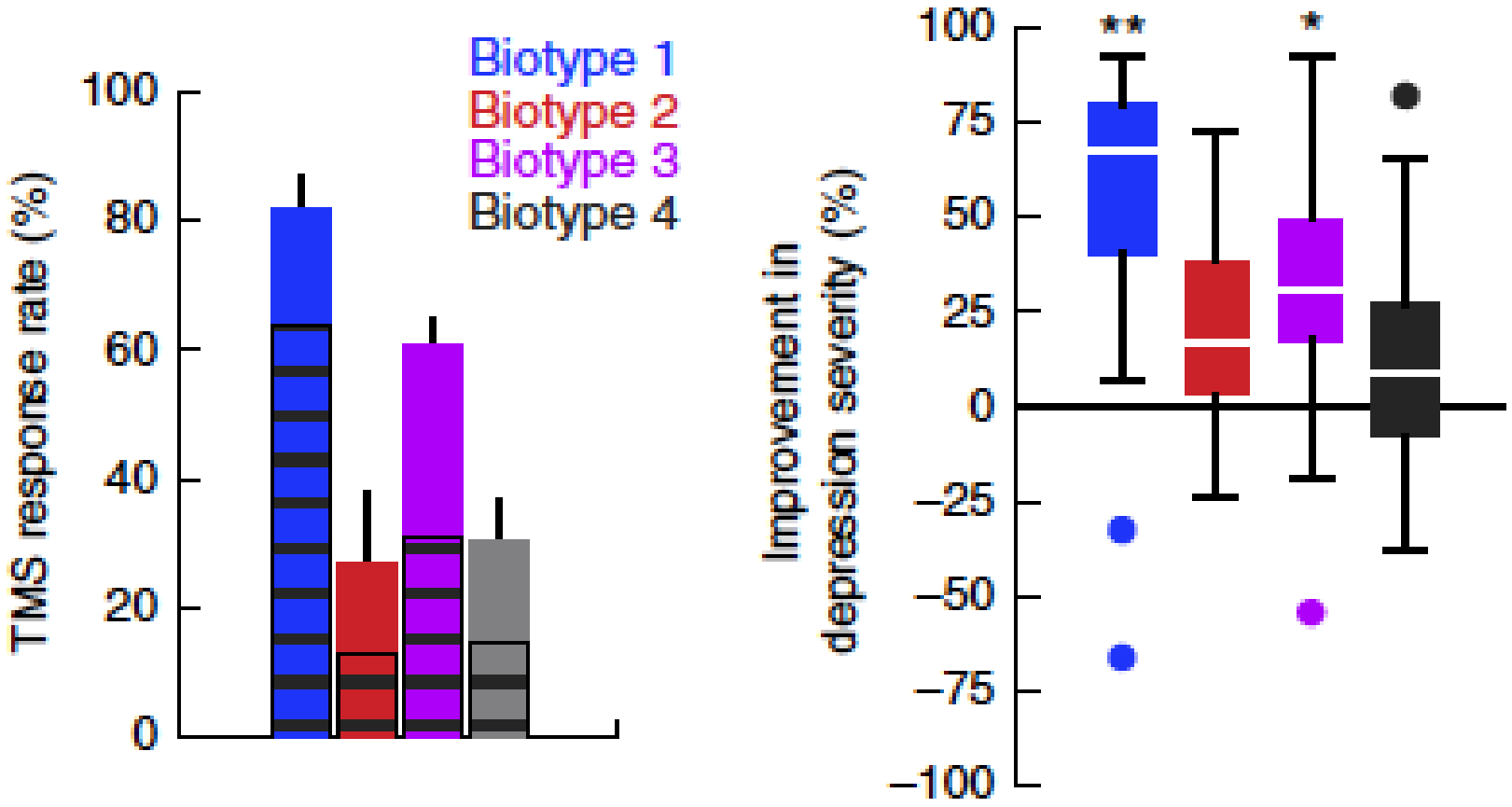
Drysdale et al., *Nature Medicine*, 2017

Clustering Patients Based on Connectivity



Drysdale et al., *Nature Medicine*, 2017

Subtypes Differ in Responsivity to Prefrontal Cortex Repetitive Transcranial Magnetic Stimulation



Drysdale et al., *Nature Medicine*, 2017

Theory-Driven Approaches to Clinical Psychiatry

2017

JAMA Psychiatry | Original Investigation

Association of Neural and Emotional Impacts of Reward Prediction Errors With Major Depression

Robb B. Rutledge, PhD; Michael Moutoussis, PhD; Peter Smittenaar, PhD; Peter Zeidman, PhD; Tanja Taylor, PhD; Louise Hrynkiewicz, BSc; Jordan Lam, BSc; Nikolina Skandali, MSc; Jenifer Z. Siegel, MSc; Olga T. Ousdal, MD, PhD; Gita Prabhu, PhD; Peter Dayan, PhD; Peter Fonagy, PhD; Raymond J. Dolan, FRS, MD

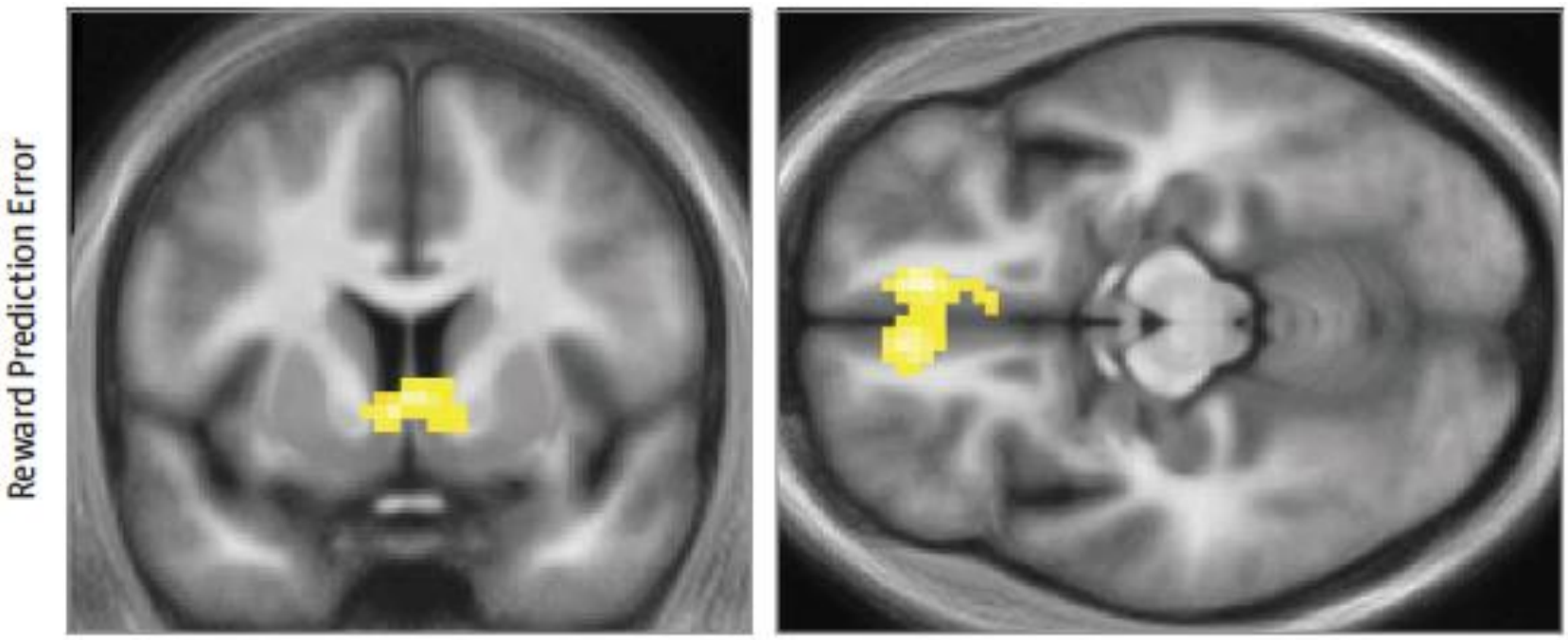
Breaking Down Behavior

$$\text{Happiness}(t) = w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j} CR_j + w_2 \sum_{j=1}^{t} \gamma^{t-j} EV_j + w_3 \sum_{j=1}^{t} \gamma^{t-j} RPE_j$$

- baseline happiness
- past rewards
- expected values
- reward prediction error

Rutledge et al., *JAMA Psychiatry*, 2017

Breaking Down Behavior



ventral striatum

medial prefrontal cortex

Rutledge et al., *JAMA Psychiatry*, 2017

Science Highlight

The American Journal of Psychiatry

2018

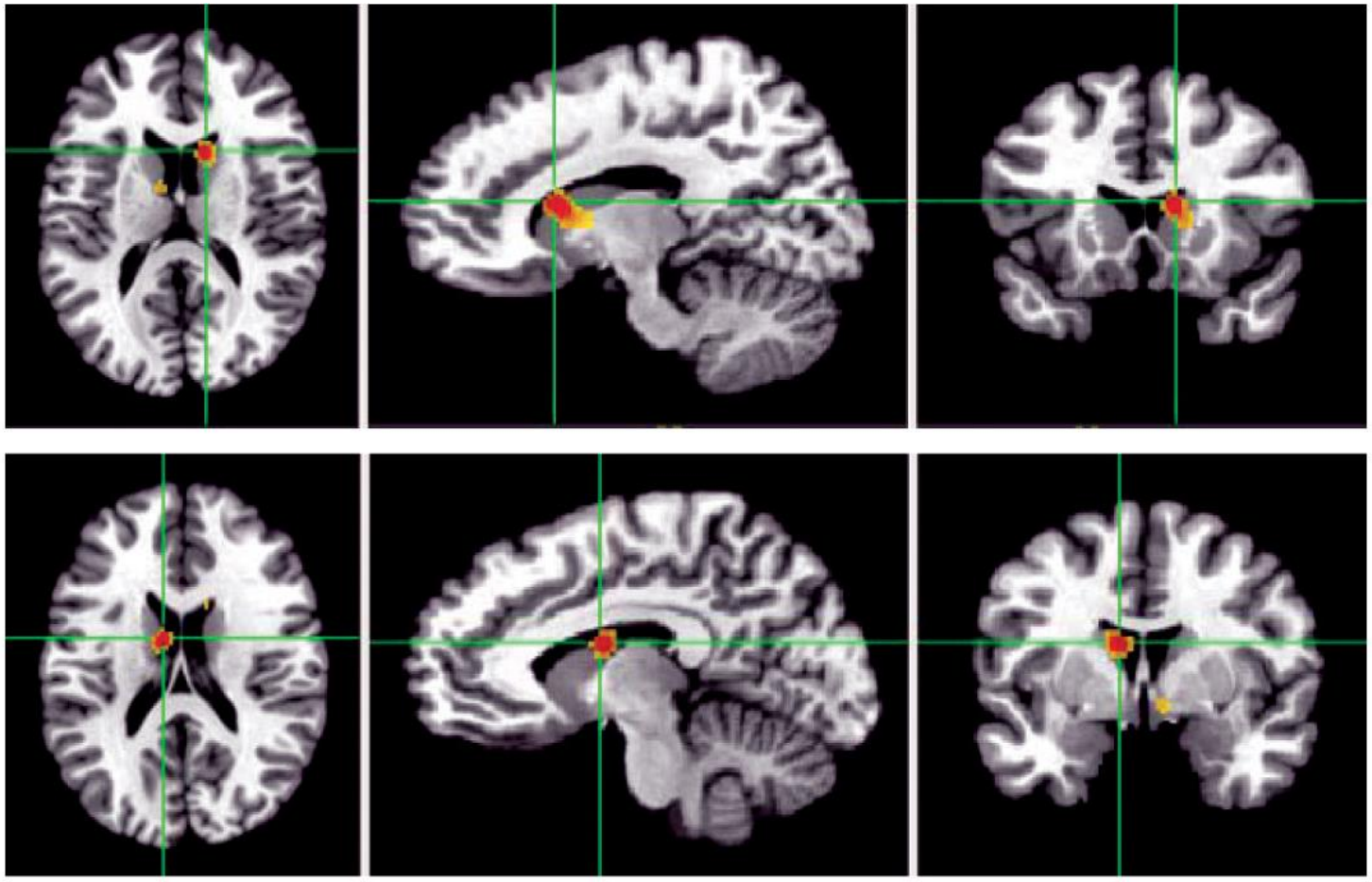
Reward Processing in Depression: A Conceptual and Meta-Analytic Review Across fMRI and EEG Studies

Hanna Keren, Ph.D., Georgia O'Callaghan, Ph.D., Pablo Vidal-Ribas, M.Sc., George A. Buzzell, Ph.D., Melissa A. Brotman, Ph.D., Ellen Leibenluft, M.D., Pedro M. Pan, M.D., Ph.D, Liana Meffert, B.Sc., Ariela Kaiser, B.A., Selina Wolke, M.Sc., Daniel S. Pine, M.D., Argyris Stringaris, M.D., Ph.D.

Show Fewer Authors

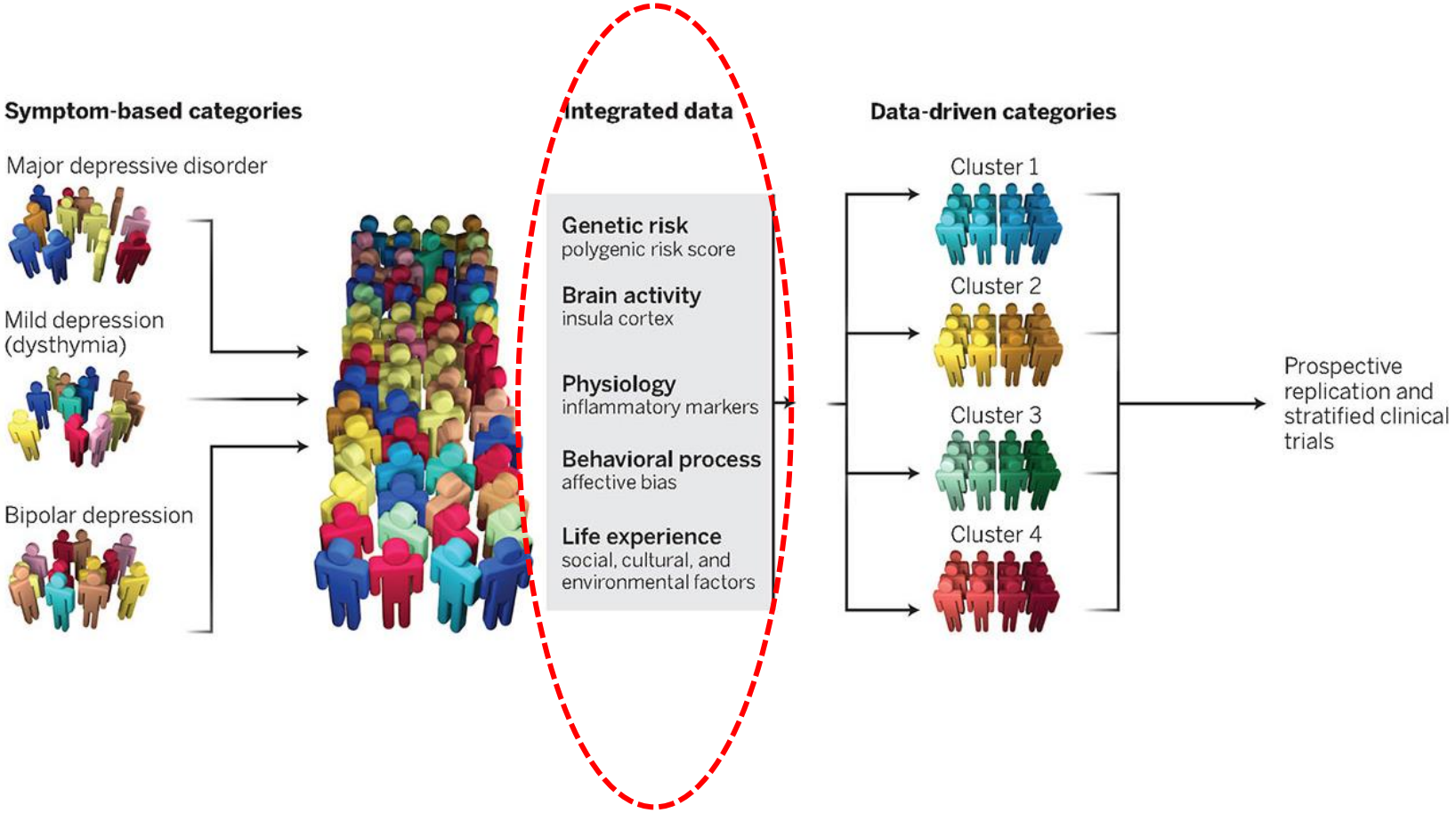
Published Online: 20 Jun 2018 | https://doi.org/10.1176/appi.ajp.2018.17101124

Reward Processing in Depression



Keren et al., *American Journal of Psychiatry*, 2018

Combining Theory- and Data-Driven Approaches



 Insel & Cuthbert, *Science*, 2015

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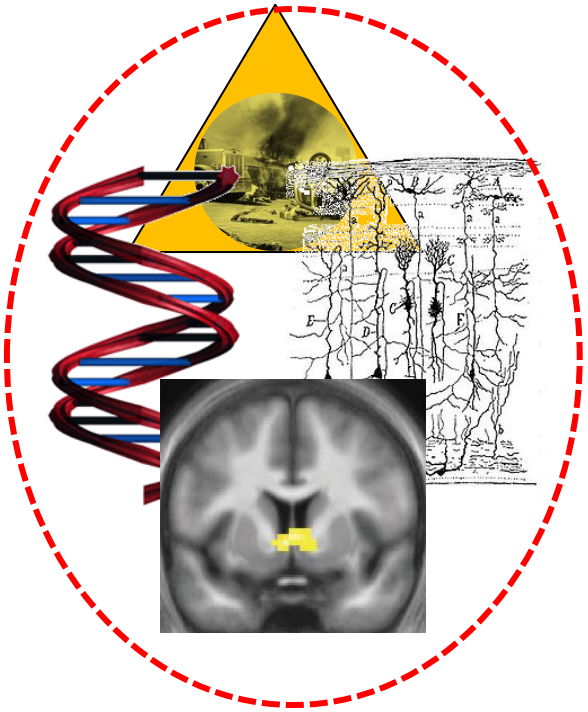
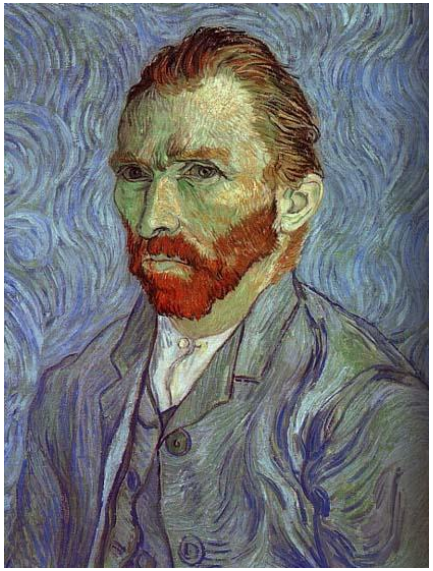
Traditional Diagnostic Framework

Disease

Symptoms



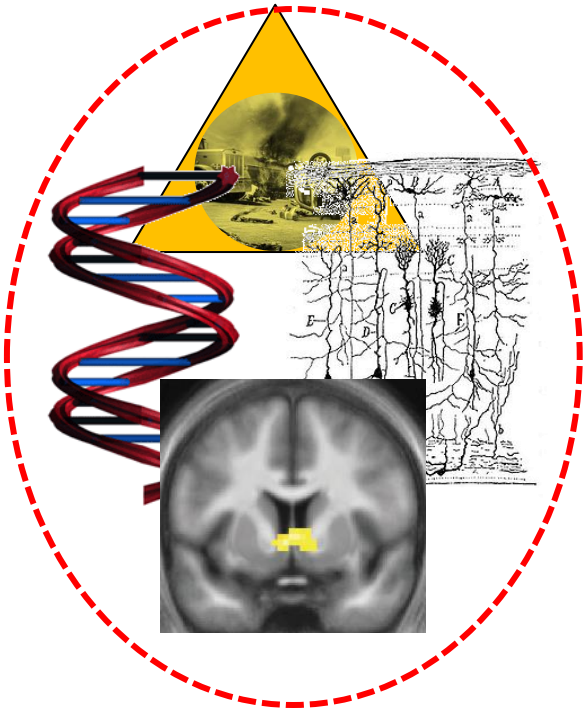


Depression

Mood, Energy,
Concentration, etc.

Research Domain Criteria (RDoC) Framework

Disease

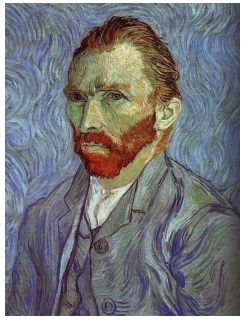


Depression

Transdiagnostic Phenotypes

RDoC
Research Domain Criteria Initiative

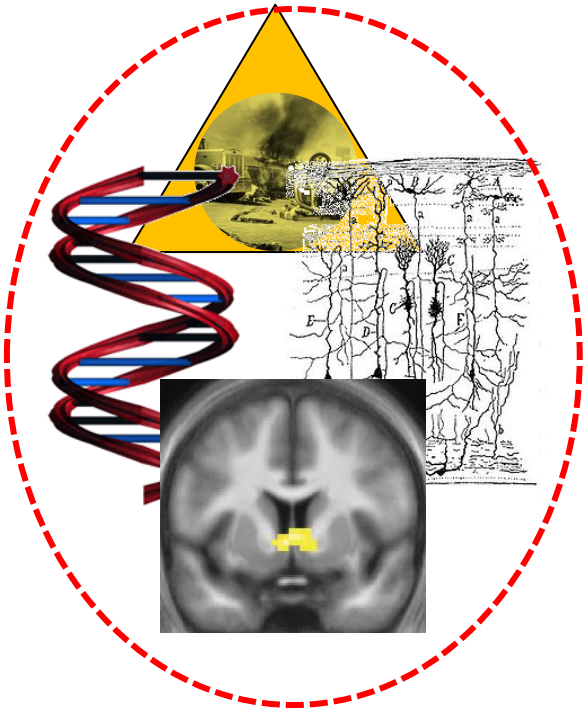
Symptoms



Mood, Energy, Concentration, etc.

Diagnosis as Outcome

Disease



Transdiagnostic Phenotypes

RDoC
Research Domain Criteria Initiative

Symptoms

Mood, Energy, Concentration, etc.

Diagnosis

Depression

NIH National Institute of Mental Health

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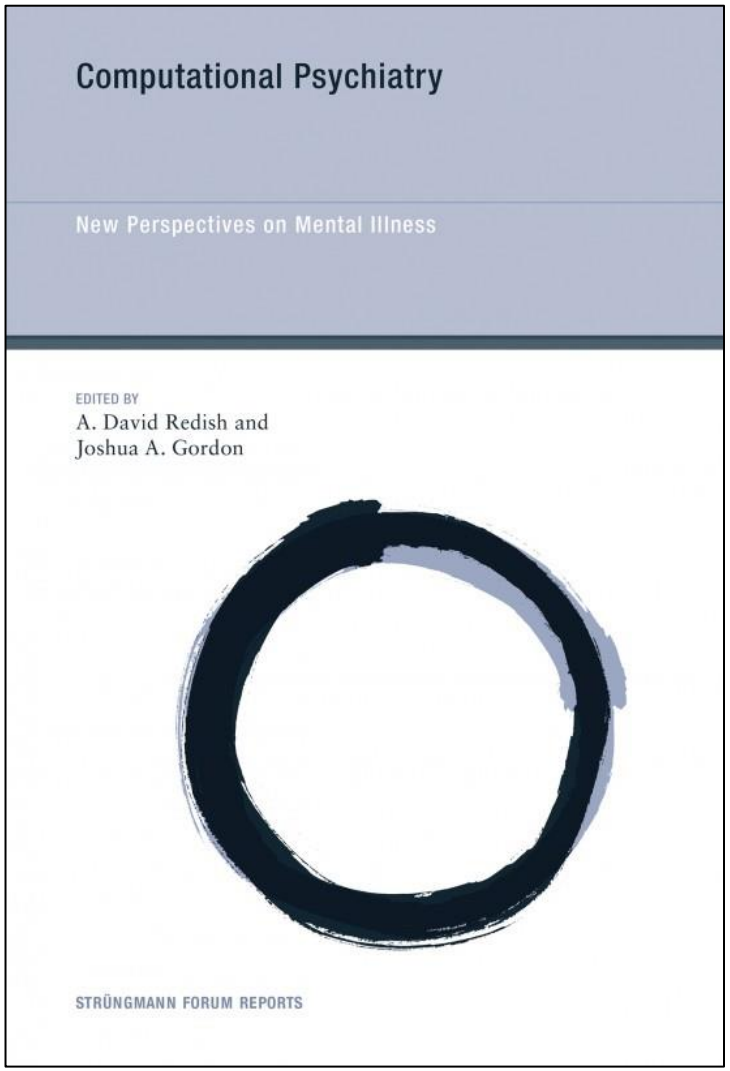
A Bayesian Approach To Precision Psychiatry



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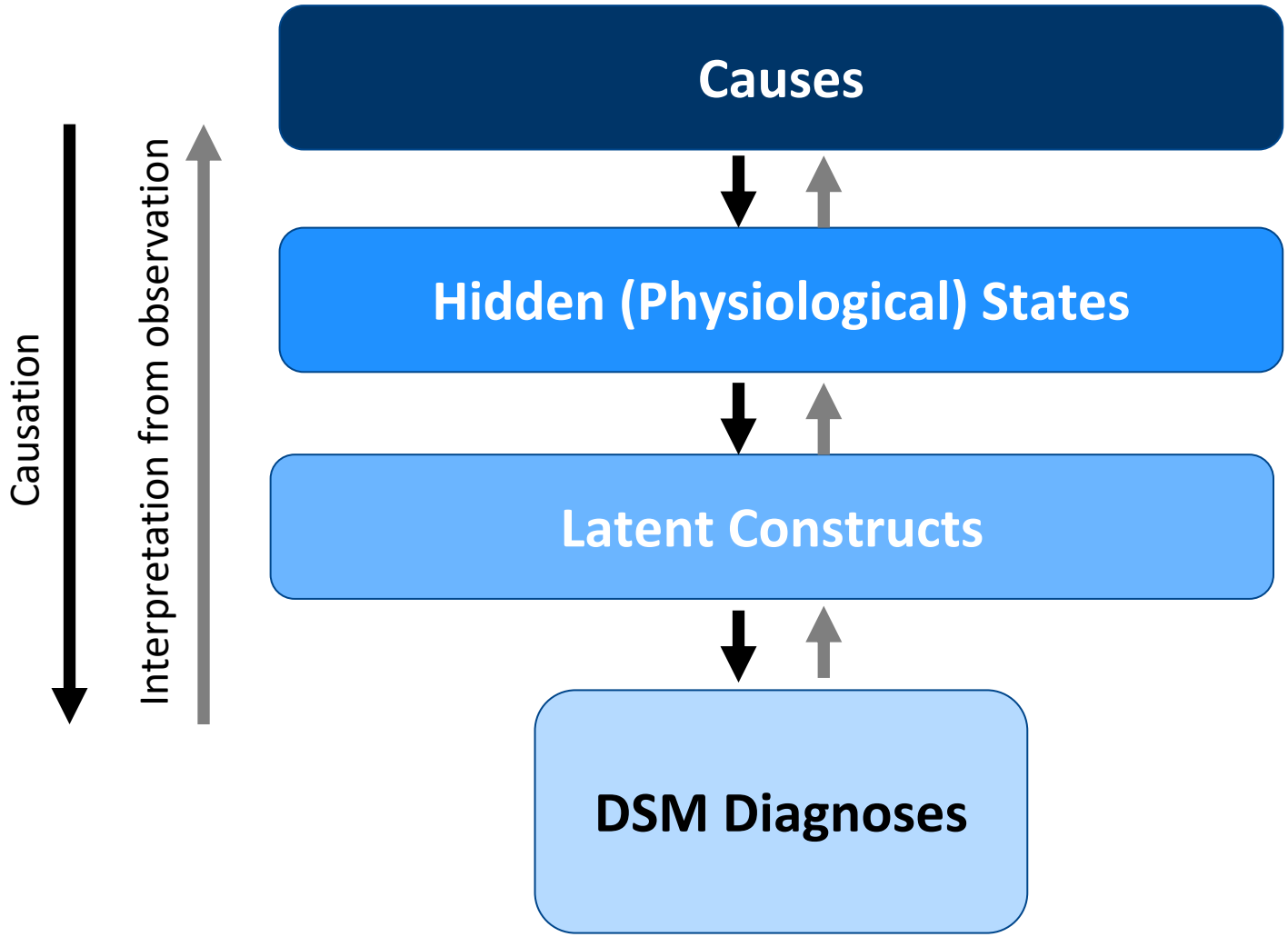
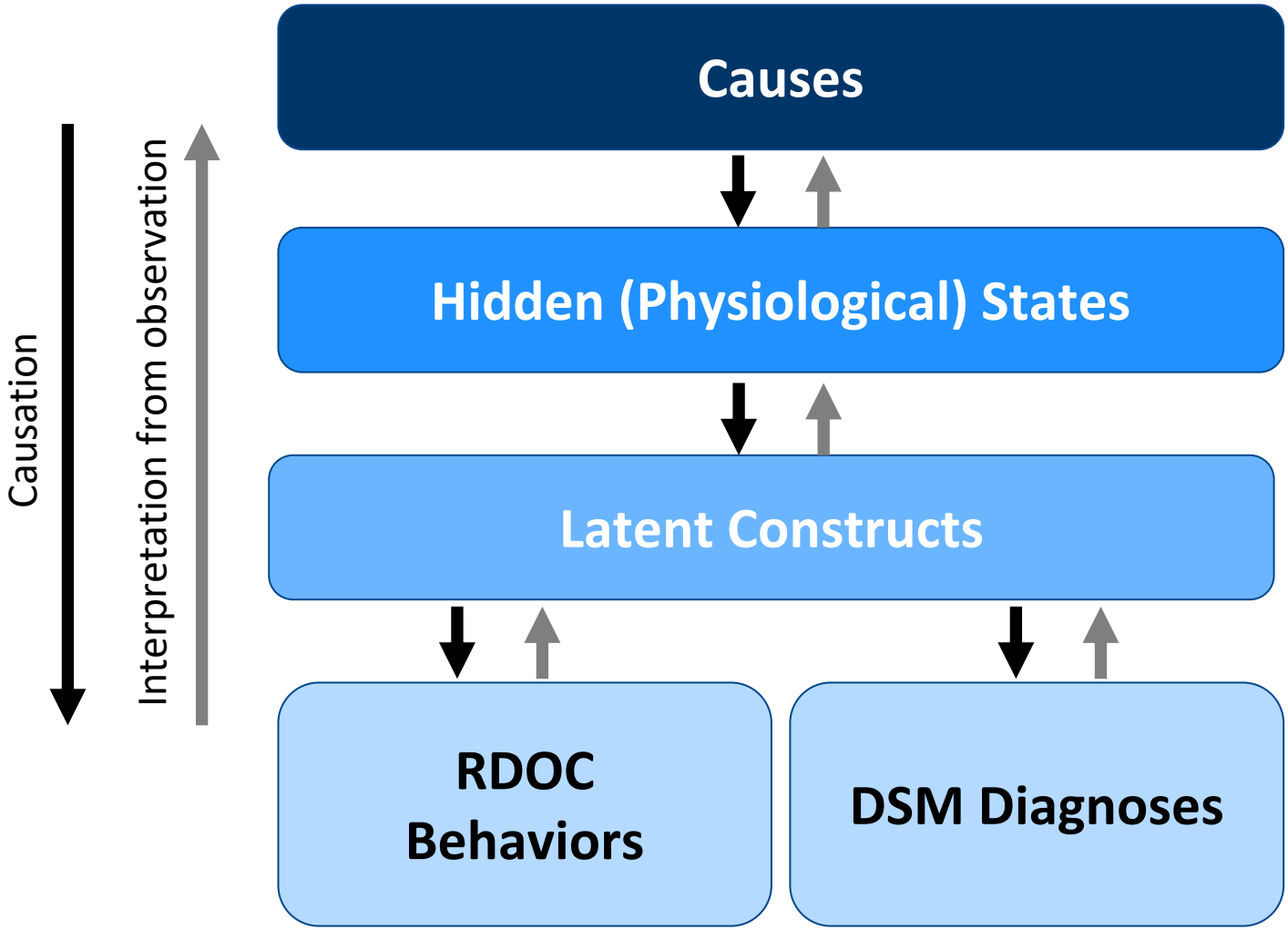
A Novel Framework for Improving Psychiatric Diagnostic Nosology

Shelly B. Flagel, Daniel S. Pine, Susanne E. Ahmari,
Michael B. First, Karl J. Friston,
Christoph Mathys, A. David Redish,
Katharina Schmack, Jordan W. Smoller,
and Anita Thapar

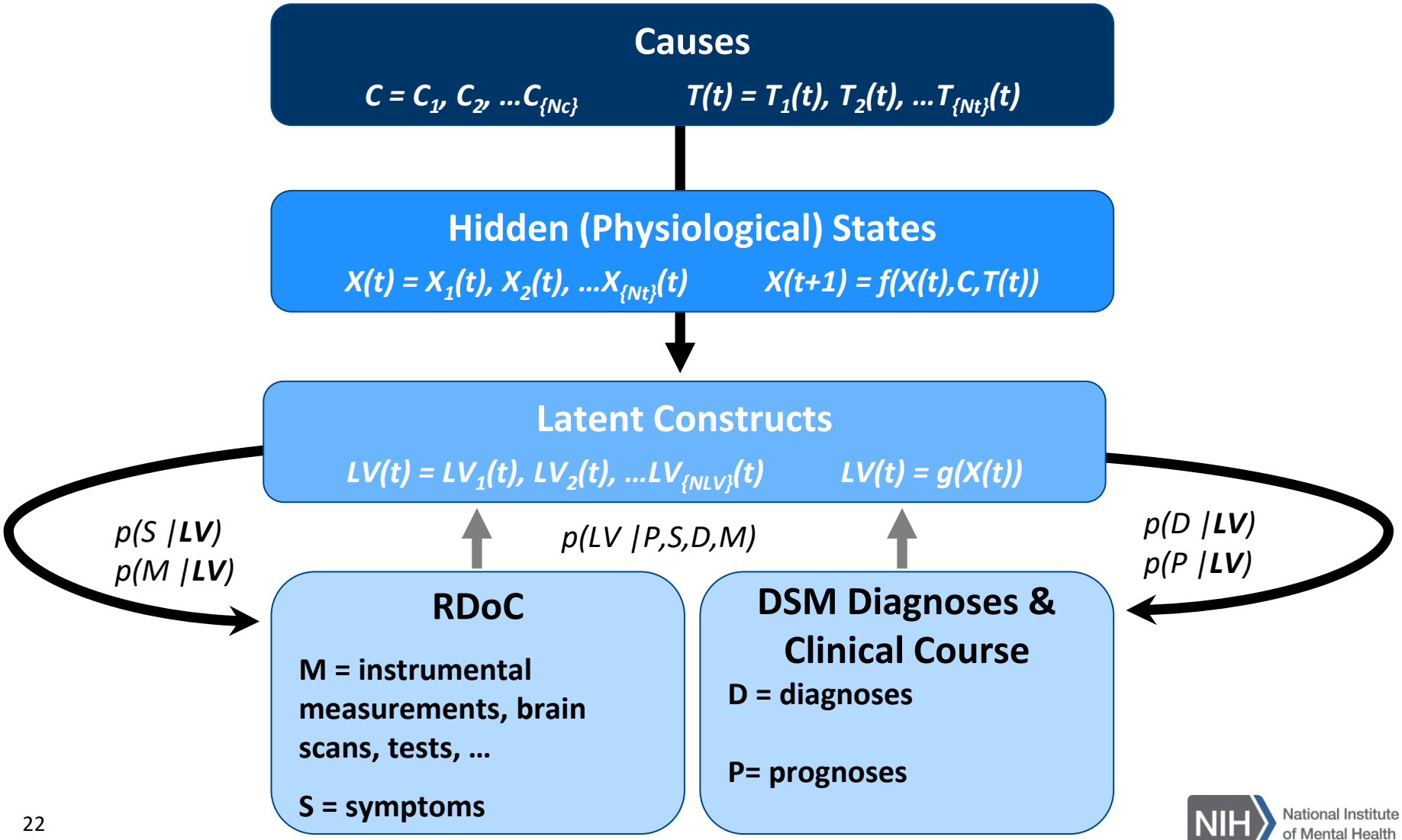
Diagnoses as Observations



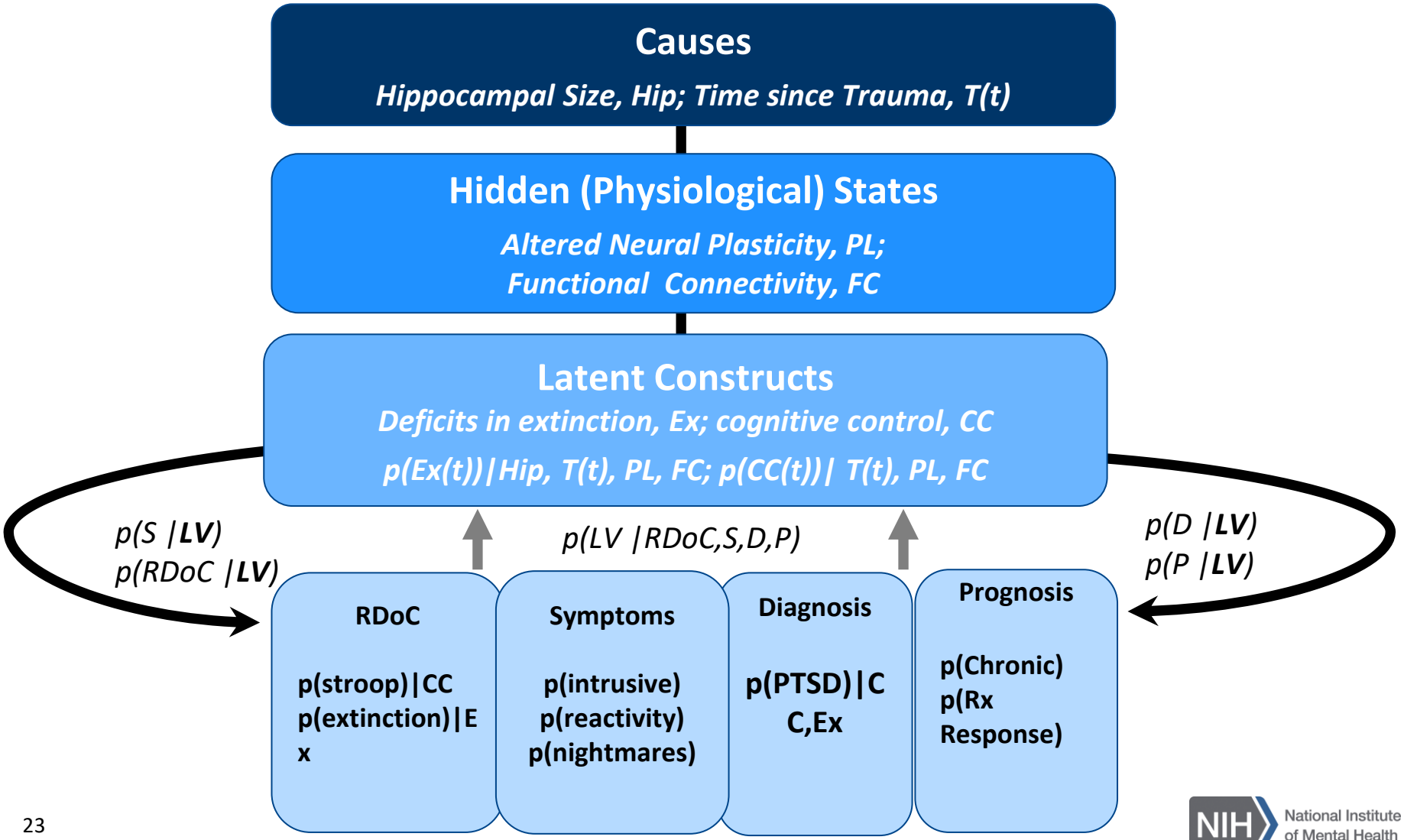
Integrating RDoC



Bayesian Approach



Example: Obsessive-Compulsive Disorder



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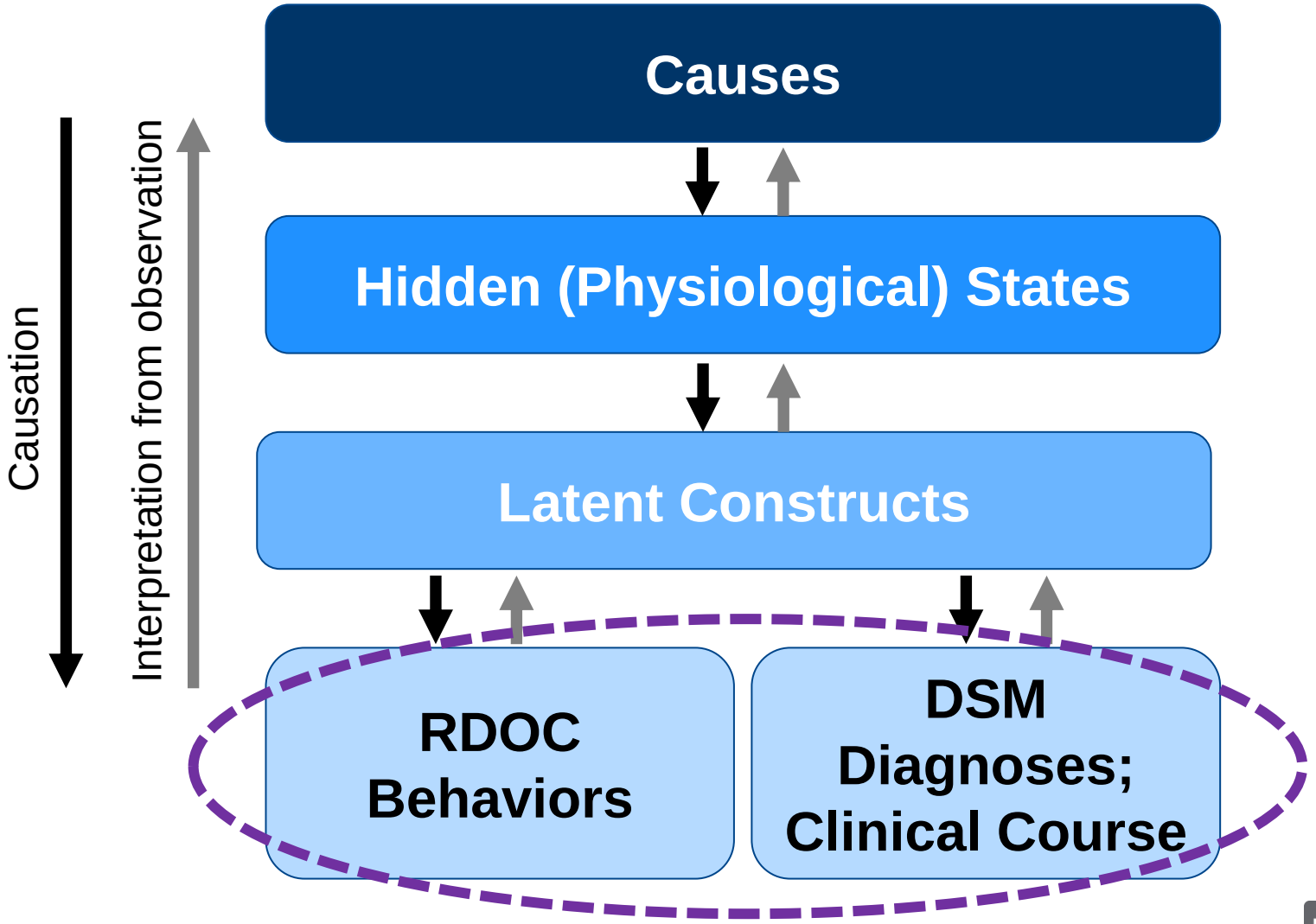

All of Us

- The NIH *All of Us* Research Program is an historic effort to advance precision medicine by collecting and studying data from **one million or more people** living in the United States

https://allofus.nih.gov

NIMH and *All of Us*: New Tasks and Measures

https://allofus.nih.gov

NIMH and *All of Us*: New Tasks and Measures

- The *All of Us* cohort provides a variety of other data (genetics, health records, scores on self-report measures) that could be **combined with behavioral tasks** to assess the utility of psychological constructs
- In line with this goal, NIMH is collaborating with *All of Us* to develop and deploy behavioral tasks focused on:
  - emotion identification;
  - sustained attention;
  - reward responsiveness/reward learning;
  - risky decision-making; and,
  - response inhibition

NIMH and *All of Us*: Advancing Computational Psychiatry

- **Data-driven Validation**: Test the relationships between and within RDoC domains/constructs
- **Theory-driven Computational Phenotypes**: Develop parameterized, mathematically formalized behavioral descriptions and associated tests and measures

NIMH and *All of Us*: Validating Constructs

- The *All of Us* cohort enables **testing and validating psychological constructs** with very large samples
- In line with this goal, NIMH has launched several funding opportunities, focused on:
  - using computational approaches to test the validity of constructs in the NIMH Research Domain Criteria (RDoC) matrix (PAR-21-263)
  - applying computational approaches to develop behavioral assays across mental-health relevant domains of function (PAR-21-264)
  - developing and optimizing tasks and measures for constructs pertaining to functional aspects of behavior or cognitive/affective processes (PAR-18-930)

NIMH Vision and Mission

NIMH envisions a world in which mental illnesses are prevented and cured.

To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

Questions