Bipolar Research Studies: Impact and Future State

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• Gloria Harrington – None

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Vision: To **personalize treatment** of bipolar disorder and **prevent recurrences** to enable those with bipolar to lead healthy and productive lives.
Bipolar Disorder

- Profound shifts in mood & energy
- Genes and environment interact
- Devastating effects on:
  - Social life
  - Vocation
  - Personal economics
Bipolar Disorder Facts

• 2 - 3% Prevalence (~6 million US adults)\textsuperscript{1}
• Average age of onset: 25
• At least 25 to 50% attempt suicide once\textsuperscript{1}
• Nearly 1 in 5 complete suicide\textsuperscript{2}
• U.S. economic burden: $45 billion annually\textsuperscript{3}
• Personal economic burden: $12,000 – $650,000\textsuperscript{4}

Emerging Bipolar Research Areas

• Induced Pluripotent Stem Cells – cell models
• Microbiome – to understand role of the gut flora
• Mobile Technology – to predict mood episodes

• Made possible through longitudinal engagement
Landmark Longitudinal Studies

• **Cardiovascular**
  Framingham Study – cardiovascular disease
  - Est. 1948; now in 3rd generation
  - 1,200+ publications; prevention & risk identification
  - Multiple cardiovascular longitudinal studies with thousands enrolled

• **Mental Health**
  STEP-BD: Systematic Treatment Enhancement Program for Bipolar Disorder
  - Est. 1998; follow-up every 3-6 months over 5 years
  - 53+ publications; 4361 patients over 22 sites; primarily a treatment and treatment outcome study

Mental health longitudinal studies – in general have small sample sizes with limited number of follow-up years
Need for Longitudinal Studies

1. Applicable to study-defined populations
2. Provide estimates of distributions and prevalence rates
3. Used to assess risk factor trends over time
4. To observe relationships of various factors that impact outcomes

Prechter Longitudinal Study of Bipolar Disorder

- Understand illness patterns in bipolar disorder:
  - through genetics
  - continued observation
  - additional research participation

- Over 1,200 enrolled

- 75% participants remain actively engaged

- Now in Year 10

Sharing of Resources

NAMI National Convention

Denver. July 6-9, 2016
Integrated Solutions for Bipolar Disorder

- Clinic
- Mobile Health
- Social Environment

Medical management
Social management
Monitoring outcomes

Biology – Genetics – iPSC (Stem Cells)
Microbiome – Biomarkers

Nutrition
Behavior
Habits

NAMI National Convention
Denver. July 6-9, 2016
Key Multi-disciplinary Collaborations

- Electrophysiology
- Metabolomics
- Phenomenology
- Environmental
- Computer Tech
- Psychology
- Genetics
- Microbiomics
- Neuropsychology
- Cell Biology - iPSC
Induced Pluripotent Stem Cells

• Ideal method to study neurodevelopmental disorders

• Adult cells coaxed back to early stage of development (pluripotent) (not embryonic)

• Grown forward to cell type of interest (brain cells)

• Modeling of neural growth and development

• Evolution of pathophysiologial development of disease states

(Melvin G. McInnis, MD)
iPSC Reprogramming Stages

- Powerful model to study cell function
- Discovery of new molecules to help create and test new medications
- Leads to understanding of how individuals react to different treatments
  - Personalized medicine

- Capture the disease genome
- Study the development of live neurons
- Reveal disease-specific molecular pathways
- Uncover disease-specific cellular phenotypes
- Perform drug screening
- Therapeutical intervention
What We’ve Learned from iPSCs

- Developmental Pattern Difference in Bipolar Cells
- Lithium pretreatment normalizes bipolar neuron calcium dynamics

Chen, Yoo, Herron
Next Steps for iPSC Research

• Lithium mechanisms – can novel interventions be developed?

• Mechanisms of other bipolar medications will be studied to advance research in therapeutics

• Developmental patterning research involves the study of the developing brain that is at risk for bipolar disorder
Microbiome: Gut-Brain Interaction

- Gut microbiome: influence on brain development, function, and behavior

- The microbiome responds to stress, diet, and medications
  - impact sleep, anxiety, mania, and depression

- Longitudinal study:
  - Leverage historical data to inform microbiome analysis
What We’ve Learned from the Microbiome

• The bacterial gut community is different in individuals with bipolar disorder.

• Specific gut bacteria associate with sleep quality, anxiety, and depression in bipolar disorder.

• Specific gut bacteria associate with intake of specific dietary nutrients.
Next Steps for the Microbiome Studies

• Can specific diets improve the bacterial complement of the gut microbiome?

• Do dietary-induced changes in the microbiome extend to improved clinical outcomes over time?
  • Better sleep
  • Lower anxiety
  • Reduced depression and mania
PRIORI: Predicting Individual Outcomes for Rapid Intervention

- n = 50
- 6 – 12 months
- 45,000 calls

AUC 0.70 – 0.81

(Emily Provost, PhD)
Computer Science & Engineering
What We’ve Learned from PRIORI

• Mood can be detected using speech characteristics
• Quality of data varies by phone models
• Area under curve (AUC) for participants from assessment to 7 days prior:

Hypomanic vs. Euthymic

Depressed vs. Euthymic

(Emily Provost, PhD)
Computer Science & Engineering
Other Mobile Technology Apps

Pre-Assessment
Day 1
Twice daily tasks

Passive/Sensor Data

UP
ask

Day 14
Twice daily tasks

Post-Assessment
Day 45
Twice daily tasks
Day 58

Kelly Ryan, PhD
Department of Psychiatry
Next Steps for Mobile Technology Studies

• Need larger sample sizes

• Need for clinical trial

  • Can we measure or redefine core features, such as psychomotor activity, using technology?

  • Can we predict changes and alter the course of bipolar disorder using PRIORI and other mobile applications?
Heinz C. Prechter Bipolar Genetics Repository

- Clinical data and biological samples
  - Bipolar disorder
  - Healthy controls

- Integrated solutions

- Longitudinal Clinical Data
- Neuropsychology
- Microbiome
- Stem Cells - iPSC
- PRIORI smartphone app
Longitudinal Studies: Engagement

1. Maintain good relationships with longitudinal members

2. Securing health-care provider support for cohort with key health issues

3. Creating an Executive Committee (community) to assist with:
   • Program planning
   • Translate study findings to community
   • Active participation in organizational aspects of the study

4. Overall, our participants report doing better by being involved in research
   • Clinicians do check-ins when there are safety concerns
   • Depression and mania scores are showing improvement over time

Key Multi-disciplinary Collaborations

- Electrophysiology
- Metabolomics
- Phenomenology
- Environmental
- Computer Tech
- Psychology
- Genetics
- Microbiomics
- Neuropsychology
- Cell Biology - iPSC
Conclusion

• Living a healthy life with bipolar disorder is possible.

Strategies to consider:

  o Work-life balance
  o Regular exercise
  o Get enough sleep
  o Eat a healthy diet
  o Collaborate with your care providers (& your research team!)
  o Engage support of friends and family

• For more information, visit us at Booth #219
• www.prechterfund.org
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