NIMH Priorities and Plans: Women’s Health Research

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Objectives

- About the NIMH
- Research Priorities
- Women’s Health Research
- Science Highlights
- Large Studies, Resources, and Repositories
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About the NIMH

• The National Institute of Mental Health (NIMH) is the lead federal agency for research on mental illnesses.

• NIMH supports more than 3,000 research grants and contracts at universities and other institutions across the country and overseas.

• NIMH intramural research programs support approximately 600 scientists working on the NIH campuses.
Objective 1: Define the mechanisms of complex behaviors

Objective 2: Chart mental illness trajectories to determine when, where, and how to intervene

Objective 3: Strive for prevention and cures

Objective 4: Strengthen the public health impact of NIMH-supported research
From Disease Origin to Recovery

Priorities

I. Identify Risk – Enhance Prediction
II. Identify biomarkers
III. Chart illness across development
IV. Develop personalized interventions

Development: Maturation/Sensitive Periods
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• **Short-term Goals:** Suicide Prevention
  - Identify implementable evidence-based practices and knowledge gaps

• **Medium-term Goals:** Neural Circuits
  - Develop technologies to interrogate neural circuits, and ultimately improve the understanding and treatment of mental health disorders

• **Long-term Goals:** Computational Psychiatry
  - Develop computational perspectives and approaches to improve the understanding and treatment of mental health disorders
Short-term Goal: Suicide Prevention

Age-Adjusted Suicide Rates in the United States (1999-2014)

- Male
- Total
- Female

Year

Suicide Rate (per 100,000)

Data courtesy of CDC
• NIMH hosted a workshop to review current themes in suicide research and to consider how approaches consistent with the Research Domain Criteria (RDoC) framework could provide new insights on the underlying mechanisms of suicide risk

• Discussion topics included gender differences and the timing of early life stress as strong influences in the trajectory of suicide risk over the life course
NIMH Initiatives for Suicide Prevention

- Detecting and Preventing Suicide Behavior, Ideation and Self-Harm in Youth in Contact with the Juvenile Justice System (PAR-16-299)
- Addressing Suicide Research Gaps: Aggregating and Mining Existing Data Sets for Secondary Analyses (RFA-MH-18-400)
Medium-Term Goal: Understanding Neural Circuits

- Understanding brain function and dysfunction
  - Characterize molecular identity, anatomy, and activity patterns in a cell-type specific manner

- Monitor and manipulate circuits for improved function
  - Drive and inhibit circuits with precise behavioral effects
• The overarching goal of the workshop was to identify how NIMH can support the development of technologies to interrogate neural circuits, and ultimately improve the understanding and treatment of mental health disorders.
Long-Term Goal: Computational Psychiatry

- Test links across multiple levels of analyses (genetic, molecular, cellular, circuit, behavior)
- Formalize behavioral analysis, defining underlying algorithms and facilitating neurobiological and clinical studies
- Provide quantitative assessment of utility of biomarkers
- Lead to an enhanced and integrative nosology
NIMH hosted a workshop to identify how NIMH can support the development of computational perspectives and approaches to improve the understanding and treatment of mental health disorders.

Addressed 4 Areas:

- Evaluation
- Computation
- Psychiatry
- Basic Fundamental Research
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NIMH’s Spending on Women’s Health (2007-2016)

Official dollars determined by PARIS queries reported to NIH Budget

* Includes ARRA funding
** Does not include AIDS dollars
NIMH’s Women’s Health Portfolio (2016)

- Sex Differences, 63%
- Other, 11%
- Perinatal Mental Health, 15%
- Postpartum Depression, 8%
- Menopause, 2%

Official dollars determined by PARIS queries reported to NIH Budget
Sex as a Biological Variable

Cahill, Nature Reviews Neuroscience, 2006

P: proestrus
O: oestrus
D: dioestrous
• Coordinates with the NIMH scientific Divisions to promote research on women’s mental health and to encourage the examination of sex and gender differences in NIMH funded research

• Works closely with the NIH Office for Research on Women’s Health and other NIH Institutes and Centers to facilitate joint funding opportunities

• Serves as a liaison to other federal agencies and external stakeholders on research issues relevant to women’s mental health
Women’s Mental Health and Sexual and Gender Minority Mental Health FOAs

• Notice of Information: NIMH High-Priority Areas for Research on Women's Mental Health During Pregnancy and the Postpartum Period

• Research on the Health of Women of Underrepresented, Understudied and Underreported (U3) Populations (PA-17-101)

• Administrative Supplement for Research on Sex/Gender Influences (PA-17-078)

• Administrative Supplements for Research on Sexual and Gender Minority Populations (PA-17-098)

• The Health of Sexual and Gender Minority (SGM) Populations (R01, R03, and R21) (PA-15-261, PA-15-262, and PA-15-263)
Collaborative Hubs for International Mental Health Research

**Latin-MH**
Brazil*, Peru, Guatemala, Colombia, Ecuador

**RedeAmericas**
Chile*, Brazil, Argentina, Colombia

**Pam-D**
Nigeria*, South Africa, Kenya, Ghana, Liberia

**SHARE**
India*, Pakistan, Afghanistan, Bangladesh, Nepal, Sri Lanka

**AFFIRM**
South Africa*, Ethiopia, Ghana, Malawi, Uganda, Zimbabwe
Global Research on Maternal Depression

- **South Asian Hub for Advocacy, Research and Education (SHARE)**
  - Developed an innovative approach for the delivery of an established psychological treatment that reduces the burden of depression in mothers in South Asia

- **Africa Focus on Intervention Research for Mental Health (AFFIRM)**
  - Tested the effectiveness of a task sharing model to provide counselling for depressed pregnant women by non-specialist health workers in a primary care setting in South Africa
• Peter Schmidt, M.D., Chief

• Studying how changes in reproductive hormones trigger mood disorders, why these hormones trigger mood disturbances only in some women, and how the pathogenic mechanisms underlying these disorders translate into novel therapies or novel uses of existing therapies
  - Postpartum Depression
  - Premenstrual Dysphoric Disorder (PMDD, a severe premenstrual syndrome)
  - Perimenopausal Depression

• Examining the role of growth and pubertal development in normal brain development, in collaboration with NICHD investigators
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Neuroscience

THE TIMING OF NEURONAL LOSS ACROSS ADOLESCENCE IN THE MEDIAL PREFRONTAL CORTEX OF MALE AND FEMALE RATS

J. WILLING * AND J. M. JURASKA

2015
Female rats lost neurons in the medial prefrontal cortex between postnatal days 35 and 45.

Males did not lose a significant number of neurons from preadolescence to adulthood.

Willing and Juraska, *Neuroscience*, 2015
Science Highlight:
Sex-Differences in Oxytocin Expression

Archival Report

Sex-Specific Effects of Stress on Oxytocin Neurons Correspond With Responses to Intranasal Oxytocin


2016
Oxytocin-sensitive Networks Contribute to Stress-related Sex Differences

In female mice, but not in male mice, social defeat induced a long-lasting increase in the # of OT neurons, OT/c-fos colocalization, and Oxt gene expression.
JAMA Psychiatry

Efficacy of a Maternal Depression Prevention Strategy in Head Start
A Randomized Clinical Trial

Michael Silverstein, MD, MPH; Yaminette Diaz-Linhart, MSW, MPH; Howard Cabral, PhD, MPH; William Beardslee, MD; Mark Hegel, PhD; Winta Haile, BA; Jenna Sander, MPH; Gregory Patts, MPH; Emily Feinberg, ScD

2017
Science Highlight: Preventing Maternal Depression

PSE = problem-solving intervention

Silverstein, JAMA Psychiatry, 2017
Science Highlight: Preventing Maternal Depression

PSE = problem-solving intervention

Silverstein, JAMA Psychiatry, 2017
Hunting the Genetic Signs of Postpartum Depression With an iPhone App

By PAM BELLUCK  MARCH 21, 2016
Power of Team Science to Investigate the Causes of Postpartum Mood Disorders

Images used with permission from all investigators
Data as of April 2017

- 13,689 PPD ACT Downloads in the US
- Eligibility and Consent
  - 10,473 Participants Enrolled
    - 160 Participants Withdrawn
    - 755 Did not complete PPD screen
- Lifetime PPD Screen
  - 7,607 PPD Cases (1,187 Potential Psychosis Cases)
  - Consent for DNA Collection
  - 5,534 Consent to Provide Saliva Sample
  - Address Confirmation
    - 4,662 Kits Distributed
    - 872 Did Not Confirm Mailing Address
- Sample Collection and Return
  - 3,039 Kits Biobanked

349 EPDS < 13
241 Child born > 6 wks early
157 Diagnosed with life-threatening illness after childbirth
293 Child died or had life-threatening illness after birth
568 Symptom onset prior to pregnancy
617 Symptom onset > 3 months postpartum
387 Symptom duration < 2 weeks

Total Cases by State

Images used with permission from all investigators
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Large Cohort Studies: All of Us Research Program

• Key element of the Precision Medicine Initiative (PMI)
  • Launched in FY 2016, now beta testing
  • Aims to enroll over 1 million participants
  • Mission: Accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us
Large Cohort Studies: ECHO

- Environmental influences on Child Health Outcomes (ECHO)
  - **Cohort:** Aim to include ~50,000 children from diverse racial, geographic, and SES backgrounds
  - **Scientific Goal:** Answer crucial questions about effects of a range of early environmental exposures on child health and development
  - **Focus:** Key pediatric outcomes that have a high public impact
Large Cohort Studies: ABCD

- Adolescent Brain Cognitive Development (ABCD) Study
  - Longitudinal study of ~10,000 children from ages 9-10 through early adulthood to assess factors that influence individual brain development trajectories and functional outcomes
  - Aim to fill the gap in research about how childhood experiences affect brain, social, emotional, and academic development
  - Federal collaborators, including NIH (NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, NINDS, OD), CDC, and DOJ, and private partners
Big Data – NIMH Data Archive (NDA)

• National Database for Autism Research (NDAR)
  • Trans-NIH initiative sharing research data and results
  • Data from 355 projects and $800M ASD research investment
  • 115,000+ participants sharing genomics, imaging, neurophysiology, clinical measures

• National Database of Clinical Trials Related to Mental Illness (NDCT)

• Research Domain Criteria database (RDoCdb)

• Adolescent Brain Cognitive Development (ABCD) Study
NIMH Repository and Genomics Resource (NIMH-RGR)

- Biospecimen repository at Rutgers University Cell & DNA Repository (RUCDR) with clinical/genetic data housed at Washington Univ. in St. Louis (since 1998)
  
  https://www.nimhgenetics.org/

- Stem Cell Center at RUCDR provides iPSC lines for research into the cellular mechanisms and druggable targets of mental illness.
To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

www.nimh.nih.gov

Research = Hope
Upcoming NIMH Event

AUTISM IN GIRLS AND WOMEN

A PANEL DISCUSSION

TUESDAY, SEPTEMBER 19, 2017 • 1:00 PM - 3:00 PM
NEUROSCIENCE CENTER (NSC) • 6001 EXECUTIVE BLVD • ROOM 7102

Event will also be available live on videocast.nih.gov

Zoe Gross
Kevin Pelphrey, Ph.D.
Pamela Ventola, Ph.D.