NIMH Updates: Programs, Plans, and Priorities

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Director, NIMH

American Association of Chairs of Departments of Psychiatry Fall Meeting
September 25, 2020

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Agenda

• NIMH Programs and Plans

• NIMH Priorities

• Addressing Urgent Priorities
Agenda

- NIMH Programs and Plans
  - NIMH Priorities
  - Addressing Urgent Priorities
To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

September 22, 2020
NIMH Budget

NIMH Budget in Appropriated Dollars and Constant 2000 Dollars

Fiscal Year

Dollars (Millions)

- Appropriation (excluding Cures)
- Appropriation in 2000 Dollars
NIMH Budget

NIMH Applications, Awards, and Success Rates for Research Project Grants

Number of Applications/Awards

Fiscal Year

2015: 507
2016: 587
2017: 571
2018: 589
2019: 638
2020 (Est): 654

Success Rate

2015: 20%
2016: 23%
2017: 21%
2018: 23%
2019: 25%
2020 (Est): 24%

NIMH Budget

National Institute of Mental Health
Strategic Plan Goals

The four Strategic Plan Goals form a broad roadmap for the Institute's research priorities, spanning fundamental science to public health impact.

- **Goal 1**: Define the Brain Mechanisms Underlying Complex Behavior
- **Goal 2**: Examine Mental Illness Trajectories Across the Lifespan
- **Goal 3**: Strive for Prevention and Cures
- **Goal 4**: Strengthen the Public Health Impact of NIMH-Supported Research
Agenda

• NIMH Programs and Plans

• NIMH Priorities
  • Genetics
  • Neural Circuits
  • Computation
  • Suicide Prevention

• Addressing Urgent Priorities
Likely Complexity
Critical Convergence?
Large-Scale Exome Sequencing Study Implicates Both Developmental and Functional Changes in the Neurobiology of Autism

F. Kyle Satterstrom,1,2,3,37 Jack A. Kosmicki,1,2,3,4,5,37 Jiebiao Wang,6,37 Michael S. Breen,7,8,9 Silvia De Rubeis,7,8,9 Joon-Yong An,10,11 Minshi Peng,6 Ryan Collins,5,12 Jakob Grove,13,14,15 Lambertus Klei,16 Christine Stevens,1,3,4,5 Jennifer Reichert,7,8 Maureen S. Mulhern,7,8 Mykyta Artomov,1,3,4,5 Sherif Gerges,1,3,4,5 Brooke Sheppard,10 Xinyi Xu,7,8 Aparna Bhaduri,17,18 Utku Norman,19 Harrison Brand,5 Grace Schwartz,10 Rachel Nguyen,20 Elizabeth E. Guerrero,21 Caroline Dias,22,23 Autism Sequencing Consortium, and iPSYCH-Broad Consortium, Catalina Betancur,24 Edwin H. Cook,25 Louise Gallagher,26 Michael Gill,26 James S. Sutcliffe,27,28 Audrey Thurm,29 Michael E. Zwick,30 Anders D. Børglum,13,14,15,31 Matthew W. State,10 A. Ercument Cicek,6,19 Michael E. Talkowski,5 David J. Cutler,30 Bernie Devlin,16 Stephan J. Sanders,10,38,* Kathryn Roeder,6,32,38,* Mark J. Daly,1,2,3,4,5,33,38,* and Joseph D. Buxbaum7,8,9,34,35,36,38,39,*

2020
Genetic Risk for ASD

Exome analysis of 35,584 samples identified 99 ASD-associated genes.
ASD Genes Enriched in Maturing Inhibitory and Excitatory Neurons

<table>
<thead>
<tr>
<th>Phenotypic distinctions</th>
<th>Functional distinctions</th>
<th>Cell type enrichment</th>
</tr>
</thead>
<tbody>
<tr>
<td>53 ASD predominant genes</td>
<td>58 gene expression regulation genes</td>
<td>Excitatory lineage</td>
</tr>
<tr>
<td>49 ASD &amp; Neuro-developmental delay genes</td>
<td>24 neuronal communication genes</td>
<td>Newborn neurons</td>
</tr>
</tbody>
</table>

**Density**

- 0 - 25
- 25 - 50
- 50 - 75
- 75 - 100
- 100 - 125
- 125 - 150

**Full-scale IQ**

- Prenatal
- Birth
- Postnatal

- Newborn neurons
- Maturing excitatory neurons
- Maturing inter-neurons
NIMH Initiatives for Genetics

• Genetic Architecture of Mental Disorders in Ancestrally Diverse Populations (PAR-20-026; PAR-20-027)

• Leveraging Electronic Medical Records for Psychiatric Genetic Research (PAR-18-904; PAR-18-905)

• From Genomic Association to Causation: A Convergent Neuroscience Approach for Integrating Levels of Analysis to Delineate Brain Function in Neuropsychiatry (PAR-17-253) expired September 8, 2020
  • From Genomic Association to Causation: A Convergent Neuroscience Approach 2.0 (Concept Clearance)
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• Addressing Urgent Priorities
Cross-hemispheric gamma synchrony between prefrontal parvalbumin interneurons supports behavioral adaptation during rule shift learning

Kathleen K. A. Cho1,2,3, Thomas J. Davidson2,4,5, Guy Bouvier4,5, Jesse D. Marshall6, Mark J. Schnitzer7,8 and Vikaas S. Sohal1,2,3

Gamma Synchrony Required for Rule Shift Performance
Gamma Synchrony Required for Rule Shift Performance

[Diagram showing experimental setup and results with statistical analysis]

NIMH Initiatives for Neural Circuits

• Multiple BRAIN Initiative Efforts
  • Cell census and atlases of mouse, NHP, human brain
  • Technologies for recording and modulating activity
  • Comprehensive circuit dissection

• NIH Blueprint for Neuroscience Research: Functional Neural Circuits of Interoception (RFA-AT-21-003)

• Utilizing Invasive Recording and Stimulating Opportunities in Humans to Advance Neural Circuitry Understanding of Mental Health Disorders (RFA-MH-20-350; RFA-MH-20-351)

• Explainable Artificial Intelligence for Decoding and Modulating Neural Circuit Activity Linked to Behavior (PAR-19-344)
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Computational Approaches

- 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
- Enhanced understanding of brain mechanisms
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

2017
Breaking Down Behavior

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

\[
\text{Happiness}(t) = w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j} CR_j + w_2 \sum_{j=1}^{t} \gamma^{t-j} EV_j + w_3 \sum_{j=1}^{t} \gamma^{t-j} RPE_j
\]
Breaking Down Behavior

ventral striatum

medial prefrontal cortex

Rutledge et al, *JAMA Psychiatry*, 2017
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.

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
NIMH Initiatives for Computational Psychiatry

• Computational Approaches for Validating Dimensional Constructs of Relevance to Psychopathology (RFA-MH-19-242) Data Mining

• Computationally-Defined Behaviors in Psychiatry (RFA-MH-19-240) Computational Phenotyping

• New Computational Methods for Understanding the Functional Role of DNA Variants that are Associated with Mental Disorders (PA-18-907; PA-18-908) Biophysical Modeling/Data Mining

• Notice of Availability of Administrative Supplements for Advancing Computational Modeling and Data Analytics Relevant to Mental Health (NOT-MH-19-004) All Three
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How to Prevent the Most Suicides in the Shortest Amount of Time?

Understand when and where individuals access health care

Identify individuals at risk

Provide effective interventions

Suicide decedents are accessing healthcare

~30% Visit within 7 days of suicide
>50% Visit within 30 days of suicide
>90% Visit within 365 days of suicide

Emergency departments (EDs) may provide a unique opportunity to prevent suicide
Progress in Risk Identification – Screening Youths

ASQ – Ask Suicide Screening Questions

Universal screening of youth in EDs with ASQ more than doubled the detection of suicide risk compared with treatment as usual

DeVylder, JAMA Netw Open, 2019

ED STARs

Validating the Computerized Adaptive Screen and associated risk stratification algorithm; early results show risk factors for suicide attempts differ by sex and whether or not youth report recent suicidal thoughts

King, J Child Psychol Psychiatry, 2019
Progress in Risk Identification – Risk Algorithms

Integrating Predictive Modeling Into Mental Health Care: An Example in Suicide Prevention

Greg M. Reger, Ph.D., M.A., Mary Lou McClure, R.N., B.S.N., David Ruskin, M.D., Sarah P. Carter, Ph.D., Mark A. Reger, Ph.D.

Predicting Suicide Attempts and Suicide Deaths Following Outpatient Visits Using Electronic Health Records

Gregory E. Simon, M.D., M.P.H., Eric Johnson, M.S., Jean M. Lawrence, Sc.D., Rebecca C. Rossom, M.D., M.S., Brian Ahmedani, Ph.D., Frances L. Lynch, Ph.D., Arne Beck, Ph.D., Beth Waitzfelder, Ph.D., Rebecca Ziebell, Robert B. Penfold, Ph.D., Susan M. Shortreed, Ph.D.
Effective Interventions Are Ready to Use

Brief suicide prevention interventions were associated with reduced subsequent suicide attempts and increased linkage to follow-up care.

### Study: Depression at follow-up

<table>
<thead>
<tr>
<th>Study</th>
<th>Hedges g (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asarnow et al,16 2011</td>
<td>-0.13 (-0.42 to 0.16)</td>
</tr>
<tr>
<td>Armitage et al,15 2016</td>
<td>0.18 (-0.14 to 0.50)</td>
</tr>
<tr>
<td>Currier et al,19 2019</td>
<td>0.31 (-0.05 to 0.66)</td>
</tr>
<tr>
<td>Grupp-Phelan et al,20 2012</td>
<td>0.57 (-0.22 to 1.37)</td>
</tr>
<tr>
<td>Grupp-Phelan et al,21 2019</td>
<td>0.05 (-0.26 to 0.36)</td>
</tr>
<tr>
<td>King et al,22 2015</td>
<td>1.23 (0.62 to 1.83)</td>
</tr>
<tr>
<td><strong>Subtotal I^2 = 72.2%; (P = .003)</strong></td>
<td><strong>0.28 (-0.02 to 0.59)</strong></td>
</tr>
</tbody>
</table>

### Study: Linkage to follow-up care

<table>
<thead>
<tr>
<th>Study</th>
<th>Hedges g (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asarnow et al,16 2011</td>
<td>0.71 (0.18 to 1.24)</td>
</tr>
<tr>
<td>Currier et al,19 2010</td>
<td>0.93 (0.50 to 1.36)</td>
</tr>
<tr>
<td>Grupp-Phelan et al,20 2012</td>
<td>1.21 (0.17 to 2.24)</td>
</tr>
<tr>
<td>Grupp-Phelan et al,21 2019</td>
<td>0.21 (-0.16 to 0.58)</td>
</tr>
<tr>
<td>O’Connor et al,24 2020</td>
<td>0.75 (0.10 to 1.40)</td>
</tr>
<tr>
<td>Ouigrin et al,25 2011</td>
<td>0.89 (0.29 to 1.49)</td>
</tr>
<tr>
<td>Spirito et al,26 2002</td>
<td>0.15 (-0.87 to 1.16)</td>
</tr>
<tr>
<td>Stanley et al,27 2015</td>
<td>0.49 (0.11 to 0.88)</td>
</tr>
<tr>
<td>Stanley et al,28 2018</td>
<td>0.26 (0.11 to 0.41)</td>
</tr>
<tr>
<td><strong>Subtotal I^2 = 55.4%; (P = .02)</strong></td>
<td><strong>0.55 (0.32 to 0.78)</strong></td>
</tr>
</tbody>
</table>

### Study: Subsequent suicide attempt

<table>
<thead>
<tr>
<th>Study</th>
<th>Hedges g (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asarnow et al,16 2011</td>
<td>0.11 (-0.63 to 0.85)</td>
</tr>
<tr>
<td>Bryan et al,17 2017</td>
<td>0.57 (-0.36 to 1.51)</td>
</tr>
<tr>
<td>Comtois et al,18 2019</td>
<td>0.29 (-0.02 to 0.60)</td>
</tr>
<tr>
<td>Grupp-Phelan et al,21 2019</td>
<td>-0.61 (-1.86 to 0.64)</td>
</tr>
<tr>
<td>Miller et al,23 2017</td>
<td>0.16 (-0.01 to 0.33)</td>
</tr>
<tr>
<td>O’Connor et al,24 2020</td>
<td>-0.05 (-1.16 to 1.06)</td>
</tr>
<tr>
<td>Stanley et al,28 2018</td>
<td>0.32 (0.03 to 0.61)</td>
</tr>
<tr>
<td><strong>Subtotal I^2 = 0.0%; (P = .72)</strong></td>
<td><strong>0.21 (0.08 to 0.33)</strong></td>
</tr>
</tbody>
</table>
Research Partnerships: Mental Health Research Network (MHRN)

MHRN is the nation’s preeminent source of population-based research on mental health, partnering with 13 health system research centers that provide care of a diverse population of over 12.5 million people in 15 states.

Testing Interventions in Healthcare Settings, Using Electronic Health Records Can Bring Them to Scale

Sample Sizes in Major NIMH Suicide Prevention Trials

<table>
<thead>
<tr>
<th>Trial (Year)</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT (2005)</td>
<td>120</td>
</tr>
<tr>
<td>DBT (2006)</td>
<td>101</td>
</tr>
<tr>
<td>ED-SAFE (2017)</td>
<td>1,376</td>
</tr>
<tr>
<td>SPOT (2020)</td>
<td>18,868</td>
</tr>
</tbody>
</table>

NIMH Initiatives in Suicide Prevention

• Practice-Based Suicide Prevention Research Centers (PAR-20-286)

• Enhancing Suicide Prevention in Emergency Care via Telehealth (RFA-MH-20-226)

• Notice of Intent to Publish a Funding Opportunity Announcement for Service-Ready Tools for Identification, Prevention, and Treatment of Individuals at Risk for Suicide (NOT-MH-20-068; NOT-MH-20-069)

• Notice of Special Interest (NOSI) in Research on Risk and Prevention of Black Youth Suicide (NOT-MH-20-055)

• Assessing Outcomes of Health System Suicide Risk Screening Programs (Concept Clearance)
Agenda

• NIMH Programs and Plans

• NIMH Priorities

• Addressing Urgent Priorities
  • COVID-19 Information and Resources
  • Mental Health Equity
COVID-19 Information

Coronavirus (COVID-19)

How to prepare and protect yourself

What to do if you think you are sick

https://www.coronavirus.gov

COVID-19 Testing
Learn about NIH’s RADx Initiative to speed development of rapid and widely accessible COVID-19 testing.

About ACTIV
Learn about NIH’s collaboration and data sharing efforts through the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

Grants and Funding
Get information for applicants and recipients and find NIH COVID-19 funding opportunities.

Treatment Guidelines
Stay up to date on the latest treatment guidelines for COVID-19 developed by a U.S. panel of experts.

https://www.nih.gov/coronavirus
COVID-19 Updates and Guidance

- Information for NIH Applicants and Recipients of NIH Funding
  - Guidance for Applicants Preparing Applications for the Fall 2020 Due Dates During the COVID-19 Pandemic (NOT-OD-20-122)
  - NIH Late Application Policy for Institutional Training Grants to PA-20-142 and PA-20-162 Due to Public Health Emergency for United States Coronavirus Disease 2019 (NOT-OD-20-105)


- NIH-Wide Strategic Plan for COVID-19 Research
Responding to COVID-19

• Why Testing is Key to Getting Back to Normal (September 8, 2020)

• NIH One Step Closer to Speeding Delivery of COVID-19 Testing Technologies to Those Who Need It Most Through RADx-UP (June 24, 2020)

https://www.nimh.gov/covid19
COVID-19 Initiatives

• NIMH-Administering
  • Notice of Special Interest (NOSI) regarding the Availability of Administrative Supplements and Urgent Competitive Revisions for Mental Health Research on the 2019 Novel Coronavirus (NOT-MH-20-047)

• NIMH-Participating
  • Digital Healthcare Interventions to Address the Secondary Health Effects Related to Social, Behavioral, and Economic Impact of COVID-19 (PAR-20-243)
  • Community Interventions to Address the Consequences of the COVID-19 Pandemic among Health Disparity and Vulnerable Populations (PAR-20-037)

https://www.nimh.nih.gov/funding/index.shtml
NIMH Efforts to Address Institutionalized Racism and Mental Health Equity

Request for Information: Fostering Innovative Research to Improve Mental Health Outcomes Among Minority and Health Disparities Populations (NOT-MH-20-073)
NIMH Initiatives in Minority Health & Health Disparities

• Effectiveness of Implementing Sustainable Evidence-Based Mental Health Practices in Low-Resource Settings to Achieve Mental Health Equity for Traditionally Underserved Populations (RFA-MH-20-400)

• Implementing and Sustaining Evidence-Based Mental Health Practices in Low Resource Settings to Achieve Equity to Outcomes (RFA-MH-20-401)

• Practice-Based Research for Implementing Evidence-Based Prevention Interventions in Primary Care Settings (RFA-MH-20-505; RFA-MH-20-506)
NIMH Vision and Mission

VISION

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

MISSION

To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.
Current Efforts to Advance Workforce Diversity

- Individual Supplement Awards
  - Research Supplements to Promote Diversity (PA-18-906; PA-18-592)

- Predoctoral Awards
  - Individual Predoctoral Fellowship to Promote Diversity (F31) (PA-19-196)
  - Mental Health Dissertation Research Grant to Increase Diversity (R36) (PAR-18-894)
  - NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) Award (F99/K00) (RFA-NS-19-011)

- Postdoctoral/Career Development Awards:
  - K99/R00 - BRAIN Initiative Advanced Postdoctoral Career Transition Award to Promote Diversity (RFA-NS-19-043)

- Other Programs
  - NIH Blueprint Program for Enhancing Neuroscience Diversity through Undergraduate Research Education Experiences (ENDURE) (RFA-NS-20-015)
  - NIMH Support for Scientific Conferences to Promote Inclusion
  - Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Institutionally-Focused Research Education Award to Promote Diversity (PAR-19-342)
  - NIH Neuroscience Development for Advancing the Careers of a Diverse Research Workforce (PAR-20-240)
  - Faculty Institutional Recruitment for Sustainable Transformation (FIRST)