State of BRAIN

BRAIN Multi-Council Working Group
Walter J. Koroshetz, MD
Joshua A. Gordon, MD, PhD
Co-chairs, NIH BRAIN MCWG
January 30, 2018
• The BRAIN Initiative to date
  • Timelines & Budgets
  • Investigators & Transitions
  • Current Funding Announcements & Clinical Trials issues

• The Science of the BRAIN
  • The Cell Census projects
  • Science Highlights
  • 4th Annual Investigator Meeting

• BRAIN: Next Steps
  • Responding to the opioid epidemic
  • Revisiting BRAIN 2025
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**Goal**: See the circuits in action to understand:

- How the brain moves, plans, executes
- How to monitor/manipulate circuits for improved function
- That disordered brain circuits cause neuro/mental/substance use disorders

**Long-term goal**: Make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention
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<thead>
<tr>
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<th>New (FY2017)</th>
<th>Since BRAIN Began (FY2014)</th>
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<tbody>
<tr>
<td>Number awards</td>
<td>110</td>
<td>345</td>
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<tr>
<td>Number investigators</td>
<td>178</td>
<td>504</td>
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<tr>
<td>Investment</td>
<td>$169.6M</td>
<td>$548.3M</td>
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THE BRAIN INITIATIVE®

BRAIN Awards

NIH National Institutes of Health
Turning Discovery into Health
## BRAIN Competing $ Available
(dollars in millions)

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<thead>
<tr>
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<td>IC BRAIN Base</td>
<td>$30.7</td>
<td>$55.4</td>
<td>$140.4</td>
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<td>CRCNS/Other</td>
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<td>$-</td>
<td>$-</td>
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<td>21st Century Cures</td>
<td>$-</td>
<td>$-</td>
<td>$-</td>
<td>$10.0</td>
<td>$86.0</td>
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<td>$336.4</td>
<td>$400.4</td>
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<td>IC Additional</td>
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<td>$4.8</td>
<td>$1.5</td>
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<tbody>
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<td>Competing</td>
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<td>$36.6</td>
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<td>$155.2</td>
<td>$261.9</td>
<td>$236.4</td>
<td>$336.4</td>
<td>$400.4</td>
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BRAIN is Just Getting Started

$4.2B: Projected total for lifetime of BRAIN

$550M: BRAIN Funding through 2017

~12% of the total

21st Century Cures
Base Budget

NIH National Institutes of Health
Turning Discovery into Health
– New BRAIN funding opportunities attract both new and early stage investigators, and they fare well in BRAIN reviews
– BRAIN should make concerted efforts to enhance outreach to women, underrepresented minority, and geographically diverse applicants
– Applicants from increasingly diverse set of disciplines
  • FY 2016, more engineers than neuroscientists applied
  • Looking to increase applications from physical scientists, such as material scientists
New MCWG Member: Karl Deisseroth, Ph.D., M.D.
D.H. Chen Professor of Bioengineering and of Psychiatry and Behavioral Sciences
Stanford University
NIDA Council Member

Roderic Pettigrew, Ph.D., M.D. stepped down as Director of NIBIB to join Texas A&M University and lead Engineering Health (EnHealth)
Jill Heemskerk, Ph.D. is Acting NIBIB Director (Member of BRAIN Coordinating Team)

Josie Briggs, M.D. retired as Director of NCCIH to become the Editor-in-Chief of the Journal of the American Society of Nephrology
David Shurtleff, Ph.D. is Acting NCCIH Director (Member of BRAIN Coordinating Team)
NIH is reopening the search and actively recruiting for BRAIN Director!

www.braininitiative.nih.gov
Currently Open in FY18

- Tools to Facilitate High-Throughput Microconnectivity Analysis
- Targeted BRAIN Circuits Projects- TargetedBCP
- Theories, Models and Methods for Analysis of Complex Data from the Brain
- Proof of Concept Development of Early Stage Next Generation Human Brain Imaging
- Development of Next Generation Human Brain Imaging Tools and Technologies
- Tools to Target, Identify and Characterize Non-Neuronal Cells in the Brain
- Research Resource Grants for Technology Integration and Dissemination
- Small Business Opportunities: Development, Optimization, and Validation of Novel Tools and Technologies for Neuroscience Research
- BRAIN Initiative Fellows: Ruth L. Kirschstein NRSA Postdoctoral Fellowship
- Biology and Biophysics of Neural Stimulation
- Next-Gen Invasive Devices for Recording/Modulation in Humans (with Clinical Studies)
Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

- The study is a clinical trial if it:
  - Involves one or more human subjects
  - Prospectively assigns human subject(s) to intervention(s)
  - Evaluates the effect of intervention(s) on the human subject(s)
  - Has a health-related biomedical or behavioral outcome

Due Dates on or after January 25, 2018

All clinical trial applications MUST be submitted to a funding opportunity that allows clinical trials
How to determine if a funding opportunity accepts clinical trials?

- Refer to Section II. Award Information
- Indicated in FOA title (new FOAs only)
  - BRAIN Initiative: Targeted BRAIN Circuits Projects- TargetedBCP (R01 - Clinical Trial Not Allowed)
  - BRAIN Initiative: Next-Generation Invasive Devices for Recording and Modulation in the Human Central Nervous System (UG3/UH3 Clinical Trial Required)
  - BRAIN Initiative: Biology and Biophysics of Neural Stimulation (R01 Clinical Trial Optional)

  ➢ If proposing a clinical trial, this FOA will only accept applications that propose mechanistic trials/studies. NIH defines a mechanistic clinical trial as follows: "A mechanistic study is designed to understand a biological or behavioral process, the pathophysiology of a disease, or the mechanism of action of an intervention."

https://grants.nih.gov/policy/clinical-trials.htm
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BRAIN Cell Census Vision – through 2025

- **Phase 1**: Pilot census projects - both models and human (FY14-16)
- **Phase 2**: Focus on mouse; begin human census (FY17-21)
- **Phase 3**: Ramp up hu/NHP census; wind down mouse (FY21-25)
Launched in FY2017: BRAIN Initiative
Cell Census Network

BICCN EXTERNAL SCIENTIFIC PANEL (ESP)

BICCN Program Team

U19 (Zeng)

U19 (Huang)

U19 (Ecker)

U24 BCDC

Data Archive

Data Archive

Research Community

Funded 11 projects ~$50M/yr for 5 years
Over 320 publications have emerged from NIH BRAIN to date.

https://www.braininitiative.nih.gov/resources/publication.aspx
Meeting offers opportunity for BRAIN investigators and trainees to interact across project areas and funding agencies.

**4th Annual Meeting: April 9-11, 2018**
- ~1000 participants expected
- Bethesda North Marriott Hotel and Conference Center (Bethesda, MD, USA)
- **Registration now OPEN!**
  www.braininitiative.org/events/Plmeeting
- Program available online
  - 5 Keynote presentations broadcast live
  - Panels focused on BICCN, data coordination, commercialization, neuroethics, diversity, and more!
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Opioid Prescriptions have started to Decrease but Opioid Fatalities are still Increasing

Opioid morphine milligram equivalents (MME) dispensed fell by over 15% from 2010-2015

![Graph showing Opioid MME in billions from 2010 to 2015](chart.png)

Source: IMS Health, U.S. Outpatient Retail Setting

- 266 in 2010
- 260 in 2011
- 253 in 2012
- 242 in 2013
- 234 in 2014
- 222 in 2015

Opioid OD Deaths US, 2000-2015

- 2015 Overdose Deaths:
  - 52,404 Any Drug
  - 33,091 Any Opioid

- ~64,000 deaths from drug overdose in 2016
- ~20,100 deaths from fentanyl/related drugs

NIH on the Opioid Epidemic and Chronic Pain

• Address rise in opioid-related fatalities via 3 pillars:
  – Improve overdose-reversal and prevention interventions
  – New medications, technologies to treat opioid addiction
  – ID safe, effective, non-addictive interventions for chronic pain

The Role of Science in Addressing the Opioid Crisis

Nora D. Volkow, M.D., and Francis S. Collins, M.D., Ph.D.
BRAIN Initiative: Notice of Support for Research on the Fundamental Neurobiology of Pain Processing

- NIH welcomes BRAIN Initiative applications targeting central nervous system nociceptive and pain circuits, as appropriate to the goals and requirements of specific BRAIN Initiative FOAs.
- It is expected that the unique opportunities of the BRAIN Initiative will enable production of detailed maps of pain circuits, and the adoption of powerful new tools for monitoring and modulating pain circuit activity, leading to significant advances in the understanding of pain and nociception.

Revisiting BRAIN in 2020 and Beyond

BRAIN 2025 Report: First years [should] emphasize technology development and validation, with a growing emphasis on problem-driven neuroscience after FY2020

- As discussed at the Feb 2017 MCWG meeting, NINDS/NIMH launched effort to assess BRAIN Initiative progress
- Looking ahead, NIH will formally revisit BRAIN 2025’s priorities to provide an updated scientific vision to guide the second half of the Initiative
- Focus on specific topics/questions that can now be interrogated given the emerging set of tools and technologies
Tentative timeline

Fall 2017: Initial call for WG nominations
Spring 2018: First public town-hall and in-person WG meeting at BRAIN PI meeting
Winter/Spring 2019: Initial draft released for public comment
Summer/Fall 2018: Country-wide workshops
Summer 2019: Final version of BRAIN strategic plan released
Winter 2020: Deadline for FY2020 FOAs
• Update the scientific vision for the NIH BRAIN Initiative, established in the BRAIN 2025 plan, to guide the second half of the Initiative
  – Review the NIH BRAIN Initiative progress and advances
  – With BRAIN 2025 as a model, identify new specific topics and questions from high priority research areas that might be interrogated given the emerging set of tools and technologies
• Identify valuable areas of new and continued technology development
• Consider the unique contributions that the NIH BRAIN Initiative can make to Neuroscience
Thank You!

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Follow us @NINDSdirector @NIMHDirector

https://www.braininitiative.nih.gov/