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

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  - Investigators & Transitions
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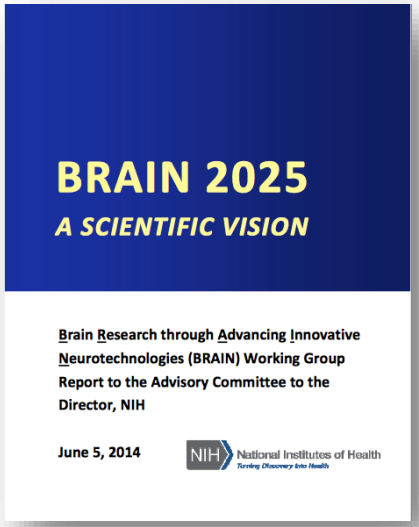
Focus on Circuit Structure and Function



FIRST FIVE YEARS → **SECOND FIVE YEARS**

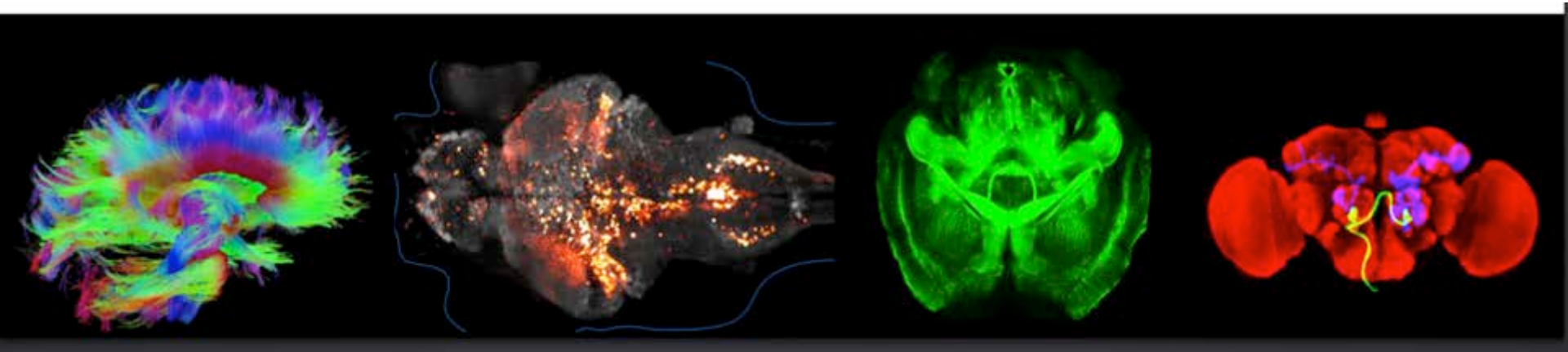
Emphasize technology development

Emphasize discovery driven science

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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BRAIN: *Where Are We?*

BRAIN Initiative announced
April 2013

1st meeting of the BRAIN MCWG
August 2014

1st BRAIN PI Meeting
November 2014

Neuroethics Division established
August 2015

BRAIN Initiative Alliance website launches
November 2016

4th NIH BRAIN awards
May, October 2017

***BRAIN 2025* Report released**
June 2014

1st NIH BRAIN awards
September 2014

1st BRAIN Initiative Alliance discussion
July 2015

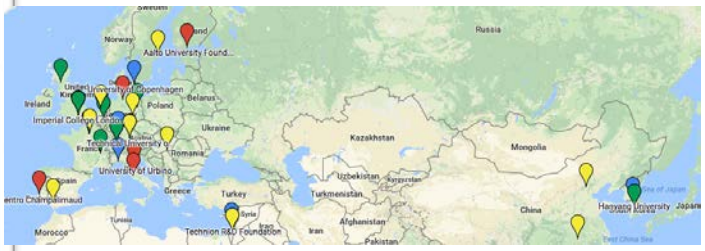
Public-Private Partnership Program established
September 2015

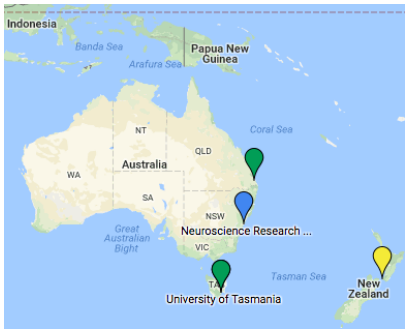
21st Century Cures Act signed into law
December 2016

4th BRAIN PI Meeting
April 2018

National Institutes of Health
Turning Discovery Into Health

BRAIN Awards





	New (FY2017)	Since BRAIN Began (FY2014)
Number awards	110	345
Number investigators	178	504
Investment	$169.6M	$548.3M

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BRAIN Competing $ Available

(dollars in millions)

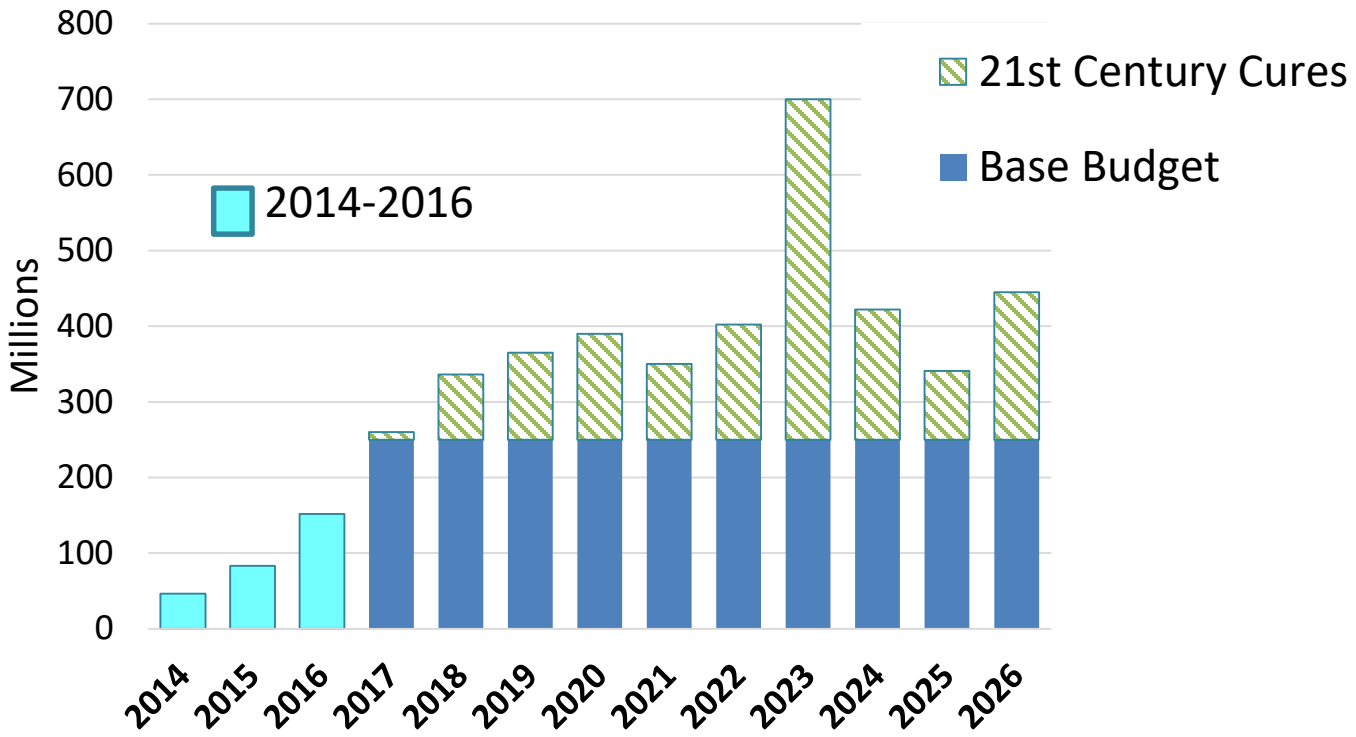
Sources	FY 2014 Actual	FY2015 Actual	FY 2016 Actual	FY 2017 Actual	FY 2018 Pres. Budget	FY 2018 House	FY 2018 Senate
IC BRAIN Base	$30.7	$55.4	$140.4	$240.4	$140.4	$240.4	$304.4
Blueprint	$10.0	$10.0	$10.0	$10.0	$-	$-	$-
CRCNS/Other	$-	$-	$-	$-	$10.0	$10.0	$10.0
21st Century Cures	$-	$-	$-	$10.0	$86.0	$86.0	$86.0
Subtotal	$40.7	$65.4	$150.4	$260.4	$236.4	$336.4	$400.4
IC Additional	$5.4	$19.7	$4.8	$1.5	$-	$-	$-
Uses	**FY 2014 Actual**	**FY2015 Actual**	**FY 2016 Actual**	**FY 2017 Actual**	**FY 2018 Pres. Budget**	**FY 2018 House**	**FY 2018 Senate**
Competing	$46.1	$36.6	$70.7	$169.5	$60.6	$156.6	$220.6
Noncompeting	$-	$46.6	$79.6	$85.7	$169.9	$169.9	$169.9
RMS	$-	$-	$4.7	$6.4	$5.6	$9.6	$9.6
Intramural	$-	$-	$0.2	$0.3	$0.3	$0.3	$0.3
Total	$46.1	$83.2	$155.2	$261.9	$236.4	$336.4	$400.4

BRAIN is Just Getting Started

$4.2B: Projected total for lifetime of BRAIN

$550M: BRAIN Funding through 2017

~12% of the total

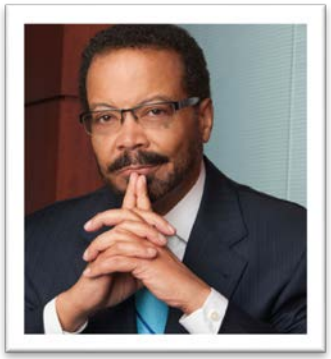


Overview of BRAIN Investigators

- 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

BRAIN Transitions

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

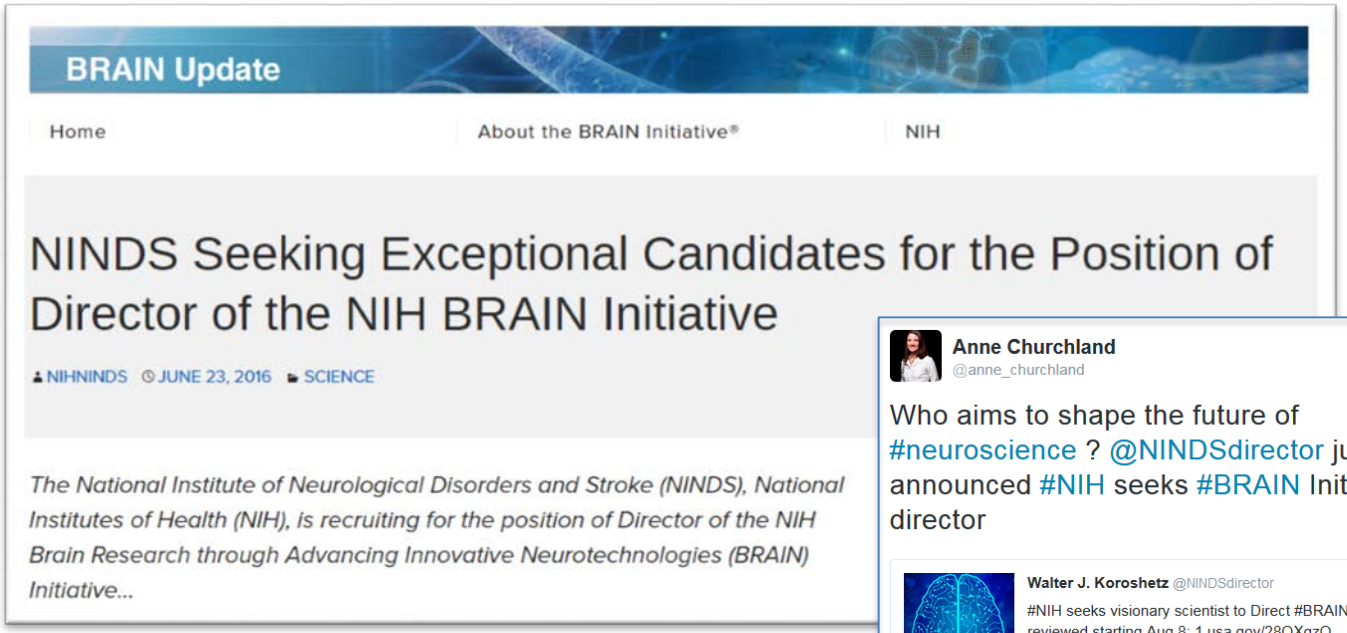


Roderic Pettigrew, Ph.D., M.D. stepped down as **Director of NIBIB** to join Texas A&M University and lead Engineering Health (EnHealth)
Jill Heemskerk, Ph.D. is Acting NIBIB Director (Member of BRAIN Coordinating Team)

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)

BRAIN Scientific Staff

NIH is reopening the search and actively recruiting for BRAIN Director!



www.braininitiative.nih.gov

20 BRAIN Funding Opportunities in FY 2018:

THE BRAIN INITIATIVE®

Many Open Now

Discovering Brain Cell Types	Tools for Circuit Diagrams Across Scales	Technology to Monitor Neural Activity	Precise Interventional Tools: Linking to Behavior	Theory, Fundamentals and Data Analysis Tools	Advancing Human Neuroscience	Integrated Approaches: From Initiative to the Brain

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)

New NIH Definition of Clinical Trial

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

Identifying the Right Funding Opportunity is Key

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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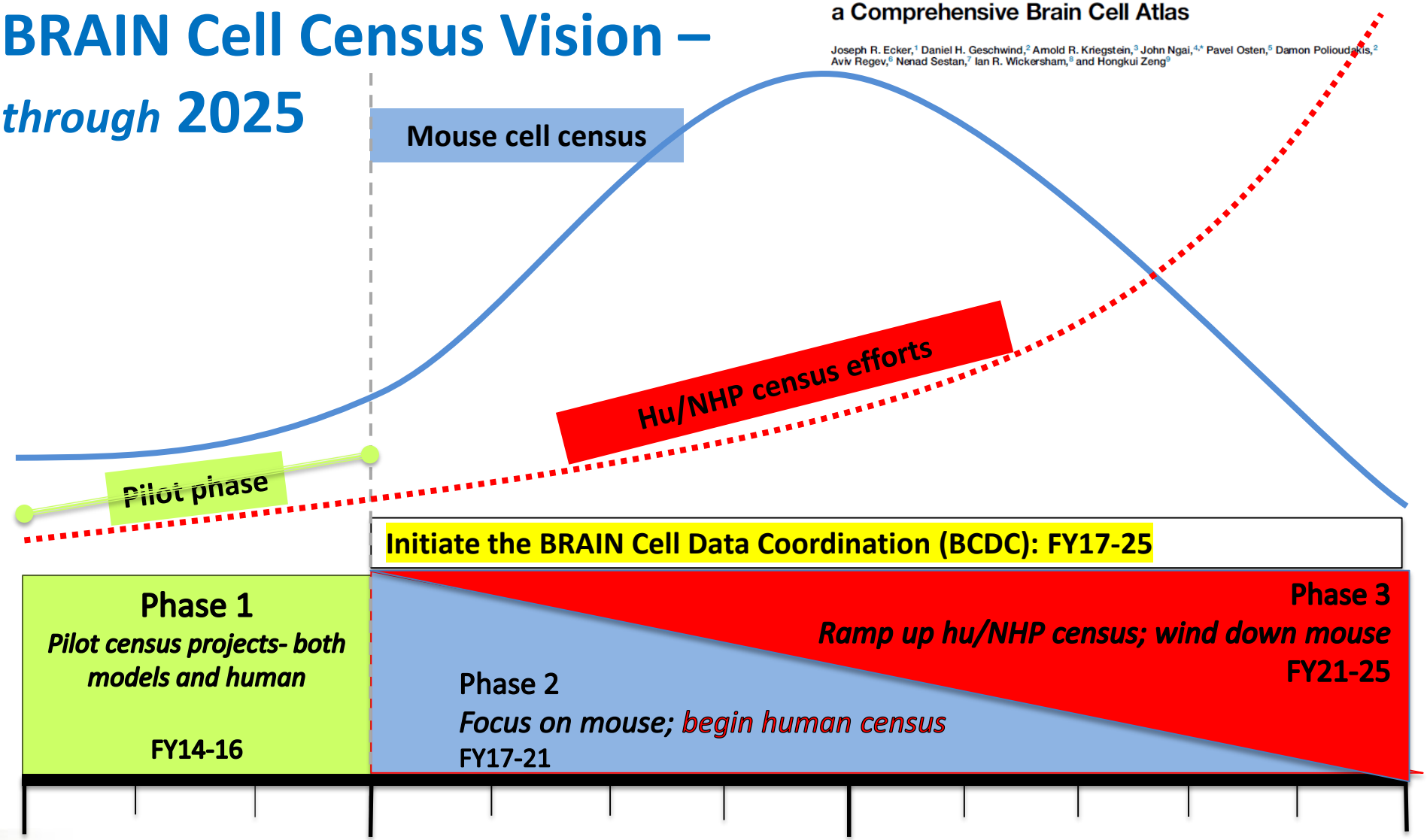
CellPress
Neuron
Perspective

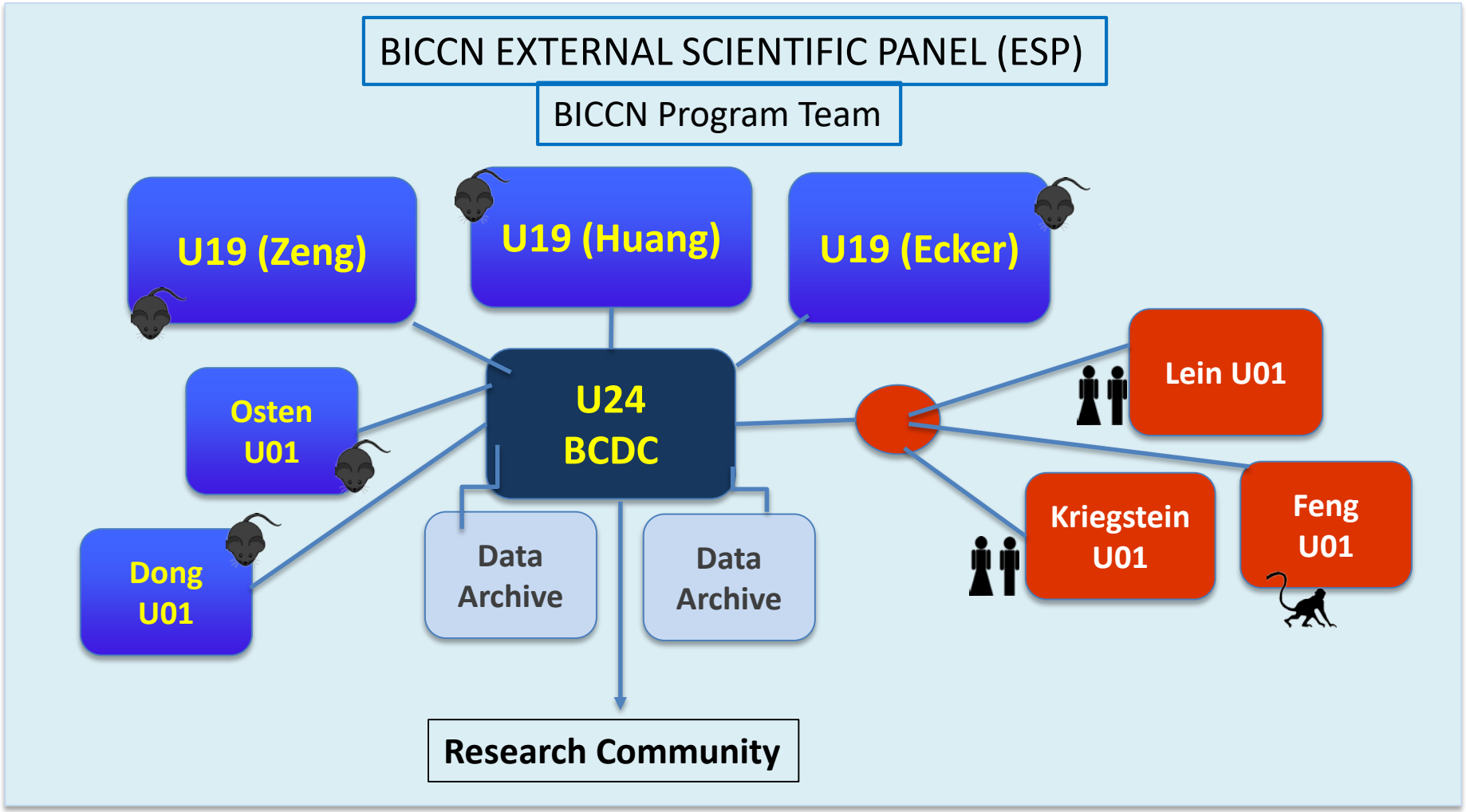
BRAIN Cell Census Vision – *through* 2025

The BRAIN Initiative Cell Census Consortium: Lessons Learned toward Generating a Comprehensive Brain Cell Atlas

Joseph R. Ecker,[1] Daniel H. Geschwind,[2] Arnold R. Kriegstein,[3] John Ngai,[4,*] Pavel Osten,[5] Damon Polioudakis,[2] Aviv Regev,[6] Nenad Sestan,[7] Ian R. Wickersham,[8] and Hongkui Zeng[9]



Launched in FY2017: *BRAIN Initiative Cell Census Network*



Funded 11 projects ~$ 50M/yr for 5 years

THE BRAIN INITIATIVE®

Exciting Advances Continuing to Emerge

frontiers in Molecular Neuroscience

LETTER

nature international weekly journal of science

Bidirectional electromagnetic control of the hypothalamus regulates feeding and metabolism

Sarah A. Stanley[1], Leah Kelly[1], Kaamashri N. Latcha[1], Sarah F. Schmidt[1], Xiaofei Yu[1], Alexander R. Nectow[1], Jeremy Sauer[2], Jonathan P. Dyke[3], Jonathan S. Dordick[2] & Jeffrey M. Friedman[1,4]

A Toolkit for Orthogonal and *in vivo* Optical Manipulation of Ionotropic Glutamate Receptors

Joshua Levitz, Andrei T. Popescu, [...], and Ehud Y. Isacoff

LETTERS

nature biotechnology

Cre-dependent selection yields AAV variants for widespread gene transfer to the adult brain

Benjamin E Deverman[1], Piers L Pravdo[1], Bryan P Simpson[1], Sripriya Ravindra Kumar[1], Ken Y Chan[1], Abhik Banerjee[1], Wei-Li Wu[1], Bin Yang[1], Nina Huber[2], Sergiu P Pasca[2] & Vivi

Neuron

Cell

Volume 88, Issue 6, 16 December 2015, Pages 1121–1135

NeuroResource

Mapping Sub-Second Structure in Mouse Behavior

Article

Neuron

Inhibition, Not Excitation, Drives Rhythmic Whisking

Highlights

- Sniffing and whisking oscillators drive different pools of facial motoneurons
-

Authors

Martin Deschênes, Jun Takatoh, Anastasia Kurnikova, ...,

Cell Stem Cell

Available online 30 March 2016

In Press, Corrected Proof — Note to users

Brief Report

Expression Analysis Highlights AXL as a Candida Entry Receptor in Neural Stem Cells

Over 320 publications have emerged from NIH BRAIN to date

https://www.braininitiative.nih.gov/resources/publication.aspx

BRAIN *Investigators Meeting*

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/PImeeting

- Program available online
  - 5 Keynote presentations broadcast live
  - Panels focused on BICCN, data coordination, commercialization, neuroethics, diversity, and more!

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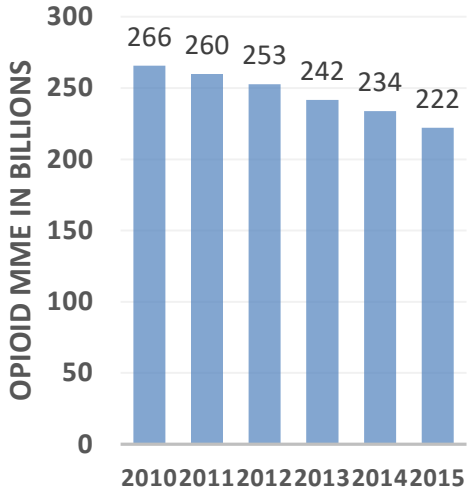
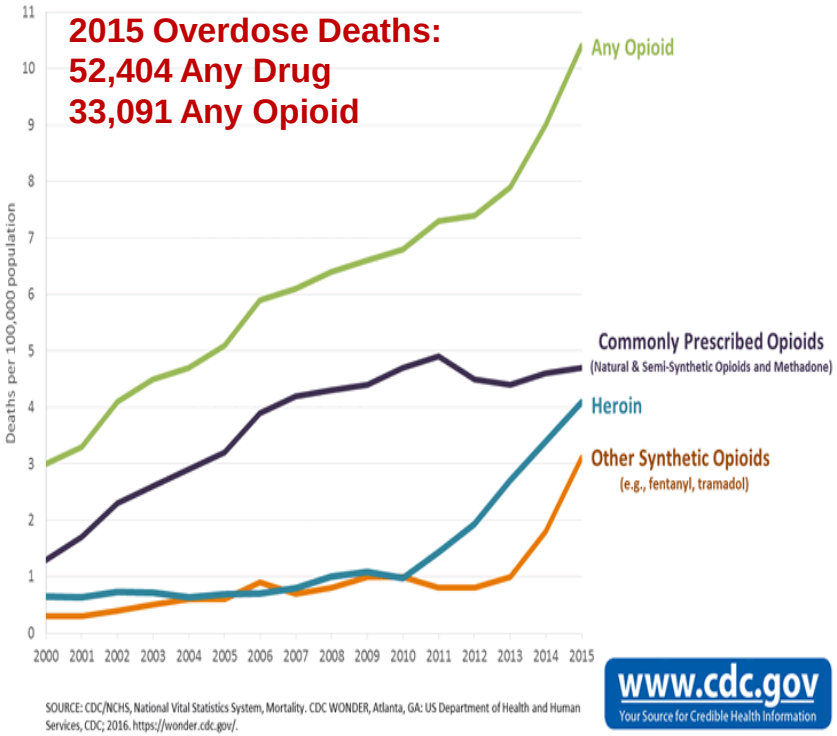
Opioid Prescriptions have started to Decrease but Opioid Fatalities are still Increasing

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



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

Opioid OD Deaths US, 2000-2015



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

National Institutes of Health
Turning Discovery Into Health

NIH on the Opioid Epidemic and Chronic Pain

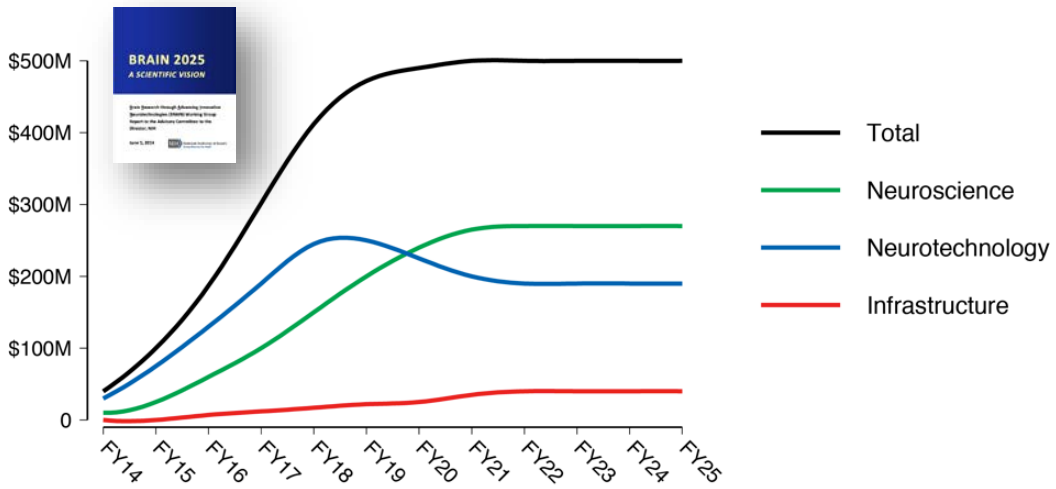
- Address rise in opioid-related fatalities via 3 pillars:
  - Improve overdose-reversal and prevention interventions
  - New medications, technologies to treat opioid addiction
  - ID safe, effective, non-addictive interventions for chronic pain

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.

https://grants.nih.gov/grants/guide/notice-files/NOT-NS-18-008.html

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

Updating the Scientific Vision of BRAIN

Tentative timeline

March 2018: Request for information on *BRAIN 2025*

Summer/Fall 2018: Country-wide workshops

Summer 2019: Final version of BRAIN strategic plan released

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

Winter 2020: Deadline for FY2020 FOAs

Preliminary Charge to the WG

- 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!

Walter J. Koroshetz, M.D.

Email: koroshetzw@ninds.nih.gov

Joshua A. Gordon

Email: joshua.gordon@nih.gov

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