

# State of BRAIN

BRAIN Multi-Council Working Group

Walter J. Koroshetz, MD

Joshua A. Gordon, MD, PhD

Co-chairs, NIH BRAIN MCWG

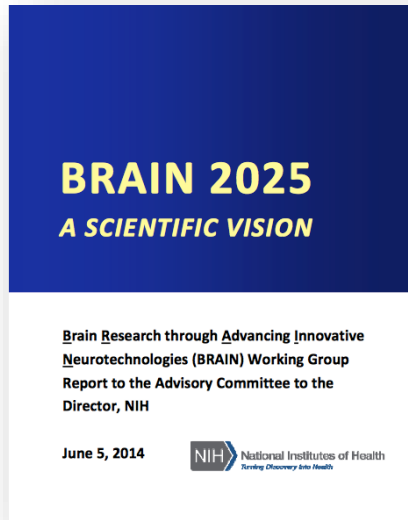
January 30, 2018

- 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
  - 4<sup>th</sup> Annual Investigator Meeting
- BRAIN: Next Steps
  - Responding to the opioid epidemic
  - Revisiting *BRAIN 2025*

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# Focus on Circuit Structure and Function

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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

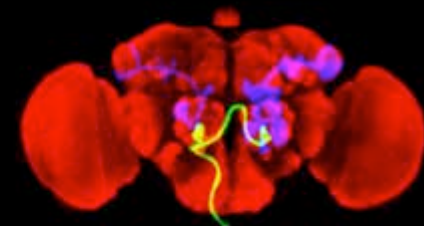
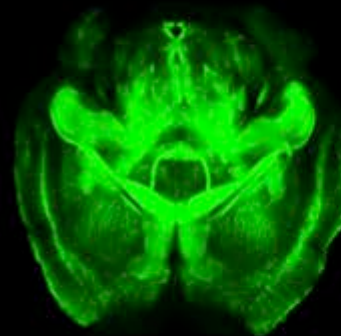
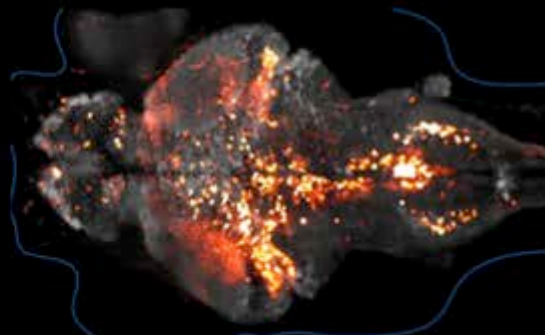
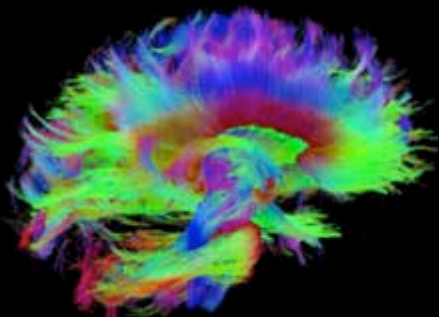
**Long-term goal:** Make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention

FIRST FIVE YEARS

Emphasize  
technology  
development

SECOND FIVE YEARS

Emphasize  
discovery  
driven science



**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*

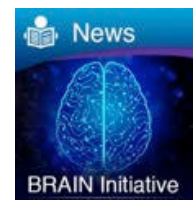
**4th NIH BRAIN awards**  
*May, October 2017*



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



**1st NIH BRAIN awards**  
*September 2014*



**1st BRAIN Initiative Alliance discussion**  
*July 2015*

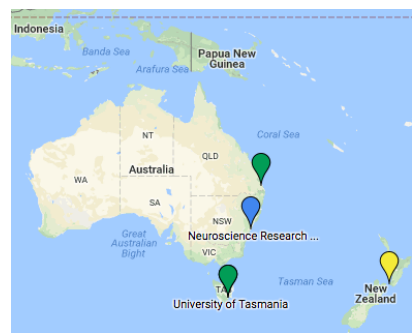
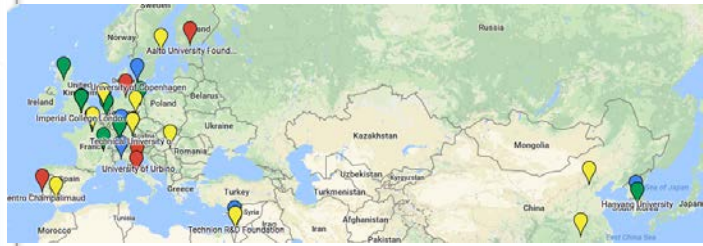


**Public-Private Partnership Program established**  
*September 2015*

**21<sup>st</sup> Century Cures Act signed into law**  
*December 2016*



**4th BRAIN PI Meeting**  
*April 2018*



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

# BRAIN Competing \$ Available

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(dollars in millions)

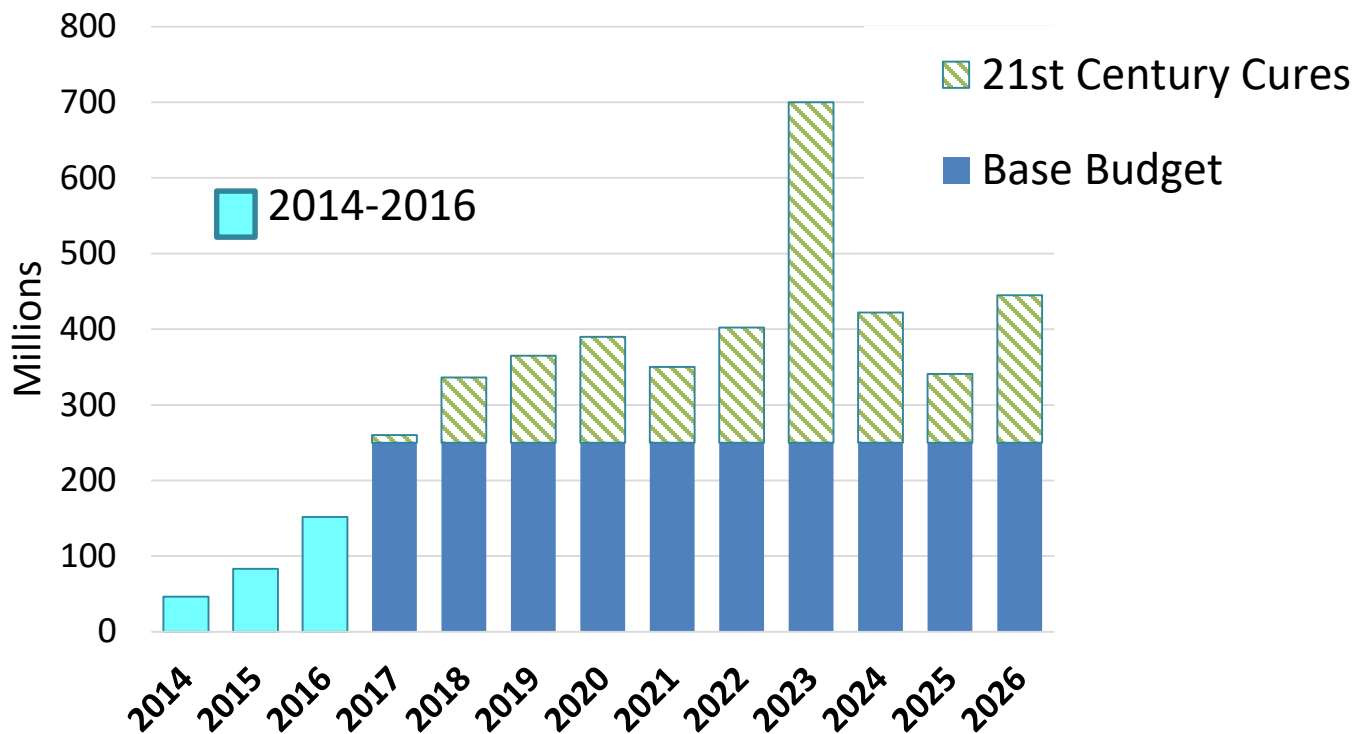
Sources	FY 2014 Actual	FY2015 Actual	FY 2016 Actual	FY 2017 Actual	FY 2018 Pres. Budget	FY 2018 House	FY 2018 Senate
IC BRAIN Base	\$30.7	\$55.4	\$140.4	\$240.4	\$140.4	\$240.4	\$304.4
Blueprint	\$10.0	\$10.0	\$10.0	\$10.0	\$-	\$-	\$-
CRCNS/Other	\$-	\$-	\$-	\$-	\$10.0	\$10.0	\$10.0
21 <sup>st</sup> Century Cures	\$-	\$-	\$-	\$10.0	\$86.0	\$86.0	\$86.0
<b>Subtotal</b>	<b>\$40.7</b>	<b>\$65.4</b>	<b>\$150.4</b>	<b>\$260.4</b>	<b>\$236.4</b>	<b>\$336.4</b>	<b>\$400.4</b>
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
<b>Total</b>	<b>\$46.1</b>	<b>\$83.2</b>	<b>\$155.2</b>	<b>\$261.9</b>	<b>\$236.4</b>	<b>\$336.4</b>	<b>\$400.4</b>



**\$4.2B:** Projected total for lifetime of BRAIN

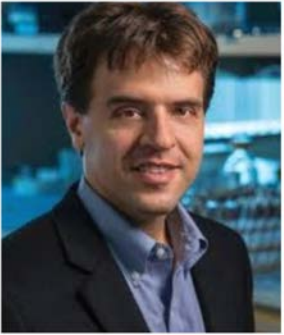
**\$550M:** BRAIN Funding through 2017

~12% of the total





- 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)

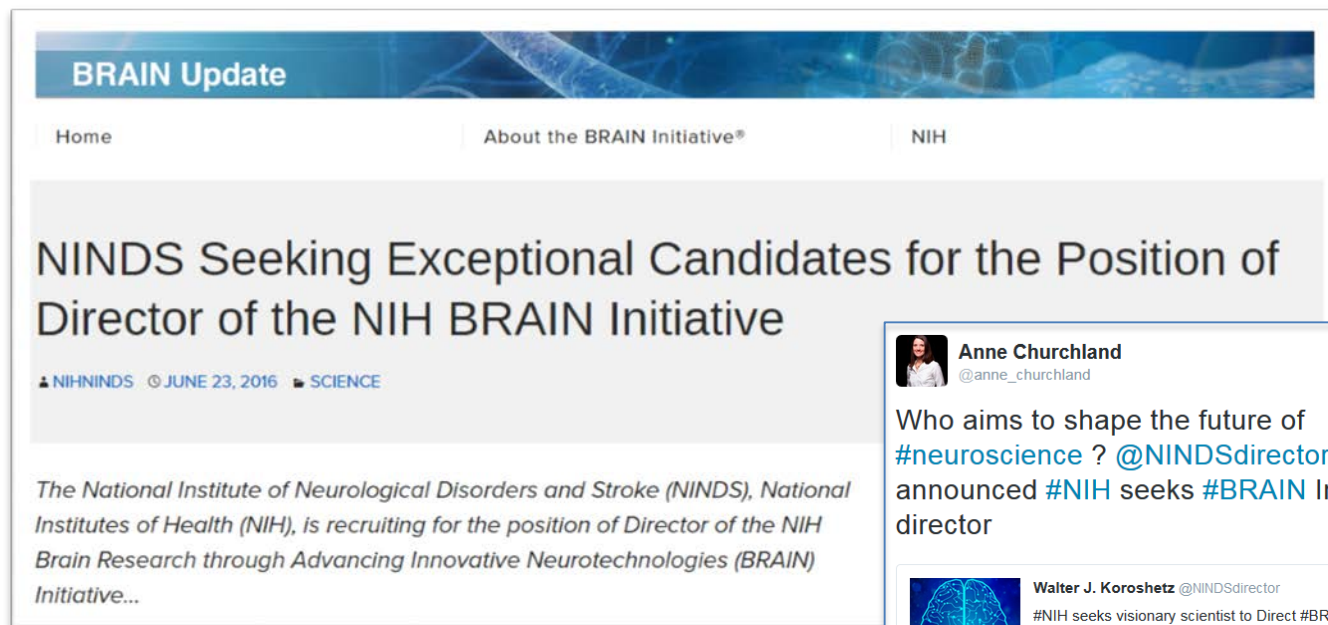
Jill Heemskerk, Ph.D. is Acting NIBIB Director (Member of BRAIN Coordinating Team)



**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!



**BRAIN Update**

Home | About the BRAIN Initiative® | NIH

## NINDS Seeking Exceptional Candidates for the Position of Director of the NIH BRAIN Initiative

NIHNINDS | JUNE 23, 2016 | SCIENCE

*The National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH), is recruiting for the position of Director of the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative...*



**Anne Churchland** @anne\_churchland Following

Who aims to shape the future of #neuroscience ? @NINDSdirector just announced #NIH seeks #BRAIN Initiative director

**Walter J. Koroshetz** @NINDSdirector  
#NIH seeks visionary scientist to Direct #BRAIN Initiative, apps reviewed starting Aug 8: 1.usa.gov/28QXgzO

RETWEETS 9 | LIKES 7

6:38 AM - 27 Jun 2016

[www.braininitiative.nih.gov](http://www.braininitiative.nih.gov)



# 20 BRAIN Funding Opportunities in FY 2018:

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*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)



**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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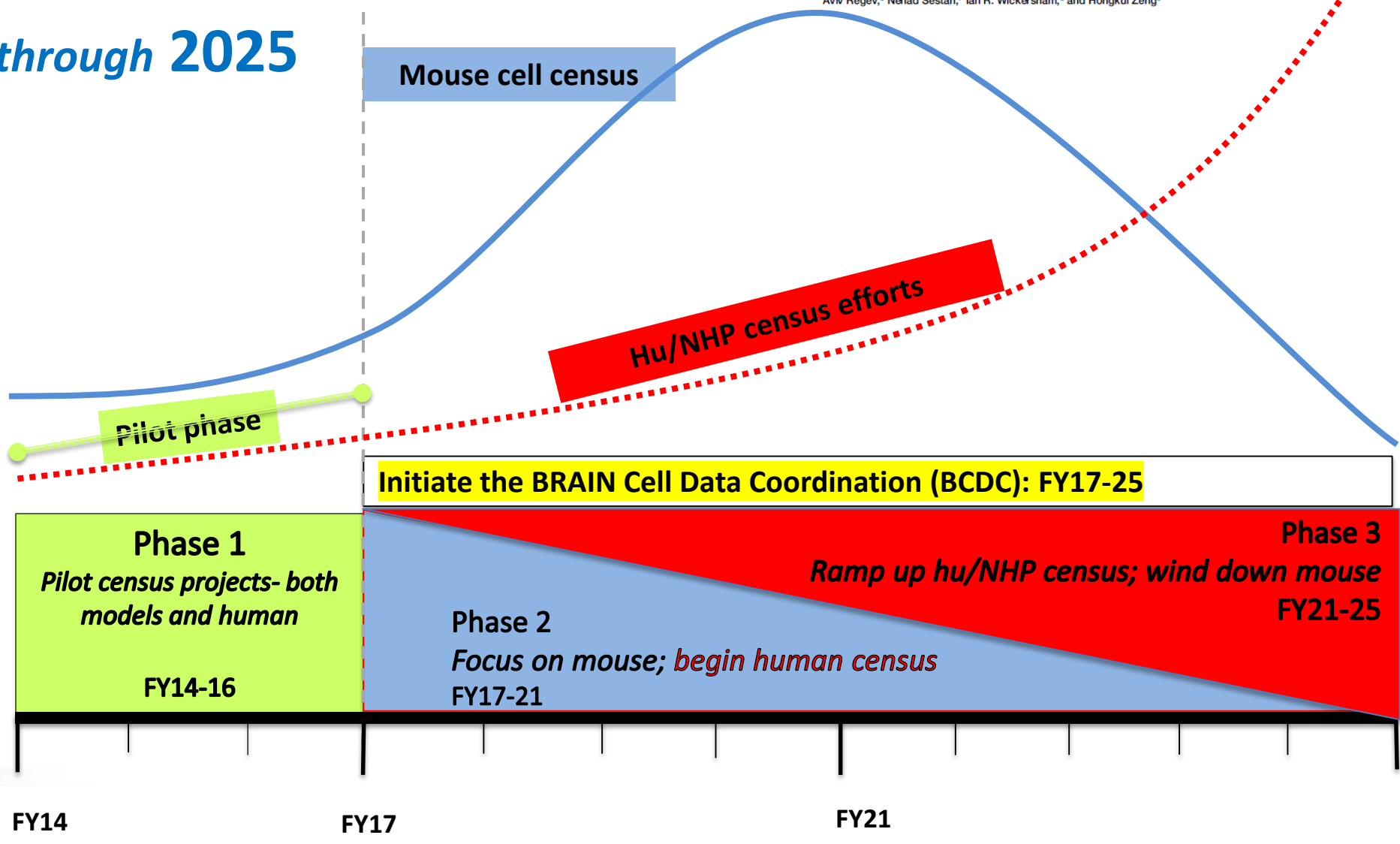


# THE BRAIN INITIATIVE®

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

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

# BRAIN Cell Census Vision – through 2025

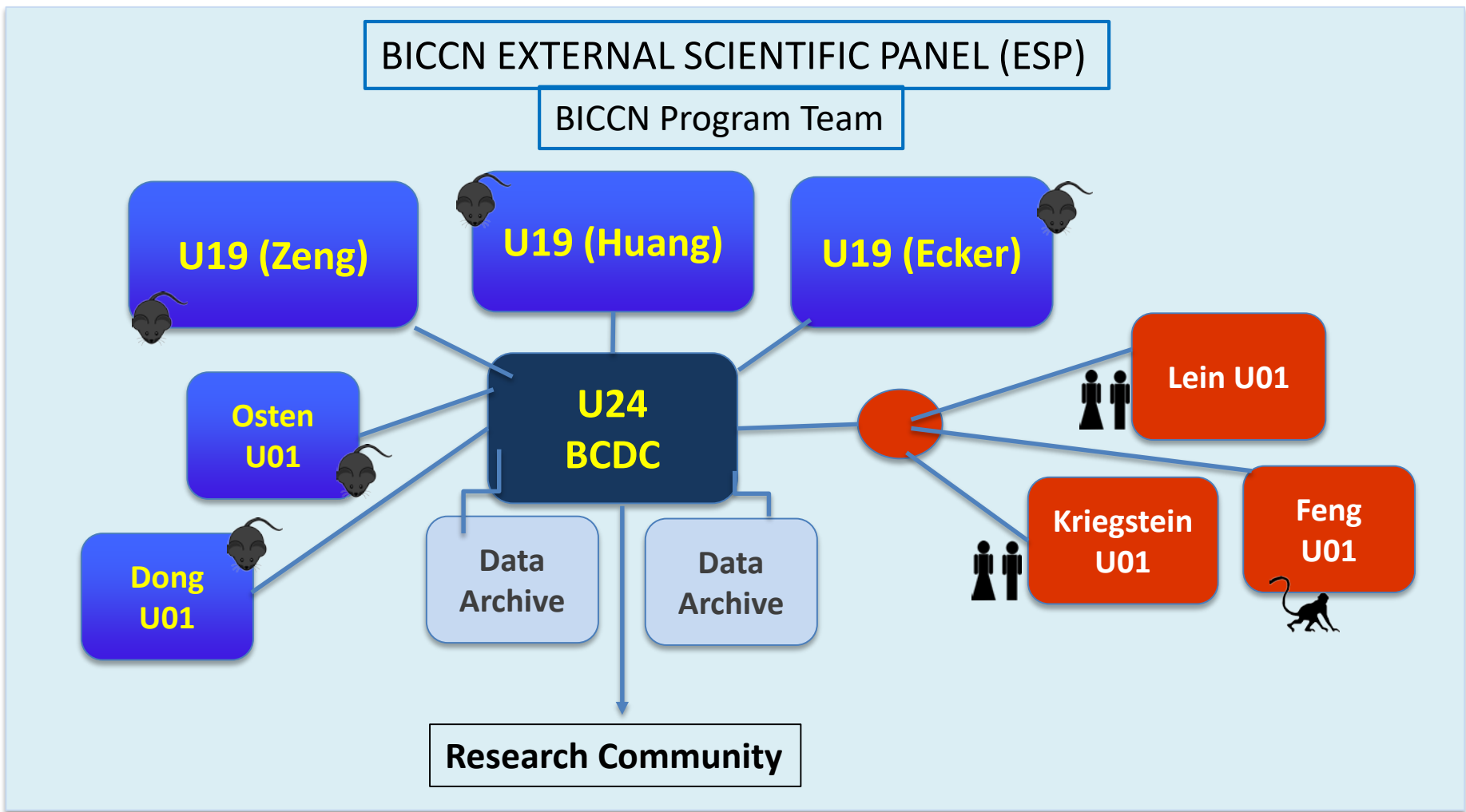






# Launched in FY2017: *BRAIN Initiative* Cell Census Network

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



## LETTER



### Bidirectional electromagnetic control of the hypothalamus regulates feeding and metabolism

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

LETTERS

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

Benjamin E. Deverman<sup>1</sup>, Piers L. Pravdo<sup>1</sup>, Bryan P. Simpson<sup>1</sup>, Sripriya Ravindra Kumar<sup>1</sup>, Ken V. Chan<sup>1</sup>, Abhik Banerjee<sup>1</sup>, Wei-Li Wu<sup>1</sup>, Bin Yang<sup>1</sup>, Nina Huber<sup>2</sup>, Sergiu P. Pasca<sup>2</sup> & Vivi



## Neuron

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

NeuroResource

### Mapping Sub-Second Structure in Mouse Behavior



Article

## 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

## Neuron

### Inhibition, Not Excitation, Drives Rhythmic Whisking

Highlights

- Sniffing and whisking oscillators drive different pools of facial motoneurons

Authors

Martin Deschênes, Jun Takahashi, Anastasia Kurnikova, ...

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.

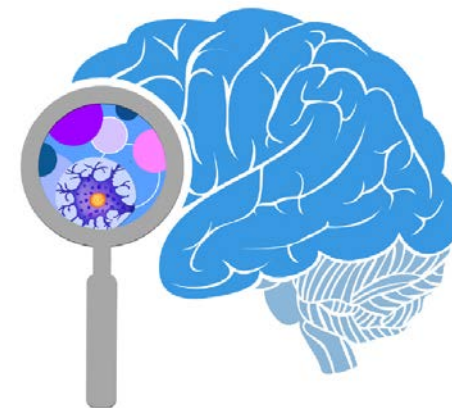
## 4<sup>th</sup> Annual Meeting: April 9-11, 2018

- ~1000 participants expected
- Bethesda North Marriott Hotel and Conference Center (Bethesda, MD, USA)
- **Registration now OPEN!**

[www.braininitiative.org/events/PImeeting](http://www.braininitiative.org/events/PImeeting)

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

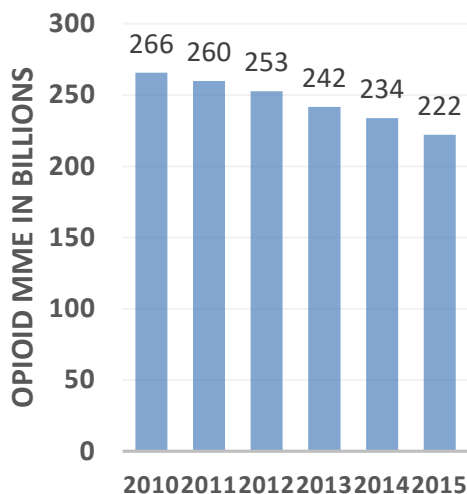
BRAIN Initiative®  
Investigators Meeting



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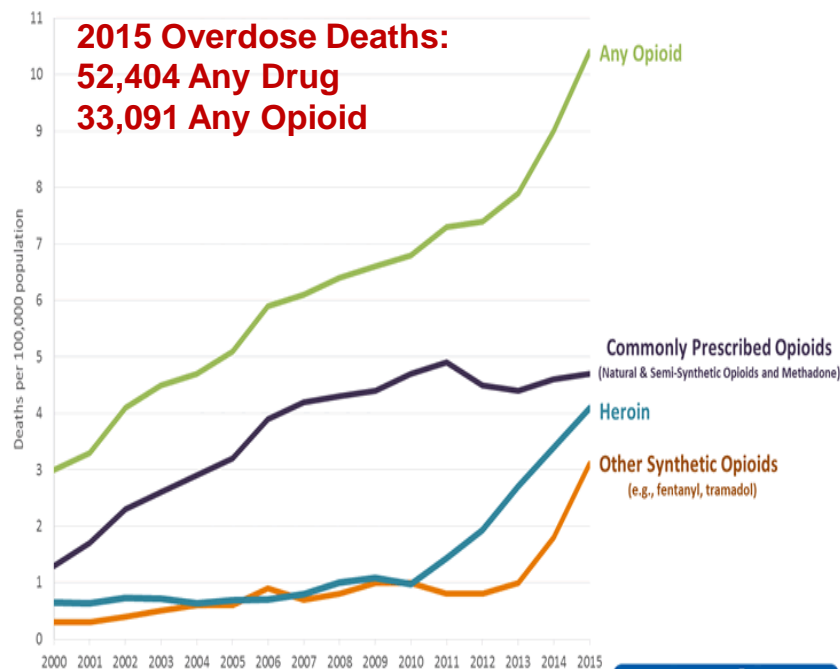
# Opioid Prescriptions have started to Decrease but Opioid Fatalities are still Increasing

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



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality, CDC WONDER, Atlanta, GA; US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.



- ~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 NEW ENGLAND JOURNAL of MEDICINE*

**SPECIAL REPORT**

## **The Role of Science in Addressing the Opioid Crisis**

Nora D. Volkow, M.D., and Francis S. Collins, M.D., Ph.D.

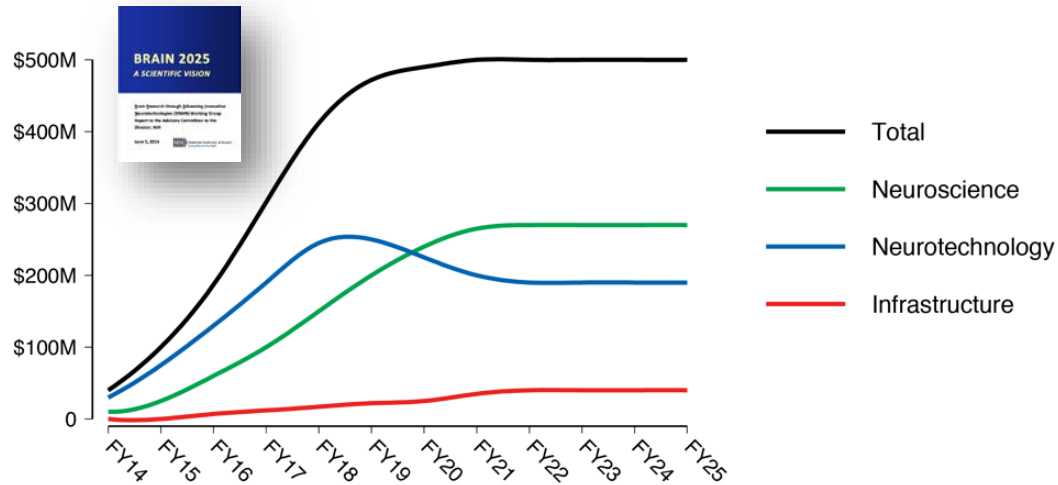
# BRAIN Initiative: Notice of Support for Research on the Fundamental Neurobiology of Pain Processing

- 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.

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

# Revisiting BRAIN in 2020 and Beyond

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***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





**March 2018:**  
Request for information on *BRAIN 2025*

**Summer/Fall 2018:**  
Country-wide workshops

**Summer 2019:**  
Final version of BRAIN strategic plan released

## 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

**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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