Congressional Neuroscience Caucus Briefing

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Neuropsychiatric Disorders Leading Cause of Disability in U.S.

Leading Categories of US DALYs 2010

1. Neuropsychiatric Disorders
   - Mental and Behavioral Disorders: 13.6%
   - Neurological Disorders: 5.1%

2. Cardiovascular and Circulatory Diseases: 16.8%

3. Neoplasms: 15.1%

4. Musculoskeletal Disorders: 11.8%

5. Diabetes, Urogenital, Blood, and Endocrine Diseases: 8.0%

6. Chronic Respiratory Diseases: 6.5%

7. Other Non-communicable Diseases: 5.1%

Percent of Total U.S. DALYs

“New directions in science are launched by new tools much more often than by new concepts. The effect of a concept-driven revolution is to explain old things in new ways. The effect of a tool-driven revolution is to discover new things that have to be explained.”

Freeman Dyson (1997) *Imagined Worlds*
Harvard University Press, Cambridge, MA
The Brain Initiative®

What is Next?

1974

Original axial CT image form Siretom CT scanner circa 1975. Physicians were fascinated by the ability to see the brain and ventricles for the first time.

2012

NIH
National Institutes of Health
Turning Discovery into Health
What If You Could See It All?
From the laboratory and collaborations of Dr. Michael Crair, Yale University
Barson, Hamodi et al. Funded FY15
Brain disorders -- a leading source of disease burden and cost in the U.S.

Recent breakthroughs are transforming how we study brain structure and function.

The BRAIN Initiative builds on this recent progress to create tools that will accelerate discovery and build the foundation we need to reduce the burden of brain disorders.
**Goal**: See the circuits in action to understand:

- How the brain moves, plans, executes
- How to monitor/manipulate circuits for improved function
- How 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
Seven High Priority Research Areas

1. Discovering diversity
2. Maps at multiple scales
3. The brain in action
4. Demonstrating causality
5. Identifying fundamental principles
6. Creating human brain research networks
7. From BRAIN Initiative to the brain
### NIH BRAIN Initiative Awards

<table>
<thead>
<tr>
<th>Category</th>
<th>New (FY2017)</th>
<th>Since BRAIN Began (FY2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number awards</td>
<td>110</td>
<td>345</td>
</tr>
<tr>
<td>Number investigators</td>
<td>178</td>
<td>504</td>
</tr>
<tr>
<td>Investment</td>
<td>$169.6M</td>
<td>$548.3M</td>
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$4.2B  Projected total for lifetime of BRAIN
$550M  BRAIN Funding through 2017: ~12% of the total
Over 315 publications have emerged from NIH BRAIN Initiative to date
**BRAIN Initiative Cell Census Network:**

- Provide a comprehensive reference of all different cell types in human, monkey, and mouse brain
- $250$ Million invested over the next $5$ years
- $9$ funded projects to support $4$ parts of the network:
  - Brain Cell Data Center
  - Mouse Brain Cell Census Center
  - Mouse Brain Cell Census Collaboratory
  - Human and Nonhuman Primate Brain Cell Census Collaboratory
K. Chan et al. 2017 *Nature Neuroscience*
Lab of Viviana Gradinaru, California Institute of Technology

Lab of Karel Svoboda, Janelia Collaboration with NIH
Anticipated outcomes

- Essential knowledge on diverse cell types and their 3D organization
- An open-access 3D digital mouse brain cell reference atlas
- A comprehensive neural circuit diagram in mouse brain
- Precision tools to monitor, map or modulate the activity of specific cells
Discoveries from BRAIN Priority Areas

- New technologies for circuit mapping
- New interventional tools for functional circuit interrogation across scales

Ting-Hao Huang et al. Development 2016;143:4073-4084

Crair, M. Yale University, BRAIN Initiative Project funded FY15
Brain activity measured while mice run on a treadmill:

From the laboratory and collaborations of Dr. Michael Crair, Yale University
Barson, Hamodi et al. Funded FY15
• Develop and improve large-scale monitoring of neural activity to produce a dynamic picture of the brain

• Link brain activity to behavior via interventional tools

Scientists reconstructed this zebrafish larva’s brain wiring from 16,000 slices. Credit: Hildebrand, Engert, Lichtman – Nature
Dr. Polina Anikeeva (MIT) is part of a Bioelectronics Group who works at the interface of materials science, electronics, and neurobiology to create devices to manipulate and record neural activity. This machine makes flexible neural probes, as shown below.
Discoveries from BRAIN Priority Areas

- Next generation human imaging technologies (phase 2 awards)
- Foundations of human imaging
- Noninvasive neuromodulation
- Next generation DBS devices for a range of disorders
- Public Private Partnership Program

Researchers are improving on FDA-approved Deep Brain Stimulation to incorporate feedback from brain to automatically adjust brain stimulation from pacemaker

www.braininitiative.nih.gov/resources/BRAIN_PPP/index
NIH BRAIN Initiative Project:
Deep Brain Stimulation Treatment for Essential Tremor

Other videos
http://www.youtube.com/watch?v=xejclvwbwsk
http://www.youtube.com/watch?v=IOHtUzW0cg
• Of 345 BRAIN awards, 80 projects involve human subjects research
• Therapeutic projects in BRAIN: 16 awards targeting nine distinct disorders
  – Developing individualized algorithms in DBS devices for Parkinson’s disease management
  – Using DBS stimulation to disrupt circuit dysfunction in OCD
  – Building next-generation device therapy for cognitive impairment associated with TBI
• In FY2017, four R01 grants awarded for neuroethics research
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

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

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

• ~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

New Notice: NIH welcomes BRAIN Initiative applications targeting central nervous system nociceptive and pain circuits

Neuroethics Division of the BRAIN Multi-Council Working Group is charged with providing input on how to address neuroethics questions raised by BRAIN Initiative research.

Neuroethics Division holds topical workshops on key issues:
- *Ethical Issues in Research with Invasive & Non-Invasive Neural Devices in Humans*
- *Workshop on Research with Human Neural Tissue*

Neuroethics Division is developing *Neuroethics Guiding Principles for NIH BRAIN Initiative*
- Principles will serve as an overarching neuroethics framework
- Will include practical suggestions on how to integrate neuroethics into BRAIN-funded research
DRAFT Neuroethics Guiding Principles for the NIH BRAIN Initiative

A solid ethical framework is a path for ensuring that scientific research is of the utmost value to the public it intends to serve. Therefore, the research supported by and the knowledge generated through the BRAIN Initiative should be regularly assessed for their ethical, legal, and societal implications.

- Need ongoing dialogue between neuroscience researchers, neuroethicists, funders, and other stakeholders
- The Guiding Principles serve to inform this dialogue, and are framed by two general points:
  1) Pursuing neuroscience research is an ethical imperative
  2) Neuroethics is vital to neuroscience research
**BRAIN 2025 Report:** First years [should] emphasize technology development and validation, with a growing emphasis on problem-driven neuroscience after FY2020.
New panel of outside scientific experts will advise the NIH Advisory Committee to the Director on updating *BRAIN 2025* to guide the second half of the Initiative

**Goals:**

- Review the NIH BRAIN Initiative progress
- Identify new topics and questions that now can be interrogated given the emerging set of tools and technologies, within a solid ethical framework to ensure the research is of the utmost value to the public it intends to serve
- Identify valuable areas of new and continued technology development
- Consider the unique contributions that the NIH BRAIN Initiative can make to neuroscience
NIH Collaborates with Federal & Non-Federal Groups

The Alliance’s Mission is to coordinate and facilitate communications from its members related to the BRAIN Initiative.

The Website is a platform for funding opportunities, news, events, achievements, resources, and more related to the BRAIN Initiative.

www.braininitiative.org
Thank You!

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