Mission-oriented R&I policies: In-depth case studies

Case Study Report

BRAIN INITIATIVE (US)

Eva Arrilucea, Hanna Kuittinen
February 2018

Case Study Report: Brain Initiative (United States)

European Commission
Directorate-General for Research and Innovation
Directorate A — Policy Development and Coordination
Unit A.6 — Open Data Policy and Science Cloud
Contact Arnold Weiszenbacher
E-mail arnold.weiszenbacher*@ec.europa.eu*
RTD-PUBLICATIONS@ec.europa.eu
European Commission
B-1049 Brussels

Manuscript completed in February 2018.

This document has been prepared for the European Commission however it reflects the views only of the authors, and the Commission cannot be held responsible for any use which may be made of the information contained therein.

More information on the European Union is available on the internet (http://europa.eu).

Luxembourg: Publications Office of the European Union, 2017

PDF	ISBN 978-92-79-80162-4	doi:10.2777/1986	KI-01-18-153-EN-N

© European Union, 2018.

Reuse is authorised provided the source is acknowledged. The reuse policy of European Commission documents is regulated by Decision 2011/833/EU (OJ L 330, 14.12.2011, p. 39).

For any use or reproduction of photos or other material that is not under the EU copyright, permission must be sought directly from the copyright holders.

EUROPEAN COMMISSION

Mission-oriented R&I policies: In-depth case studies

Case Study Report

Brain Initiative (United States)

Eva Arrilucea

Hanna Kuittinen

A Study coordinated by the Joint Institute for Innovation Policy

February 2018 Directorate-General for Research and Innovation

Table of Contents

1 Summary of the case study 1
2 Context and objectives of the initiative 4
2.1 Contextual factors and origins of initiative 4
2.2 Strategic and operative objectives and milestones of the initiative 7
3 Resources and management 9
3.1 Governance and management model 9
3.2 Financing model 10
3.3 Key actors and key technologies and platforms involved in the initiative 13
3.4 Monitoring system and evaluation of the initiatives 16
3.5 Level and type of citizen engagement in the initiative 16
4 Policy instruments and wider policy-mix used for implementing the initiative 17
4.1 Description of the R&I policy instruments used for implementing of the initiative 17
4.2 Connection with other policies 21
4.3 Key turning points of the initiative and policy adaptation measures 24
5 Realised or expected outputs, outcomes and impacts 26
5.1 Outputs and New Instruments 26
5.2 Outcomes 26
5.3 Impacts 26
5.4 Summary of the key indicators. 27
6 Conclusions and lessons learned 29
6.1 Identification and assessment of key strengths and weaknesses of the initiative 29
6.2 Lessons learned and key messages for European R&I policy 29
References 31

1 Summary of the case study

This document analyses the case study of mission-oriented R&I policy initiatives in the field of BRAIN studies and more concretely, the US BRAIN Initiative.

The following table describes the main components of the case study:

	BRAIN INITIATIVE
Title:	The Brain Initiative
Country:	USA
Thematic area:	Health
Objective(s):	The Brain Initiative seeks to deepen understanding of the inner workings of the human mind and to improve how we treat, prevent, and cure disorders of the brain.
Main Governing Body	Private-Public Partnership
Timeline:	2013-2025
Budget:	USD 1.36 billion (public and private funding from 2013 to 2016) and USD 1.5 billion (part of public funding estimated from 2017 to 2025).
Brief description of the case (250 words)	On April 2, 2013, President Obama launched the BRAIN Initiative as part of a broader White House Neuroscience Initiative to "accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought." The challenge is to map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity flowing within those circuits, and understand how their interplay creates our unique cognitive and behavioural capabilities
Implementation and organisation (a brief description of the governance and policy instruments used)	The BRAIN Initiative is a **public-private partnership** including National Institutes of Health NIH, National Science Foundation NSF, Defense Advanced Research Projects Agency DARPA, Intelligence Advanced Research Projects Activity IARPA, Food and Drug Administration FDA and several private foundations, institutes, universities, companies and international partners.
Observed / expected outputs, outcomes, and impacts	• Since the beginning of BRAIN Initiative, there are almost 300 publications classified in seven research categories: cell types, circuit diagrams, monitor neural activity, interventional tools, theory and data analysis tools, human neuroscience and integrated approaches. • **New tools and technologies.** In general, technologies that are emerging from BRAIN Initiative are diverse and range from transgenic animals to sophisticated instrumentation to computational tools. Some examples are: DREADD (Designer Receptor Exclusively Activated by a Designer Drug) technology, to experimentally control circuits in animal's brains in order to understand their function; optogenetics, a technique that allows researchers to control neuronal activity with light; miniature fluorescence microscopes, a new technology to record from thousands of neurons simultaneously; a neuroprosthetic device that translates "thoughts" into movement; diagrams ranging in scale; Brainbow, to colour neurons with fluorescent dye; CLARITY, a tissue-preservation method; photoacoustic imaging, a technique that blends the speed of precision of light with the penetrating ability of sound to interrogate neural activity; Z-brain, an open-source anatomical atlas of the entire zebrafish brain; miniaturised and highly sensitive electrophysiology and optical imaging instruments; improvements in functional magnetic resonance imaging (fMRI) • **New platforms**. The International Brain Station, a virtual platform for collaboration and data sharing for neuroscientists worldwide, Neurodata Without Borders, another platform to share physiological data, NeuroNex, a National Research Infrastructure for Neuroscience. • 306 publications

	BRAIN INITIATIVE
	• BRAIN Initiative has inspired similar large-scale brain research projects around the world, including Japan, Australia, Canada, China, South Korea and Israel.
Main elements of mission-oriented R&I initiative: [1]	
Directionality:	**YES.** Neurological disorders are one of the main causes of death over the world and entails a substantial and increased cost in the US.
Intentionality:	**YES.** The initiative has specific and well-articulated **targets**: • Accelerate the development and application of new neurotechnologies; • Enable researchers to produce a dynamic picture of the brain functioning in real time; • Explore how the brain records, processes, uses, stores, and retrieves vast quantities of information; • Shed light on the complex links between brain function and behaviour, incorporating new theories and computational models; • Help bring safe and effective products to patients and consumers.
Clearly set timeline and milestones:	**YES.** The initiative has defined scientific **milestones** with clear horizons: • Discovering diversity; • Maps at multiple scales; • The brain in action; • Demonstrating causality; • Identifying fundamental principles; • Advancing human neuroscience; • From BRAIN Initiative to the brain.
Mobilises public and private investments:	**YES.** The BRAIN Initiative is a **public-private partnership** including National Institutes of Health NIH, National Science Foundation NSF, Defense Advanced Research Projects Agency DARPA, Intelligence Advanced Research Projects Activity IARPA, Food and Drug Administration FDA and several private foundations, institutes, universities, companies and international partners.
Focused on new knowledge creation (basic research, TRLs 1-4):	**YES.** the BRAIN Initiative has a primary focus on technology development in the first five years (2016-2020),
Focused on knowledge application (applied research, TRLs 5-9):	**YES.** The BRAIN Initiative has a goal in the period (2021-2025) on integrating technologies to make fundamental new discoveries about the brain.
Demand articulation (involves instruments for inducing demand):	**TO CERTAIN DEGREE.** In this first part of the initiative (2016-2020) the main focus is on technology development.
Multi-disciplinary (inter-disciplinary and/or trans-disciplinary):	**YES:** This challenge can only be achieved through innovative, multidisciplinary investigation at all levels of nervous system function – behavioural, electrophysiological, anatomical, cellular, and molecular. In parallel, advances in theory, computation, and analytics will be essential to understand and manage the large quantities of new data that will soon flow from neuroscience laboratories
Joint coordination (multi-level and/or horizontal governance of policies/finance):	**YES. Brain Initiative Alliance** is held by many participants that come from the public and private sectors, including agencies of the federal government agencies, private industry leaders, philanthropists, non-profit organisations, foundations, colleges and universities. The alliance seeks to inform and engage the public and the scientific community

[1] Assessment: Yes, To certain degree, No or Not known.

	BRAIN INITIATIVE
	about scientific successes emerging from the BRAIN Initiative, and opportunities for further discovery.
Reflexivity (flexible policy design, timely monitoring):	**YES. The BRAIN Multi-Council Working Group** coordinates and focuses effort across **NIH**. The Multi-Council Working Group provides ongoing oversight of the long-term scientific vision of the BRAIN initiative in the context of the evolving neuroscience landscape. It also serves as a forum for initial "concept clearance," the review of ideas for new initiatives before they become funding announcements.
Openness (connected to international agendas and networks):	**YES.** Cross boundaries in interdisciplinary collaborations is one of the main principles for BRAIN Initiative. In fact, a significative number of grants have gone to non-US researchers and there is an open debate about the creation of a Global Brain Initiative
Involvement of citizens:	**TO CERTAIN DEGREE.** To develop the document strategic vision[2] four workshops with scientific stakeholders were organised in the summer of 2013, and **public feedback sessions** (included patient advocacy groups and members of the lay public) followed publication of the preliminary report in September 2013.

[2] "Brain 2025. A scientific Vision ". Op.cit.

2 Context and objectives of the initiative

This Chapter contains the contextual factors and origins of the BRAIN Initiative, as well as strategic and operative objectives and milestones.

2.1 Contextual factors and origins of initiative

Progress in neuroscience has been limited by the technologies available during any given area. Over the past decade, however, remarkable technological advances have created new ways for studying and understanding the brain. Recognising that we are on the threshold of a revolution in modern neuroscience, the BRAIN Initiative was launched in 2013.[3]

The Brain Research Through Advancing Innovative Neurotechnologies, the **BRAIN Initiative** is part of an ambitious, public-private collaborative effort aimed at developing new experimental tools to revolutionise the understanding of the brain. The BRAIN Initiative seeks to deepen understanding of the inner workings of the human mind and to improve how disorders of the brain are treated, prevented and cured.

On April 2, 2013, President Obama launched the BRAIN Initiative as part of a broader White House Neuroscience Initiative to "*accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought.*" The challenge is to map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity flowing within those circuits, and understand how their interplay creates our unique cognitive and behavioural capabilities. This challenge can only be achieved through innovative, multidisciplinary investigation at all levels of nervous system function – behavioural, electrophysiological, anatomical, cellular, and molecular. In parallel, advances in theory, computation, and analytics will be essential to understand and manage the large quantities of new data that will soon flow from neuroscience laboratories (see Figure 1).

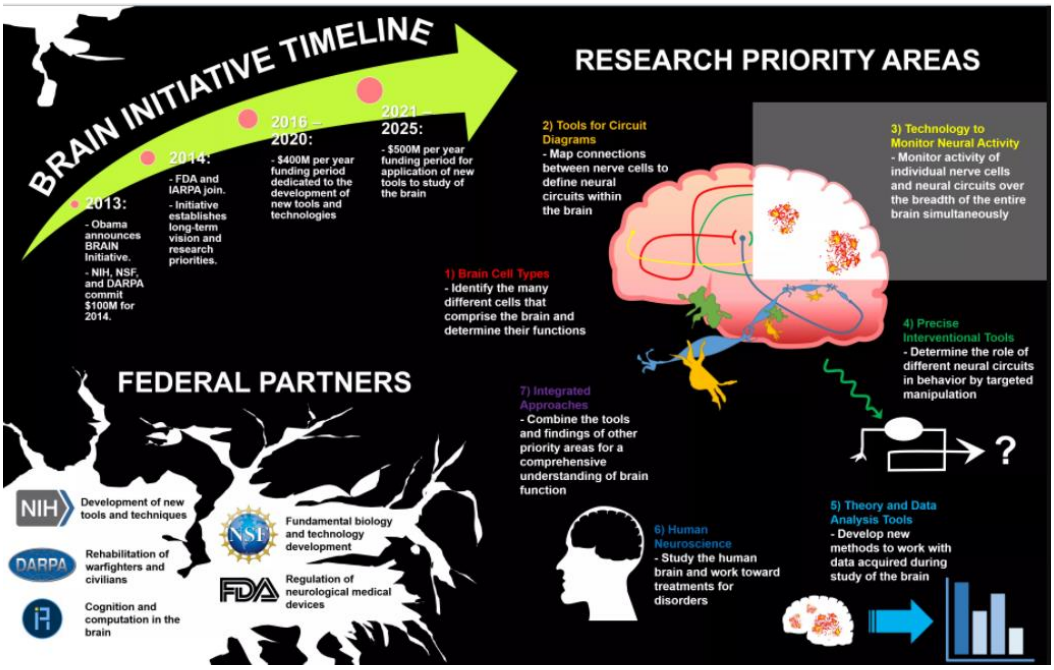

Figure 1: Brain Initiative Infographic. Source: Science in the News. Harvard University. The graduate School of Arts and Science (2016)

[3] Jorgenson LA et al. (2015). "The BRAIN Initiative: developing technology to catalyse neuroscience discovery. Phil. Trans. R. Soc. B 370: 20140164. http://dx.doi.org/10.1098/rstb.2014.0164

In response to this challenge, the National Institutes of Health (NIH) convened a working group of the Advisory Council to the NIH Director to develop a rigorous plan for achieving this scientific vision. The vision that guides the Initiative is contained in the document "Brain 2025. A scientific Vision"[4].

Although this is not the first attempt of US government to foster brain research (President Bush Announced the project on the Decade of the Brain DOB in 1990[5]), BRAIN Initiative is the first one explicitly directed toward the development of new tools to enable scientists to monitor and modulate brain circuit activity.[6]

	Drivers	Barriers
Political		• A total of 24% of countries stand-alone neurological health policies, although there is a major deficit in low- and middle-income countries.[7] • Expertise in a given project does not necessarily reside in a single country and there are not enough cross-national mechanisms of funding to support international teams or a global brain initiative.
Economic		• The former director of the National Institute of Mental Health, Dr. Thomas Insel, estimated that the total cost of serious mental illness in the US in 2002 exceeded USD 317 billion. In the last 15 years, that cost has only grown.[8]
Societal	• Neurological disorders ranked as the leading cause group of disability-adjusted life-years (DALYs) in 2015 and the second leading cause group of deaths.[9] • The burden of neurological disorders has increased substantially over the past 25 years because of expanding population	• There are unresolved ethical and societal questions related to the application of Neurotechnologies, and monitored and modify human brain activity that should be discussed not only with experts but with the citizens as a whole. [10]

[4] National Institutes of Health (2014). "Brain 2025. A scientific Vision". Available at: https://braininitiative.nih.gov/pdf/BRAIN2025_508C.pdf
[5] More information about this project available here: http://www.loc.gov/loc/brain/
[6] Martin C, Chun M (2016) "The BRAIN Initiative: building, strengthening and sustaining". Neuron 92, Nov 2. Elsevier Inc.
[7] World Health Organisation (2017). "Atlas Country Resources for Neurological Disorders".2nd edition. ISBN 978-92-4-156550-9
[8] Ramos K, Rommelfanger K, Greely H, Koroshetz W (2017). "Neuroethics and the NIH BRAIN Initiative". of Responsible Innovation, DOI: 10.1080/23299460.2017.1319035
[9] GBD 2015 Neurological Disorders Collaborator Group (2017). "Global, regional and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". Lancet Neural 2017; 16: 877-97. http://dx.doi.org/10.1016/
[10] The NIH component of the BRAIN Initiative has utilised an iterative model of integrating ethics into the scientific trajectory of the Initiative, with the creation of a Neuroethics Division of the NIH BRAIN Initiative Multi-Council Working Group. The Division serves as a resource of expertise, to help the BRAIN Initiative navigate issues involving ethics.

	Drivers	Barriers
	numbers and ageing, despite substantial decreases in mortality rates from stroke and communicable neurological disorders. The number of patients who will need care by clinicians with expertise in neurological conditions will continue to grow in coming decades. • The prevalence of neurological diseases increases because of the growing and ageing global population. In particular, Alzheimer's disease and other dementias had increases in prevalence and mortality, especially in some high-income regions.	
Technological	• Neural coding and neural circuit dynamics are conceptual foundations upon which to base a mechanistic understanding of the brain. • New molecular generic and cellular tools are generating insights into the diverse neuronal cell types in brain. • Novel anatomical techniques are providing new opportunities for tracing the interconnections between brain regions. • Innovative electrical and optical recording tools are allowing to measure the patterns of electrical activity. • Large brain data sets can be turning into information and knowledge to accelerate the initiatives. • The advances generated by other brain-related initiatives can foster new discoveries in BRAIN Initiative.[11]	• Progress toward the BRAIN Initiative scientific goals is limited by the experiments that are technically possible. Developing these novel technologies will require intense collaboration between neuroscientists and scientists in biological, physical, engineering, mathematical, and statistical and behavioural sciences.[12] • Every practicing neuroscientist's productivity is limited due to computational resources, access to data or algorithms, or struggling with determining which data and algorithms are best suited to answer the most pressing questions. Each project related to brain research will require computational capabilities (including collecting, storing, exploring, analysing, modelling and discovering data) that will bring a whole suite of new challenges.[13]
Legal	• A total of 41% of countries report the existence of legislation on epilepsy, and	

[11] Yuste R, Bargmann C (2017). "Toward a Global Brain Initiative". Cell 168, March 9. Elsevier Inc

[12] At a meeting in Pasadena, Calif., on Jan. 17 (2013) to explore the data storage needs of the proposed mapping project, computer scientists, neuroscientists and nanoscientists concluded that it would require three petabytes of storage capacity to capture the amount of information generated by just one million neurons in a year. If the brain contains between 85 and 100 billion neurons, that means that the complete brain generates about 300 000 petabytes of data each year. Source: The New York Times 2013/02/26. "Connecting the dots".

[13] Global Brain Workshop (2016). "Grand Challenges for Global Brain Science". http://brainx.io/

	Drivers	Barriers
	30% report the existence of legislation relating to people with dementia; 29% of countries report legislation on "other" neurological disorders.[14]	

2.2 *Strategic and operative objectives and milestones of the initiative*

The main goal of the Brain Initiative is to develop new technologies to explore how the brain's cells and circuits interact at the speed of thought, ultimately uncovering the complex links between brain function and behaviour. Some of the main **strategic targets** are:[15]

- Accelerate the development and application of new neurotechnologies. Support multi-disciplinary teams and stimulate research to rapidly enhance current neuroscience technologies and catalyse innovative scientific breakthroughs;

- Enable researchers to produce a dynamic picture of the brain functioning in real time. Stimulate collaborative efforts to improve current imaging technologies and create new methods to visualise brain function at higher resolution and across wide space and time scales;

- Explore how the brain records, processes, uses, stores, and retrieves vast quantities of information. Integrate expertise from diverse fields of science for large-scale interrogation and monitoring of brain cells and circuits in real-time and across a variety of model systems;

- Shed light on the complex links between brain function and behaviour, incorporating new theories and computational models. Uncover links between brain activity, behaviour, and cognition with precise interventional tools, novel informatics methods, and pioneering models of how the brain functions;

- Help bring safe and effective products to patients and consumers. Enhance the transparency of the regulatory landscape to promote the advancement of safe neurological medical devices.

Scientific milestones are classified in short and long term. The following areas have been identified for the initiative:[16]

- Discovering diversity. Identify and provide experimental access to the different brain cell types to determine their roles in health and disease;

- Maps at multiple scales. Generate circuit diagrams that vary in resolution from synapses to the whole brain;

- The brain in action. Produce a dynamic picture of the functioning brain by developing and applying improved methods for large-scale monitoring of neural activity;

- Demonstrating causality. Link brain activity to behaviour with precise interventional tools that change neural circuit dynamics;

[14] World Health Organisation (2017) op.cit.
[15] Brain Initiative: http://www.braininitiative.org
[16] In "Brain 2015. A scientific Vision". Op.cit.

- Identifying fundamental principles. Produce conceptual foundations for understanding the biological basis of mental processes through development of new theoretical and data analysis tools;

- Advancing human neuroscience. Develop innovative technologies to understand the human brain and treat its disorders; create and support integrated human brain research networks;

- From BRAIN Initiative to the brain. Integrate new technological and conceptual approaches produced in the preceding milestones to discover how dynamic patterns of neural activity are transformed into cognition, emotion, perception, and action in health and disease.

To achieve these goals, the BRAIN Initiative has a primary focus on technology development in the first five years (2016-2020), shifting in the second five years (2021-2025) to a primary focus on integrating technologies to make fundamental new discoveries about the brain. The distinction between these phases is a matter of emphasis and opportunity. Discovery-based science motivates technology development in the first phase, and further technology development will be needed as the focus shifts to discovery in later years.

3 Resources and management

3.1 Governance and management model

The BRAIN Initiative is a **public-private partnership** including National Institutes of Health NIH, National Science Foundation NSF, Defense Advanced Research Projects Agency DARPA, Intelligence Advanced Research Projects Activity IARPA, Food and Drug Administration FDA and several private foundations, institutes, universities, companies and international partners.

The BRAIN Multi-Council Working Group[17] coordinates and focuses effort across **NIH**. This WG includes a member from the Advisory Council of each of the 10 Institutes and Centres that contribute to the NIH BRAIN Initiative, with additional at-large members appointed to supplement the working group's expertise. In addition, the working group includes ex officio members from DARPA, FDA, IARPA and NSF – four of NIH's federal partners involved in the BRAIN initiative. The Multi-Council Working Group provides ongoing oversight of the long-term scientific vision of the BRAIN initiative, as endorsed by the ACD, in the context of the evolving neuroscience landscape. It also serves as a forum for initial "concept clearance," the review of ideas for new initiatives before they become funding announcements. In addition, the working group ensures that each of the BRAIN IC Advisory Councils is informed about BRAIN initiatives, awards and progress – a critical point as the individual IC Advisory Councils will perform the formal second level of review of BRAIN Initiative applications. Finally, the working group regularly offers an assessment of the progress of current projects and programmes supported by the BRAIN Initiative.

While coordination is encouraged, each partner sets its own priorities and makes its own funding decisions.

Neuroscience research in general and the BRAIN Initiative specifically generate many important ethical questions related to the conduct and use of neuroscience research. In recognition of this, NIH has established a **Neuroethics Division** of the BRAIN Multi-Council Working Group (MCWG), that will recommend overall approaches for how the NIH BRAIN Initiative might handle issues and problems involving ethics.

In addition to the NIH White House Brain Initiative, the **Brain Initiative Alliance** is held by many participants that come from the public and private sectors, including agencies of the federal government agencies, private industry leaders, philanthropists, non-profit organisations, foundations, colleges and universities. The alliance seeks to inform and engage the public and the scientific community about scientific successes emerging from the BRAIN Initiative, and opportunities for further discovery. Alliance members have committed financial and/or in-kind staff support to manage and host this website, which serves as a portal for visitors to access a wide variety of information related to the BRAIN Initiative:

- Federal Institutions: Defense Advanced Research Projects Agency (DARPA), National Institutes of Health (NIH), National Science Foundation (NSF), The Intelligence Advanced Research Projects Activity and U.S. Food and Drug Administration;
- Foundations: Brain and Behaviour Research Foundation, Kavli Foundation, National Photonics Initiative, Pediatric Brain Foundation, Simons Foundation;
- Institutes: Allen Institute for Brain Science, Janelia/Howard Hughes Medical Institute, Salk Institute for Biological Studies;
- Universities: Boston University-Center for Systems Neuroscience, Carnegie Mellon University-BrainHub, Neurotechnology Architecting Network, Pacific Northwest

[17] The current composition of the working group is available here: https://www.braininitiative.nih.gov/pdf/BRAIN_MCWGroster_Aug172017_508Comp.pdf

Neuroscience Neighbourhood, University of Arizona-Center for Innovation in Brain Science, University of California System-Cal BRAIN, University of Pittsburg-Brain Institute, University of Texas system-UT System Neuroscience, University of Utah-Neuroscience Gateway;

- Industry: Blackrock Microsustems, Boston Scientific, GE, GlaxoSmithKline, Google, Inscopix, Lawrence Livermore National Laboratory, Medtronic, NeuroNexus, NeuroPace, Ripple, Second Sight;
- International Organisations: Autralian National Health and Medical Research Council, Brain Canada Goundation, Denmark's Lundbeck Foundation.

3.2 Financing model

In 2014, the BRAIN Initiative Working Group[18] proposed a total 12-year budget estimated of USD 4.5 billion: USD 400 million per year (2016-2020) and USD 500 million per year subsequently (2021-2025) (see Figure 2).

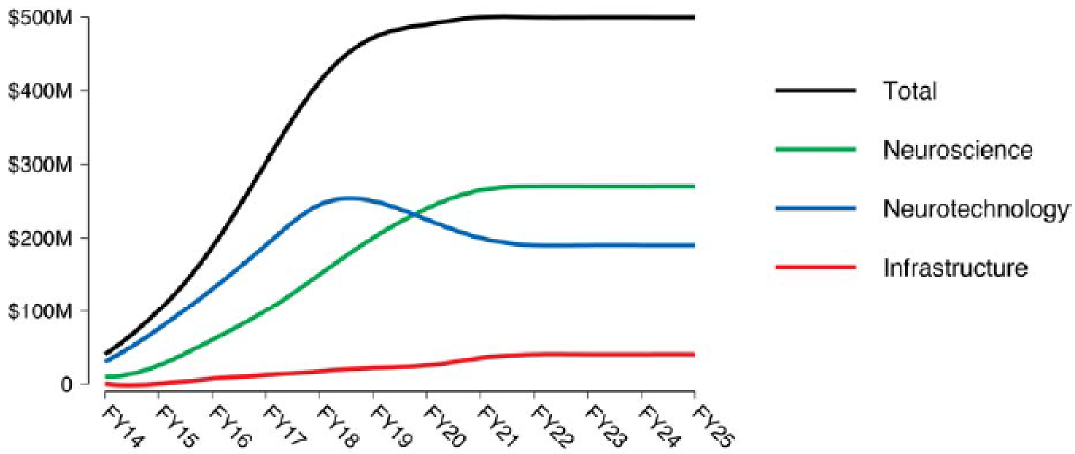

Figure 2: Proposed 12-year budget for the BRAIN Initiative. Source. BRAIN Initiative Working Group.[19]

BRAIN Initiative as launched with a budget of USD 110 million in FY2014 from the Defense Advanced Research Project Agency (DARPA), National Institutes of Health (NIH) and the National Science Foundation (NSF). Since then, **a total of USD 1.36 billion of funding have been allocated by public and private sectors.**

USD 439 million are requesting in FY2017 for the BRAIN Initiative[20], approximately USD 139 million (46%) more than the effort's estimated FY2016 funding level of USD 323 million (see Figure 3). Proposed FY2017 funding includes an estimated USD 195 million in funding for NIH, USD 118 million for DARPA, USD 74 million for NSF, USD 9 million for the DOE Office of Science, and USD 43 million for the Intelligence Advanced Research Projects Activity (IARPA).

---

[18] In "Brain 2015. A scientific Vision". Op.cit.
[19] In "Brain 2015. A scientific Vision". Op.cit.
[20] Federal Research and Development Funding: FY2017. Congressional Research Service 7-5700 R44516. Available at: https://fas.org/sgp/crs/misc/R44516.pdf

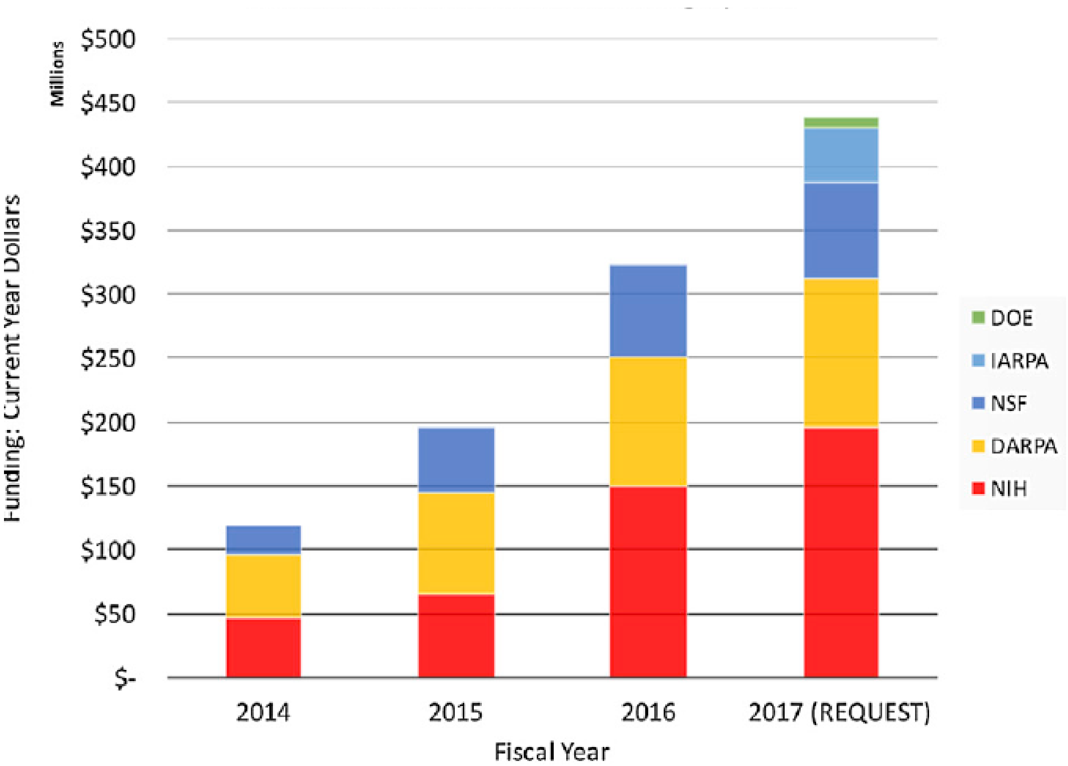

Figure 3: Federal BRAIN Initiative funding by year. Source: Martin C et al (2016).

For next years, the 21th Century Cures Act (2016) [21] signed by President Obama authorises the National Institutes of Health at the following levels:

- USD 34.851 billion for 2018;
- USD 35.585 billion for 2019;
- USD 36.472 billion for 2020.

In addition, this bill creates a USD 4.8 billion "NIH Innovation Account" over a 10-year period that supports four Initiatives: Precision Medicine Initiative (USD 1.4 billion), Cancer Moonshot (USD 1.8 billion), Regenerative Medicine (USD 30 million) and **BRAIN (USD 1.5 billion).** The following Figure 4 summarises the funding for these projects:

[21] An Act to Accelerate the Discovery, Development and Delivery of 21st Century Cures, and for Other Purposes. Public Law 114-255 114th Congress Dec.13, 2016. Available via: https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

Funding for NIH Innovation Projects under the Cures Act				
Fiscal Year	Precision Medicine Initiative	BRAIN	Cancer Moonshot	Regenerative Medicine
2017	$40,000,000	$10,000,000	$300,000,000	$2,000,000
2018	$100,000,000	$86,000,000	$300,000,000	$10,000,000
2019	$186,000,000	$115,000,000	$400,000,000	$10,000,000
2020	$149,000,000	$140,000,000	$195,000,000	$8,000,000
2021	$109,000,000	$100,000,000	$195,000,000	
2022	$150,000,000	$152,000,000	$194,000,000	
2023	$419,000,000	$450,000,000	$216,000,000	
2024	$235,000,000	$172,000,000		
2025	$36,000,000	$91,000,000		
2026	$31,000,000	$195,000,000		
TOTAL	**$1,455,000,000**	**$1,511,000,000**	**$1,800,000,000**	**$30,000,000**

Figure 4: Funding for NIH Innovation Projects under the Cures Act. Source NIH.

Having into account the priority areas identified in the strategy BRAIN 2025, the budget distribution is reflected in the following Figure 5:

BRAIN 2025 Priority Area	Innovation Project Funds
Discovering Diversity	$150,000,000
Maps at Multiple Scales	$150,000,000
The Brain in Action	$150,000,000
Demonstrating Causality	$100,000,000
Identifying Fundamental Principles	$75,000,000
Advancing Human Neuroscience	$386,000,000
From BRAIN Initiative to the Brain	$500,000,000

Figure 5: Brain 2025 Priority Areas and Funds. Source: NIH

Each scientific goal is critical to the integrated purpose of the BRAIN Initiative, but different goals require different types and amounts of resources and funding. Progress in different areas may also occur at different rates and during different stages of the Initiative. For example, initial instrumentation and technology costs are expected to be particularly high in developing new recording methods for use in humans and improving techniques to create circuit maps of whole brains. Over time, the Initiative will increasingly transition to concerted, team-science application of promising research methods with the need for more sophisticated data management, analysis, and data sharing approaches. Supporting development of infrastructure for data science and data sharing platforms will be large-scale, high-cost projects. Dissemination of new technologies may best be addressed by multiple strategies including training courses, supplements to NIH-funded grants, and establishment of centres to help investigators adopt new technologies. Moving new technologies into human testing, projected to accelerate after 2020, will also require addressing additional scientific and regulatory hurdles, with higher associated costs.[22]

3.3 Key actors and key technologies and platforms involved in the initiative

There are several private and public stakeholders deeply involved in the initiative:

Food and Drug Administration (FDA)[23]

FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. It is also responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health. FDA also has responsibility for regulating the manufacturing, marketing and distribution of tobacco products to protect the public health and to reduce tobacco use by minors. Finally, FDA plays a significant role in the Nation's counterterrorism capability. FDA fulfils this responsibility by ensuring the security of the food supply and by fostering development of medical products to respond to deliberate and naturally-emerging public health threats.

FDA supports the BRAIN Initiative by enhancing the transparency and predictability of the regulatory landscape for neurological devices and assisting developers and innovators of medical. Also, by making as transparent as possible the regulatory framework applicable to neurological devices and thereby helping to bring safe and effective products to patients and consumers.

National Institutes of Health[24]

NIH's mission is to seek fundamental knowledge about the nature and behaviour of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. The goals of the agency are:

- To foster fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health;
- To develop, maintain, and renew scientific human and physical resources that will ensure the Nation's capability to prevent disease;
- To expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research; and
- To exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

The NIH component of the BRAIN initiative is guided by its long-term scientific plan, BRAIN 2025.[25] NIH supports over 230 projects from cross-disciplinary researchers.[26] Also, it

[22] From the NIH document: "Implementation of Funding Plan for the NIH Innovation Projects Under the 21st Century Cures Act" available at: https://www.nih.gov/sites/default/files/research-training/initiatives/nih-cures-innovation-plan.pdf
[23] Food and Drug Administration. https://www.fda.gov/
[24] National Institutes of Health: https://www.nih.gov/
[25] "Brain 2025. A scientific Vision". Op.cit.
[26] Funded awards available here: https://braininitiative.nih.gov/funding/fundedAwards.htm

counts on the BRAIN Neuroethics Division[27] to raise ethical challenges and server as a resource of expertise to help the BRAIN Initiative navigate issues involving ethics.

NIH centres involved in BRAIN initiative are: National Center for Complementary and Integrative Health, National Eye Institute, National Institute on Aging, National Institute on Alcohol Abuse and Alcoholism, National Institute of Biomedical Imaging and Bioengineering, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institute of Drug Abuse, National Institute of Deafness and Other Communication Disorders, National Institute of Neurological Disorders and Stroke and National Institute of Mental Health.

The **NIH Blueprint for Neuroscience Research** includes all the institutes that support research on the nervous system and, since its inception in 2004, has supported the development of new tools, training opportunities and other resources to assist neuroscientists. In 2009, the Blueprint Grand Challenges were launched to catalyse research with the potential to transform our basic understanding of the brain and our approaches to treating brain disorders.

National Science Foundation (NSF)[28]

The National Science Foundation (NSF) is an independent federal agency created by Congress in 1950 to promote the progress of science; to advance the national health, prosperity, and welfare and to secure the national defence. In many fields such as mathematics, computer science and the social sciences, NSF is the major source of federal backing.

The National Science Foundation fosters BRAIN Initiative by bringing together a wide range of scientific and engineering disciplines from national and international communities. NSF empowers those communities to cooperatively pursue and reveal the fundamental principles and processes underlying memories, thoughts and complex behaviours. The NSF BRAIN Initiative aims to generate an array of physical and conceptual tools needed to determine how healthy brains function over the lifespan of humans and other organisms; and to develop a workforce to create and implement these tools to establish a more comprehensive understanding of how thoughts, memories and actions emerge from the dynamic activities in the brain.

Through the BRAIN Awards, NSF makes targeted, cross-disciplinary investments in research, technology and workforce development to enable scientific understanding of the full complexity of the brain. Total funding for Understanding the Brain NSF Initiative was USD 109 million in 2015, USD 146.9 million in 2016 and USD 141.6 million in 2017, of which USD 50 million, USD 73 million and USD 74 million respectively was for BRAIN project directly.

Defense Advanced Research Projects Agency (DARPA)[29]

DARPA is the agency of the US Department of Defense responsible for the development of emerging technologies for use by the military. DARPA is supporting the BRAIN initiative through a number of programmes, continuing a legacy of DARPA investment in neurotechnology that extends back to the 1970s.

---

[27] About the Neuroethics Division: https://www.braininitiative.nih.gov/about/neuroethics.htm
[28] National Science Foundation: https://www.nsf.gov
[29] Defense Advanced Research Projects Agency DARPA https://www.darpa.mil

Allen Institute for Brain Science[30]

The Allen Institute for Brain Science is a leader in large-scale brain research and open, public sharing of data, tools and knowledge for scientists worldwide through the Allen Brain Atlas.[31]

As part of a ten-year project launched in March 2012 to understand the neural code, the Allen Institute has created a set of large-scale programmes to understand the fundamentals of the brain through its components, computations and cognition. These programmes build upon the Institute's abilities to create unique resources for scientists, exemplified in the two most recent resources: the Allen Cell Types Database, the first major scientific step to create a searchable standards database for the brain, and the Allen Brain Observatory, the first tool of its kind to provide a highly standardised survey of cellular-level activity in the visual system of the mouse.

In March 2012, the Allen Institute for Brain Science embarked upon a ten-year project to understand the neural code: how brain activity leads to perception, decision making, and ultimately action. The Allen Institute's expansion, with a USD 300M investment from philanthropist Paul G. Allen in the first four years, was based on the recent unprecedented advances in technologies for recording the brain's activity and mapping its interconnections. More than USD 60M annually will be spent to support Allen Institute projects related to the BRAIN Initiative.

The Kavli Foundation[32]

The Kavli Foundation is dedicated to advancing science for the benefit of humanity, promoting public understanding of scientific research, and supporting scientists and their work. The Foundation's mission is implemented through an international programme of research institutes, scientific society collaborations, initiatives and cross-disciplinary meetings in the fields of astrophysics, nanoscience, neuroscience, and theoretical physics as well as prizes in the fields of astrophysics, nanoscience, and neuroscience.

The Kavli Foundation anticipates supporting activities that are related to BRAIN Initiative with approximately USD 4 million dollars per year over the next ten years. This figure includes a portion of the expected annual income from the endowments of existing Kavli Institutes and endowment gifts to establish new Kavli Institutes over the coming decade. This figure also includes the Foundation's continuing commitment to supporting project meetings and selected other activities.

The Simons Foundation[33]

Cofounded in New York City by Jim and Marilyn Simons, the Simons Foundation exists to support basic scientific research. The foundation's support of scientists takes the form of direct grants to individual investigators and projects, through their academic institutions. The Foundation makes grants in four areas: Mathematics and Physical Sciences, Life Sciences, autism research (SFARI) and Education & Outreach. In 2013, the foundation also launched an internal research division, the Center for Computational Biology (formerly known as the Simons Center for Data Analysis). A second internal research division, the Center for Computational Astrophysics, was launched in 2016.

The Simons Foundation seeks to create strong collaborations and foster cross-pollination of ideas between investigators, as these interactions often lead to unexpected breakthroughs and new understanding. In an effort to directly foster such interaction between scientists, in 2012 the foundation launched a new collaborative funding model,

---

[30] Allen Institute for Brain Science: https://www.alleninstitute.org/
[31] Available at: http://www.brain-map.org/
[32] The Kavli Foundation: http://www.kavlifoundation.org/
[33] The Simons Foundation: https://www.simonsfoundation.org/

the Simons Collaborations, which bring funded investigators together to work on a timely and important problem. To date, five Simons Collaborations have been launched in and across mathematics, physics and the life sciences (Simons Collaboration on the Global Brain, launched in 2014, uses new technologies for monitoring the brain with powerful computational and modelling techniques).

Intelligence Advanced Research Projects IARPA[34]

The Intelligence Advanced Research Projects Activity (IARPA) is an organisation within the Office of the Director of National Intelligence that invests in high-risk, high-payoff research to tackle some of the most difficult challenges in the Intelligence Community. As part of this mission, IARPA sponsors several applied research programmes that use multidisciplinary approaches to advance the understanding of cognition and computation in the brain. In FY2017, IARPA has a budget of USD 43 million for activities related to BRAIN Initiative.

3.4 Monitoring system and evaluation of the initiatives

The Brain Multi-Council Working Group regularly offers an assessment of the progress of current projects and programmes supported by the BRAIN Initiative. Up to now eight meetings have been held: August 2017, May 2017, February 2017, August 2016, February 2016, July 2015, March 2015 and August 2014.

In addition, scientific meetings on the BRAIN Initiative and the annual BRAIN Investigator Meeting have helped to inform the NSF and NIH Brain staff on new scientific opportunities as they emerge.

NIH plans to set up a committee to review BRAIN 2025 and compare it to the progress of the Initiative. This newly-assembled group will evaluate the current scientific landscape, and may update the report to guide NIH from 2019 through 2025.

3.5 Level and type of citizen engagement in the initiative

To develop the document strategic vision[35] four workshops with scientific stakeholders[36] were organised in the summer of 2013, and **public feedback sessions** (included patient advocacy groups and members of the lay public) followed publication of the preliminary report in September 2013.

[34] IARPA: https://www.iarpa.gov
[35] "Brain 2025. A scientific Vision". Op.cit.
[36] The Society of Neuroscience, the neuroscience members of the National Academy of Sciences and the leaders of the professional societies of clinicians specialised in disorders of the nervous system among others.

4 Policy instruments and wider policy-mix used for implementing the initiative

4.1 Description of the R&I policy instruments used for implementing of the initiative

Funding opportunities related to BRAIN Initiative came mainly from six different sources: National Institutes of Health (NIH), National Science Foundation (NSF), Intelligence Advanced Research Projects (IARPA), Defense Advanced Research Project Agency (DARPA), Simons Foundation and The Kavli Foundation.

The main programmes of **NIH** related to BRAIN Initiative are:

- NIH Funded Awards in the following areas: tools for cells and circuits, large scale recording and modulation (new technologies, optimisation and new concepts and early stage research), new generation human imaging, next generation human invasive devices, non-invasive neuromodulation, understanding neuronal circuits and cross-cutting priorities (Neuroethics, informatics, technology dissemination and training).

- BRAIN Initiative Public-Private Partnership Program, to facilitate partnerships between clinical investigators and manufacturers of latest-generation stimulating and/or recording devices that are FDA-designated as Class III (invasive, posing significant risk of harm), to conduct clinical research in the CNS. As part of the BRAIN Initiative, NIH is interested in reducing barriers to negotiating such partnerships and also ensuring that new clinical studies leverage manufacturers existing data demonstrating safety and utility of these devices, data that are very costly to obtain and pose a substantial barrier to research progress.

- Cell Census Consortium was initiated in 2013 through a NIH funding opportunity announcement (FOA)[37] to pursue pilot demonstration projects aimed at developing classification strategies for generating a systematic inventory or cell census of cell types and their connections in the brain. Ten pilot projects have been funded in developing, validating, and scaling up emerging genomic and anatomical mapping technologies for creating a complete inventory of neuronal cell types and their connections in multiple species and during development. These projects lay the foundation for a larger and longer-term effort to generate whole-brain cell atlases in species including mice and humans. To coordinate the projects, funded groups have been organised into the BRAIN Initiative Cell Census Network BICCN.

BOX 1. NIH Grants Process

NIH advertises availability of grant support through funding opportunity announcements (FOAs). There are three different types of FOAs: Parent Announcement, Program Announcements (PAs) and Request for Applications(RFA).

The main **types of grant funding** could be:

1. Research Grants: NIH Research Project Grant Program, NIH Small Grant Program, NIH Support for Conferences and Scientific Meetings, NIH Academic Research Enhancement Award, NIH Exploratory/Developmental Research Grant Award, NI Clinical Trial Planning Grant, Small Business Technology Transfer, Small Business Innovative Research, NIH High Priority Short Term Project Award, Research Project Cooperative Agreement, NIH Pathway to Independence Award.

2. Program Project/Center Grants: Research Program Project Grant, Exploratory Grants, Center Core Grants, Specialized Center.

[37] "BRAIN Initiative: Transformative Approaches for Cell-Type Classification in the Brain". https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-14-215.html

3. Resource Grants: Resource-Related Research Projects, Education Projects, Resource Access Program

4. Trans-NIH Programs: Biomedical Information Science and Technology Initiative (BISTI), NIH Blueprint for Neuroscience Research, Research Supplements to Promote Diversity in Health-Related Research, Administrative Supplements, New and Early Stage Investigators Policies, Genome-Wide Association Studies, NIH Common Fund, NIH Basic Behavioural and Social Science Research Opportunity Network, Presidential Early Career Award for Scientists and Engineers (PECASE), Stem Cell Information, Counter ACT Program.

After the application is submitted there is a **Peer Review Process** to ensure the grant applications are evaluated in a way that is fair and free of bias. NIH has two stage review:

1. Scientific Review Group (SRG), composed of non-federal scientists. Each SRG is led by a Scientific Review Officer, an NIH extramural staff responsible for ensuring that each application receives an objective and fair initial peer review, and that all applicable laws, regulations and policies are followed;

2. Institute / Center National Advisory Councils / Boards, composed of both scientific and public representatives. Members are chosen by the respective IC and are approved by the Department of Health and Human Services. For certain committees, members are appointed by the President of the United States. The Institute/Center director makes final funding decisions based on staff and Advisory Council/Board advice.

Also, **NIH Blueprint for Neuroscience Research** has an array of tools available to researchers and the general public:

- Blueprint Non-Human Primate Atlas is an online database of gene expression in the rhesus macaque brain from birth to four years old. The atlas is publicly accessible and allows users to search for gene expression data by gene, brain region, and age. It is expected to aid research on human brain development and developmental disorders;

- Blueprint Resources Antibodies Initiative for Neurodevelopment (BRAINdev) is funding the targeted manufacture and distribution of high quality monoclonal antibodies for neurodevelopment research;

- Gene Expression Nervous System Atlas (GENSAT) and the Cre Driver Network are projects that have developed, characterised and continue to distribute transgenic mouse lines (GFP reporters and Cre drivers) to serve as tools for research on the central nervous system;

- Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) triad of services include a resources registry, data commons, and cloud-based virtual machine with popular neuroimaging software pre-installed. These services help researchers save time, meet data sharing requirements, and leverage cloud-based computing on increasingly larger data sets;

- Neuroscience Information Framework (NIF) is an online portal to neuroscience information that includes a customized search engine, a curated registry of resources and direct access to more than 100 databases;

- NIH Toolbox for Assessment of Neurological and Behavioural Function is a set of integrated tools for measuring neurologic and behavioural function, and for generating data that can be used and compared across diverse clinical studies;

- Blueprint Training Programs help undergraduate and graduate students pursue interdisciplinary careers in neuroscience;

- NIH Blueprint Enhancing Neuroscience Diversity through Undergraduate Research Experiences (ENDURE) supports undergraduates from underrepresented groups in a two-year neuroscience research programme and encourages matriculation into PhD programmes;

- Blueprint Science Education Awards.

IARPA currently active neuroscience **programmes** include: [38]

- Integrated Cognitive – Neuroscience Architectures for Understanding Sense making (ICArUS), which uses models to understand how the human brain is able to make sense of sparse, ambiguous data;

- Knowledge Representation in Neural Systems (KRNS), which seeks insights into the brain's representation of conceptual knowledge;

- Machine Intelligence from Cortical Networks (MICrONS), which will reverse-engineer the algorithms of the brain to revolutionise machine learning;

- Strengthening Human Adaptive Reasoning and Problem-solving (SHARP), which will develop non-invasive neural interventions for optimising reasoning and problem-solving.

National Science Foundation support BRAIN Initiative with the following tools:

- NeuroNex Program. This programme solicits proposals that will develop and disseminate innovative neurotechnologies and/or theoretical frameworks that will transform the understanding of the linkages between neural activity and cognition and behaviour across different systems, environments, and species, while also providing an avenue for widespread dissemination of these technologies and theoretical frameworks as well as broad training opportunities;

- Understanding the Brain Program. NSF's goal is to enable scientific understanding of the full complexity of the brain, in action and in context, through targeted, cross-disciplinary investments in research, technology, and workforce development. Understanding the Brain activities promise innovative and integrated solutions to challenges in our ability to predict how collective interactions between brain function and our physical and social environment enable complex behaviour. NSF's strategic investments will support research and infrastructure designed to transform our view of who we are and how we relate to and interact with each other and our ever-changing environment.

The Kavli Foundation supports the BRAIN Initiative through a variety of **mechanisms**:

- Kavli Coffee Hours. Soon after the BRAIN Initiative was announced in 2013, The Kavli Foundation introduced Kavli BRAIN Coffee Hours at university campuses across the country, aiming to help scientists forge new professional networks, and develop collaborations with entirely new disciplines that have well-established traditions of tool development and dissemination;

- Neurodata Without Borders[39]. In mid-2014, The Kavli Foundation, along with a consortium of researchers and foundations with a shared interest in breaking down the obstacles to data sharing, initiated a programme called Neurodata Without Borders. NWB continues to fund pilot programmes that break down the geographic, institutional, technological and policy barriers that impede the flow of neuroscience data to the scientific community;

- Kavli Institutes. In 2015, The Kavli Foundation established three new Kavli Neuroscience Institutes which joined 17 existing Kavli Institutes around the globe focusing on research

[38] More information available at: https://www.iarpa.gov/index.php/research-programs/neuroscience-programs-at-iarpa

[39] More info about Neurodata Without Borders: http://www.nwb.org/

in the Foundation's core science fields of neuroscience, nanoscience, astrophysics, and theoretical physics. Kavli Institutes provide unrestricted endowed funds that enable scientists to flexibly pursue transformative research questions.

The **Simons Foundation** support the BRAIN Initiative through the following programmes:

- Simons Collaboration on the Global Brain (SCGB), that aims to expand the understanding of the role of internal brain processes in order to discover the nature, role and mechanisms of the neural activity associated with cognition. SCGB investigators seek to identify and characterise general principles of neural coding and dynamics in order to uncover a mechanistic understanding of brain function;

- The Simons Foundation also supports other large-scale programmes performing science consistent with that of the BRAIN Initiative: the Simons Foundation Autism Research Initiative, which supports basic research into the underlying causes of autism, and the neuroscience group of the Simons Foundation's Center for Computational Biology, which aims to understand how the brain analyses large and complex datasets streamed by sensory organs, combining experimental and theoretical approaches.

DARPA's main programmes related to BRAIN Initiative are:

- Electrical Prescriptions (ElectRx). The ElectRx program aims to help the human body heal itself through neuromodulation of organ functions using ultraminiaturised devices, approximately the size of individual nerve fibres, which could be delivered through minimally invasive injection;

- Hand Proprioception and Touch Interfaces (HAPTIX). The HAPTIX program aims to create fully implantable, modular and reconfigurable neural-interface microsystems that communicate wirelessly with external modules, such as a prosthesis interface link, to deliver naturalistic sensations to amputees;

- Neural Engineering System Design (NESD). The NESD program aims to develop an implantable neural interface able to provide unprecedented signal resolution and data-transfer bandwidth between the brain and the digital world;

- Neuro Function, Activity, Structure and Technology (Neuro-FAST). The Neuro-FAST program seeks to enable unprecedented visualisation and decoding of brain activity to better characterize and mitigate threats to the human brain, as well as facilitate development of brain-in-the loop systems to accelerate and improve functional behaviours. The programme has developed CLARITY, a revolutionary tissue-preservation method, and builds off recent discoveries in genetics, optical recordings and brain-computer interfaces;

- Reliable Neural-Interface Technology (RE-NET). The RE-NET program seeks to develop the technologies needed to reliably extract information from the nervous system, and to do so at a scale and rate necessary to control complex machines, such as high-performance prosthetic limbs;

- Restoring Active Memory (RAM). The RAM program aims to develop and test a wireless, fully implantable neural-interface medical device for human clinical use. The device would facilitate the formation of new memories and retrieval of existing ones in individuals who have lost these capacities as a result of traumatic brain injury or neurological disease;

- Restoring Active Memory-Replay (RAM Replay). The RAM Replay program will investigate the role of neural "replay" in the formation and recall of memory, with the goal of helping individuals better remember specific episodic events and learned skills. The programme aims to develop novel and rigorous computational methods to help investigators determine not only which brain components matter in memory formation and recall, but also how much they matter;

- Revolutionizing Prosthetics. The Revolutionizing Prosthetics program aims to continue increasing functionality of DARPA-developed arm systems to benefit Service members and others who have lost upper limbs. The dexterous hand capabilities developed under the programme have already been applied to small robotic systems used to manipulate unexploded ordnance, reducing the risk of limb loss among soldiers;

- System-Based Neurotechnology for Emerging Therapies (SUBNETS). The SUBNETS program seeks to create implanted, closed-loop diagnostic and therapeutic systems for treating neuropsychological illnesses;

- Targeted Neuroplasticity Training (TNT). The TNT program seeks to advance the pace and effectiveness of cognitive skills training through the precise activation of peripheral nerves that can in turn promote and strengthen neuronal connections in the brain. TNT will pursue development of a platform technology to enhance learning of a wide range of cognitive skills, with a goal of reducing the cost and duration of the Defense Department’s extensive training regime, while improving outcomes.

4.2 Connection with other policies

Several large-scale initiatives have been launched in the last years in many different countries (see Figure 6). Even though the initiatives are not connected to one another, numerous actions are being carried out to share information and knowledge among them.

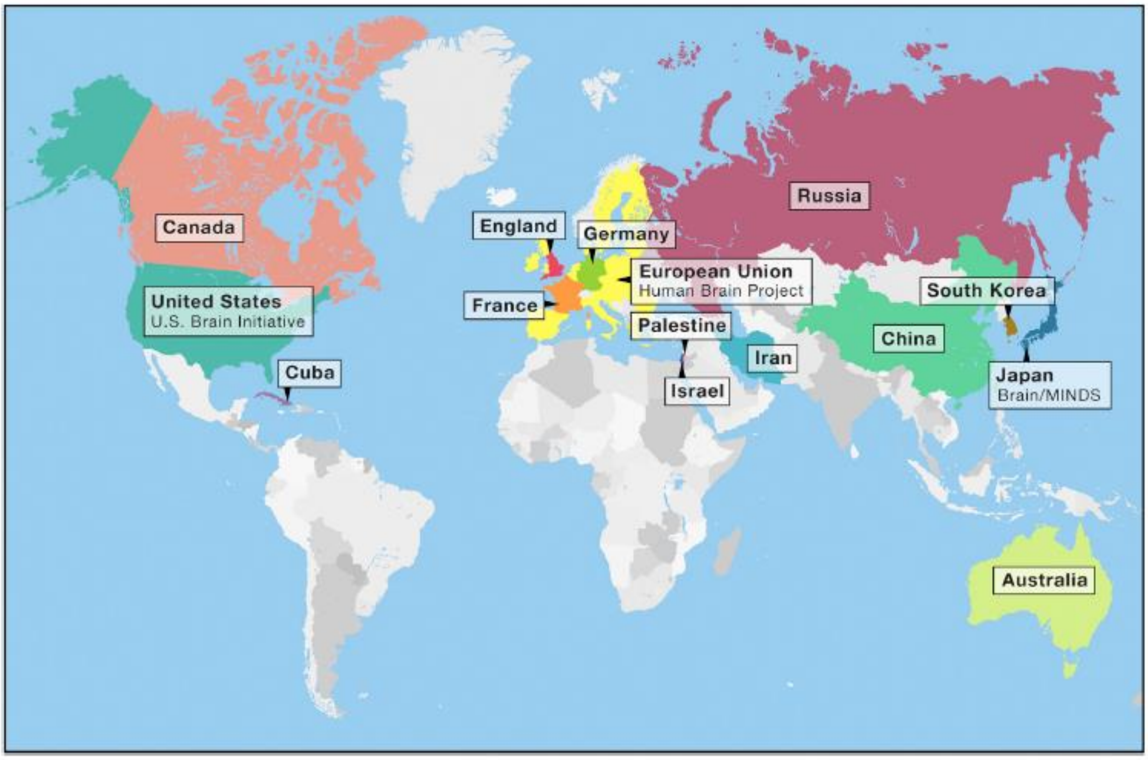

Figure 6: World Map Depicting Brain Initiatives and Related Programmes around the World. Source: Yuste and Bargmann (2017)

There are other large projects with clear interactions with BRAIN Initiative in US:

Precision Medicine Initiative

Precision Medicine is an emerging individualised approach for disease prevention and treatment[40,41,42]. Launched with a USD 215 million investment in the President's 2016 Budget, this initiative aims to accelerate biomedical discoveries and provide clinicians with new tools, knowledge and therapies to select which treatments will work best for which patients. Precision medicine, not designed for an "average patient" is an innovation approach to disease prevention and treatment that takes into account individual differences in people's genes, environments and lifestyles. To support this initiative, the **National Institutes of Health** coordinates with the Food and Drug Administration (FDA)[43] and the Office of the National Coordinator for Health Information Technology (ONC)[44]. Department of Energy[45] and Department of Veteran's Affairs[46] are also involved. The main objectives of the PM Initiative are:

- More and better treatments for cancer;
- Creation of a voluntary national research cohort of one million of Americans who volunteer or participate in research[47];
- Commitment to protecting privacy;
- Regulatory modernisation; and
- Public-private partnerships.

The 21th Century Cures Act, through "NIH Innovation Account" estimates additional financing of USD 1.4 billion over a 10-year period (2017-2026) (see Figure 4). Having into account the planned activities of the initiative, the budget distribution for next years is reflected in following Figure 7.

---

[40] Precision Medicine Initiative (2015) https://obamawhitehouse.archives.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative

[41] The White House. Office of the Press Secretary. https://obamawhitehouse.archives.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative

[42] Collins F.S, Varmus M.D (2015). A new Initiative on Precision Medicine. The New England Journal of Medicine 372;9 Feb. 26.

[43] FDA is a federal agency of the U.S Department of Health and Human Services.

[44] The Office of the National Coordinator for Health Information Technology is a staff division of the Office of the Secretary, within the U.S Department of Health and Human Services.

[45] The U.S Department of Energy (DOE (is a Cabinet-level department of the U.S. Government.

[46] The U.S Department of Veterans Affairs is a federal cabinet-level agency.

[47] All of Us Research Program. https://allofus.nih.gov/

All of Us Activity	Innovation Project Funds (numbers are approximate)
Health Care Provider Organization Network	$479,000,000
Engagement Partners	$50,000,000
Outreach to Participants and Researchers	$25,000,000
Biobank	$422,000,000
Data and Research Center	$237,000,000
Best Practices Research and Publication	$29,000,000
Biological Factors including Genetic Analyses	$148,000,000
Consumer/Mobile Technologies	$65,000,000

Figure 7: Precision Medicine Initiative activities and associated funds. Source: NIH

Beau Biden Cancer Moonshot

Biden Foundation[48] is a non-profit organisation governed by a Board of Directors. Its main mission is to identify policies that advance the middle class, decrease economic inequality and increase opportunity for all people. Biden Foundation works around sex pillars: advancing community colleges, ensuring LGBTQ equality, supporting military families, ending violence against women, protecting children and strengthening the middle class.

One of the most relevant initiatives born out of the Biden Foundation is **Biden Cancer Initiative,** whose aim is to develop and drive implementation of solutions to accelerate progress in cancer prevention, detection, diagnosis, research and care, and to reduce disparities in cancer outcomes.

In 2009, Senators Barack Obama and Joe Biden presented a plan to combat cancer with a stimulus package of USD 10 billion for National Institutes of Health. As a result, in 2016 Obama's government launched the federal initiative **Cancer Moonshot** to accelerate cancer research, improve access to therapies for more patients and increase the ability to prevent and detect cancer early.

The Cancer Moonshot Initiative, now funded through 21st Century Cures Act, continued to run the programme under former Vice President Jose Biden's Leadership as a non-profit organisation named **Biden Cancer Initiative[49]** launched in June 2017. Since part of the White House Cancer Moonshot's leaders and also the objectives are very similar in both initiatives. Biden's initiative is considered to be the continuation of the first one.

The 21th Century Cures Act, through "NIH Innovation Account" estimates additional financing of USD 1.8 billion over a 10-year period (2017-2026) (see Figure 4) Having into account the planned activities of the initiative, the budget distribution is reflected below in Figure 8:

[48] About Biden Foundation: https://bidenfoundation.org/
[49] Biden Cancer Initiative: https://bidencancer.org/

Cancer Moonshot Activities	Innovation Funds
Network for Direct Patient Engagement	$18,000,000
Cancer Immunotherapy Translational Science Network	$35,000,000
Therapeutic Target Identification to Overcome Drug Resistance	$27,000,000
Creation of a Data Ecosystem for Sharing and Analysis	$12,000,000
Fusion Oncoproteins in Pediatric Cancer	$10,000,000
Symptom Management Research	$6,000,000
Implementation of Evidence-based Approaches to Prevention	$26,000,000
Retrospective Analysis of Biospecimens from Patients Treated with Standard of Care	$15,000,000
Creation of Human Tumor Atlas	$36,000,000
Technology Development	$44,000,000
Other Cancer Moonshot Priority Activities (e.g., Partnership for Accelerating Cancer Therapies)	$71,000,000

Figure 8: Cancer Moonshot activities and associated funds for next years. Source: NIH

Regenerative Medicine Innovation Project[50]

Regenerative medicine is an emerging area of science that holds great promise for treating and possibly even curing a variety of injuries and diseases. Regenerative medicine includes using stem cells and other technologies, such as engineered biomaterials and gene editing. Stem cell-based approaches are under development in labs around the world, and some have already moved into clinical trials. Such progress notwithstanding, much work remains to be done toward the development of safe and effective regenerative medicine interventions to realise the full potential of this field.

The 21st Century Cures Act establishes a Regenerative Medicine Innovation Project to accelerate the field by supporting clinical research on adult stem cells while promoting the highest standards for carrying out scientific research and protecting patient safety. In recognition of the integral role of the Food and Drug Administration (FDA) in the successful development of this field, NIH is leading the RMIP in coordination with that agency.

The Cures Act authorises USD 30 million in federal awards over four years (2017–2020) for the RMIP. Importantly, the Act requires that award recipients match the federal award in at least an equal amount with non-federal funds, which will amplify the federal investment and could help stimulate collaboration across the public and private sectors.

4.3 Key turning points of the initiative and policy adaptation measures

The following table shows the major changes and turning points of US Brain Initiative, as well as a description of the main flexibility mechanisms and policy adaptation measures.

Major changes / turning points of the initiative	Description of the flexibility mechanism / policy adaptation measures
• President Obama launched the BRAIN Initiative as part of a broader White House Neuroscience Initiative to "accelerate the development and application of new technologies that will enable researchers to produce dynamic	• In response to this challenge, the National Institutes of Health (NIH) convened a working group of the Advisory Council to the NIH Director to develop a rigorous plan

[50] Regenerative Medicine Innovation Project https://www.nih.gov/rmi

Major changes / turning points of the initiative	Description of the flexibility mechanism / policy adaptation measures
pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought.”	for achieving this scientific vision: “Brain 2025. A scientific Vision”.
• Neuroscience research in general and the BRAIN Initiative specifically generate many important ethical questions related to the conduct and use of neuroscience research.	• NIH has established a Neuroethics Division of the BRAIN Multi-Council Working Group (MCWG), that will recommend overall approaches for how the NIH BRAIN Initiative might handle issues and problems involving ethics.
• The BRAIN Initiative is a public-private partnership including public agencies and several private foundations, institutes, universities, companies and international partners, which raises a considerable governance challenge.	• The BRAIN Initiative Alliance coordinates and focuses all the public and private efforts.

5 Realised or expected outputs, outcomes and impacts

Since BRAIN is still a young initiative, and in line with the purposes of the vision, most of the results are new instruments and technologies. This list is not exhaustive, just for illustrative purposes since other results could be also relevant:

5.1 Outputs and New Instruments

- Since the beginning of BRAIN Initiative there are almost 300 publications[51] classified in seven research categories: cell types, circuit diagrams, monitor neural activity, interventional tools, theory and data analysis tools, human neuroscience, and integrated approaches.

- New tools and technologies. In general, technologies that are emerging from BRAIN Initiative are diverse and range from transgenic animals to sophisticated instrumentation to computational tools. Some examples are: DREADD (Designer Receptor Exclusively Activated by a Designer Drug) technology, to experimentally control circuits in animal's brains in order to understand their function; optogenetics, a technique that allows researchers to control neuronal activity with light; miniature fluorescence microscopes, a new technology to record from thousands of neurons simultaneously; a neuroprosthetic device that translates "thoughts" into movement52; diagrams ranging in scale[53]; Brainbow, to colour neurons with fluorescent dye; CLARITY, a tissue-preservation method; photoacoustic imaging, a technique that blends the speed of precision of light with the penetrating ability of sound to interrogate neural activity[54]; Z-brain, an open-source anatomical atlas of the entire zebrafish brain[55]; miniaturised and highly sensitive electrophysiology and optical imaging instruments; improvements in functional magnetic resonance imaging (fMRI)

- New platforms. The International Brain Station, a virtual platform for collaboration and data sharing for neuroscientists worldwide, Neurodata Without Borders, another platform to share physiological data, NeuroNex56, a National Research Infrastructure for Neuroscience.

- 306 publications emerged from the initiative[57] (last query, Jan 2018).

5.2 Outcomes

- BRAIN Initiative has inspired similar large-scale brain research projects around the world, including Japan, Australia, Canada, China, South Korea and Israel.

5.3 Impacts

According to the Brain 2025 Strategy, it is too early to talk about impacts from this Initiative: "*It may take at least 20 years for discoveries in basic neuroscience to lead to treatments and cures for brain disorders. It may take ten years to elucidate the functions of the brain to a degree that provides a clear path for our colleagues in medicine,*

---

[51] Database consulted on 29 November 2017. Full list available here: https://braininitiative.nih.gov/resources/publication.aspx

[52] More info about this brain-machine interface: http://www.braininitiative.org/achievements/melding-mind-and-machine/

[53] Finished in 2015, the reconstruction represents the largest portion of mammalian brain ever rendered in full detail. More info about this project available at: http://www.braininitiative.org/achievements/making-the-connection/

[54] Yao J, Wang L (2015) "High-speed label-free functional photoacoustic microscopy of mouse brain in action". Nature Methods 12, 407-410.

[55] Randlett O, Wee C, Naumann E et al (2015). "Whole-brain activity mapping onto a zebrafish brain atlas". Nature Methods 12, 1039-1046.

[56] More info about NeuroNex: https://dbiblog.nsfbio.com/2016/06/28/neuronex/

[57] Publications available at: https://www.braininitiative.nih.gov/resources/publication.aspx

engineering and the biotechnology and pharmaceutical industries. It may ten additional years for them to transform this knowledge into practical and effective medical advances".

5.4 Summary of the key indicators.

The next table shows the main indicators related to US Brain Initiative:

<table>
<tr><th>Key indicators</th><th></th></tr>
<tr><td>Timeline:</td><td>2013-2025</td></tr>
<tr><td>Objective and targets:</td><td>The Brain Initiative seeks to deepen understanding of the inner workings of the human mind and to improve how we treat, prevent, and cure disorders of the brain.</td></tr>
<tr><td>Total budget:</td><td>USD 1.36 billion (2013-2016) and USD 1.5 billion (2017-2025)</td></tr>
<tr><td>Annual budget:</td><td>
<table>
<tr><th>Year</th><th>Requested public budget</th><th colspan="2">Real budget</th></tr>
<tr><td>2014</td><td>-</td><td>USD 110 million (public) and USD 110 million (private)</td><td rowspan="3">USD 1.36 billion (total public and private)</td></tr>
<tr><td>2015</td><td>-</td><td>USD 200 million (public)</td></tr>
<tr><td>2016</td><td>USD 400 million</td><td>USD 320 million (public)</td></tr>
<tr><td>2017</td><td>USD 400 million</td><td colspan="2" rowspan="9">USD 1.5 billion from NIH Innovation Account. There is no official data about other federal agencies or private investors.</td></tr>
<tr><td>2018</td><td>USD 400 million</td></tr>
<tr><td>2019</td><td>USD 400 million</td></tr>
<tr><td>2020</td><td>USD 400 million</td></tr>
<tr><td>2021</td><td>USD 500 million</td></tr>
<tr><td>2022</td><td>USD 500 million</td></tr>
<tr><td>2023</td><td>USD 500 million</td></tr>
<tr><td>2024</td><td>USD 500 million</td></tr>
<tr><td>2025</td><td>USD 500 million</td></tr>
</table>
</td></tr>
<tr><td>Share of budget, public funding:</td><td rowspan="2">There is no official data about public and private funding sources for BRAIN Initiative</td></tr>
<tr><td>Share of budget, private investment:</td></tr>
<tr><td>Leverage effect (additional public/private investments the initiative has triggered):</td><td>Although there is no yet official data about Brain Initiative leverage effect, in 2013 State of the Union, President Obama emphasised that every dollar invested to map the human genome returned US 140 to American economy.</td></tr>
<tr><td>Key (official/public) indicators applied for</td><td>Brain Initiative monitoring is up to the Brain Multi-Council Working Group. Using as a reference the goals and milestones defined in the</td></tr>
</table>

Key indicators	
monitoring the progress towards the targets:	strategy BRAIN 2025, this Group meets regularly, analyses the progress of the initiative and establishes the measures to be taken.
Other key indicators (e.g. outputs/outcomes/impacts):	There is no an official Management Control Panel with numerical key indicators.

6 Conclusions and lessons learned

6.1 Identification and assessment of key strengths and weaknesses of the initiative

Strengths	Weaknesses
• Cross boundaries in interdisciplinary collaborations is one of the main principles for BRAIN Initiative. In fact, a significative number of grants have gone to non-US researchers and there is an open debate about the creation of a Global Brain Initiative. • Platforms for sharing data, in public integrated repositories for data analysis tools with an emphasis on ready accessibility and effective central maintenance. • Accountability to NIH, the taxpayer, and the basic, translational, and clinical neuroscience communities. • The BRAIN Initiative has attracted bipartisan support and has specifically been called out positively in annual appropriations language from both the House and US Senate.	• Among the stakeholders there are not members of the neurotechnology industry. • Though technological innovation is one of the main focus of BRAIN Initiative, it should be accompanied by scalable technological dissemination to make the transformative techniques accessible to the widest spectrum of researchers.58 • Some of the platforms and infrastructures needed for the project could be far too expensive for individual laboratories to acquire, implement and maintain.[59]

6.2 Lessons learned and key messages for European R&I policy

- To focus the initiatives on **specific targets** allows tangible outcomes to be achieved early on, which can then be scaled up and disseminated for widespread use, and open previously inaccessible scientific questions.[60]

- If the initiative begins with a **clear vision** and a roadmap for the first years, it serves as a guide for all the stakeholders involved and makes it possible to monitor and plan the initiative in the most efficient and effective way.

- It is important to create an **environment for the initiative** that sustains the momentum and enthusiasm not only with scientists but with the citizens and policy-makers. Continual outreach and explanation of the Initiative's importance is critical to ensure the support and to encourage communication between private and public sectors, and the public. Not only BRAIN Initiative but also other successful ones such as National Nanotechnology Initiative[61] or Materials Genome Initiative[62] have a balance between a solid vision and a powerful network of support.[63]

- The initiatives with a **strong political support and consensus** stand higher chances of success. The BRAIN Initiative has attracted bipartisan support and has specifically

[58] Joshi P, Ghosh K (2016). "View from Silicon Valley: Maximizing the Scientific Impact f Global Brain Initiatives through Entrepreneurship". Neuron 92, Nov 2. Elsevier.Inc.
[59] Alivisatos P, Chun M, Church G et al (2015). "A national network of neurotechnology centers for the BRAIN Initiative". Neuron 88, Nov 4. Elsevier Inc.
[60] Martin C et al (2016) op.cit.
[61] National Nanotechnology Initiative: https://www.nano.gov/
[62] Materials Genome Initiative: https://www.mgi.gov/
[63] Martin C et al (2016) op.cit.

been called out positively in annual appropriation language from both the House and US Senate.[64]

- It is important to have **large, feasible scientific goals** with smaller, intermediate goals, but a lack of prior understanding should not impede future innovation. Although some of the BRAIN initiative's objectives also seem fantastic, experts in the field built the milestones through a collective planning process, coming to a consensus on goals for the project. The spectrum of planned research objectives span from risky, but potentially revolutionary, tools to important, but more attainable, applications of current methods that are likely achievable given the state of the field. Although it may not be possible to fully understand the brain, the proposed development of tools will certainly improve our current knowledge.[65]

- The development of tools that are significantly easier to use, cheaper, or more efficient than before can produce the biggest impacts on society.

---

[64] Idem.

[65] Filsinger G (2016). "The BRAIN Initiative. Structuring Large-Scale Initiatives in the US". Harvard University. Available at: http://sitn.hms.harvard.edu/flash/2016/the-brain-initiative-structuring-large-scale-science-initiatives-in-the-u-s/

References

Alivisatos P, Chun M, Church G et al (2015). "A national network of neurotechnology centers for the BRAIN Initiative". Neuron 88, Nov 4. Elsevier Inc.

Collins F.S, Varmus M.D (2015). A new Initiative on Precision Medicine. The New England Journal of Medicine 372;9 Feb. 26.

GBD 2015 Neurological Disorders Collaborator Group (2017). "Global, regional and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". Lancet Neural 2017; 16: 877-97. http://dx.doi.org/10.1016/

Filsinger G (2016). "The BRAIN Initiative. Structuring Large-Scale Initiatives in the US". Harvard University. Available at: http://sitn.hms.harvard.edu/flash/2016/the-brain-initiative-structuring-large-scale-science-initiatives-in-the-u-s/

Jorgenson LA et al. (2015). "The BRAIN Initiative: developing technology to catalyse neuroscience discovery. Phil. Trans. R. Soc. B 370: 20140164. http://dx.doi.org/10.1098/rstb.2014.0164

Joshi P, Ghosh K (2016). "View from Silicon Valley: Maximizing the Scientific Impact f Global Brain Initiatives through Entrepreneurship". Neuron 92, Nov 2. Elsevier Inc.

Martin C, Chun M (2016) "The BRAIN Initiative: building, strengthening and sustaining". Neuron 92, Nov 2. Elsevier Inc.

National Institutes of Health (2014). "Brain 2025. A scientific Vision". Available at: https://braininitiative.nih.gov/pdf/BRAIN2025_508C.pdf

Ramos K, Rommelfanger K, Greely H, Koroshetz W (2017). "Neuroethics and the NIH BRAIN Initiative". of Responsible Innovation, DOI: 10.1080/23299460.2017.1319035

Randlett O, Wee C, Naumann E et al (2015). "Whole-brain activity mapping onto a zebrafish brain atlas". Nature Methods 12, 1039-1046.

World Health Organisation (2017). "Atlas Country Resources for Neurological Disorders".2nd edition. ISBN 978-92-4-156550-9

Yao J, Wang L (2015) "High-speed label-free functional photoacoustic microscopy of mouse brain in action". Nature Methods 12, 407-410.

Yuste R, Bargmann C (2017). "Toward a Global Brain Initiative". Cell 168, March 9. Elsevier Inc

Getting in touch with the EU

IN PERSON
All over the European Union there are hundreds of Europe Direct Information Centres.
You can find the address of the centre nearest you at: http://europa.eu/contact

ON THE PHONE OR BY E-MAIL
Europe Direct is a service that answers your questions about the European Union.
You can contact this service
– by freephone: 00 800 6 7 8 9 10 11 (certain operators may charge for these calls),
– at the following standard number: +32 22999696 or
– by electronic mail via: http://europa.eu/contact

Finding information about the EU

ONLINE
Information about the European Union in all the official languages of the EU is available on the Europa website at: http://europa.eu

EU PUBLICATIONS
You can download or order free and priced EU publications from EU Bookshop at: http://bookshop.europa.eu. Multiple copies of free publications may be obtained by contacting Europe Direct or your local information centre (see http://europa.eu/contact)

EU LAW AND RELATED DOCUMENTS
For access to legal information from the EU, including all EU law since 1951 in all the official language versions, go to EUR-Lex at: http://eur-lex.europa.eu

OPEN DATA FROM THE EU
The EU Open Data Portal (http://data.europa.eu/euodp/en/data) provides access to datasets from the EU. Data can be downloaded and reused for free, both for commercial and

non-commercial purposes.

On April 2, 2013, President Obama launched the BRAIN Initiative as part of a broader White House Neuroscience Initiative to "accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought." The challenge is to map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity flowing within those circuits, and understand how their interplay creates our unique cognitive and behavioural capabilities.

Studies and reports

Publications Office