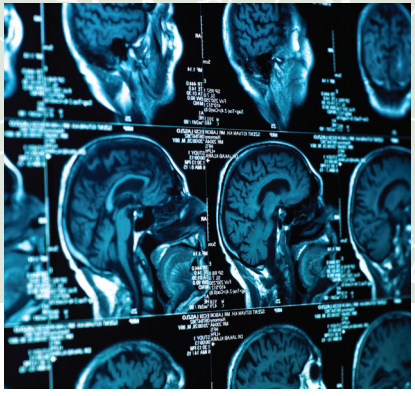
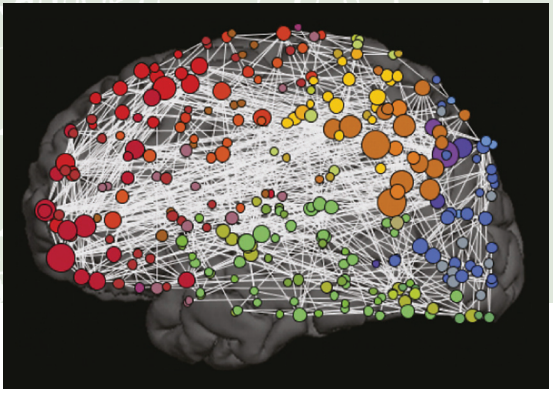
BOARD ON HEALTH SCIENCES POLICY

# Forum on Neuroscience and Nervous System Disorders

## 2014 Annual Report





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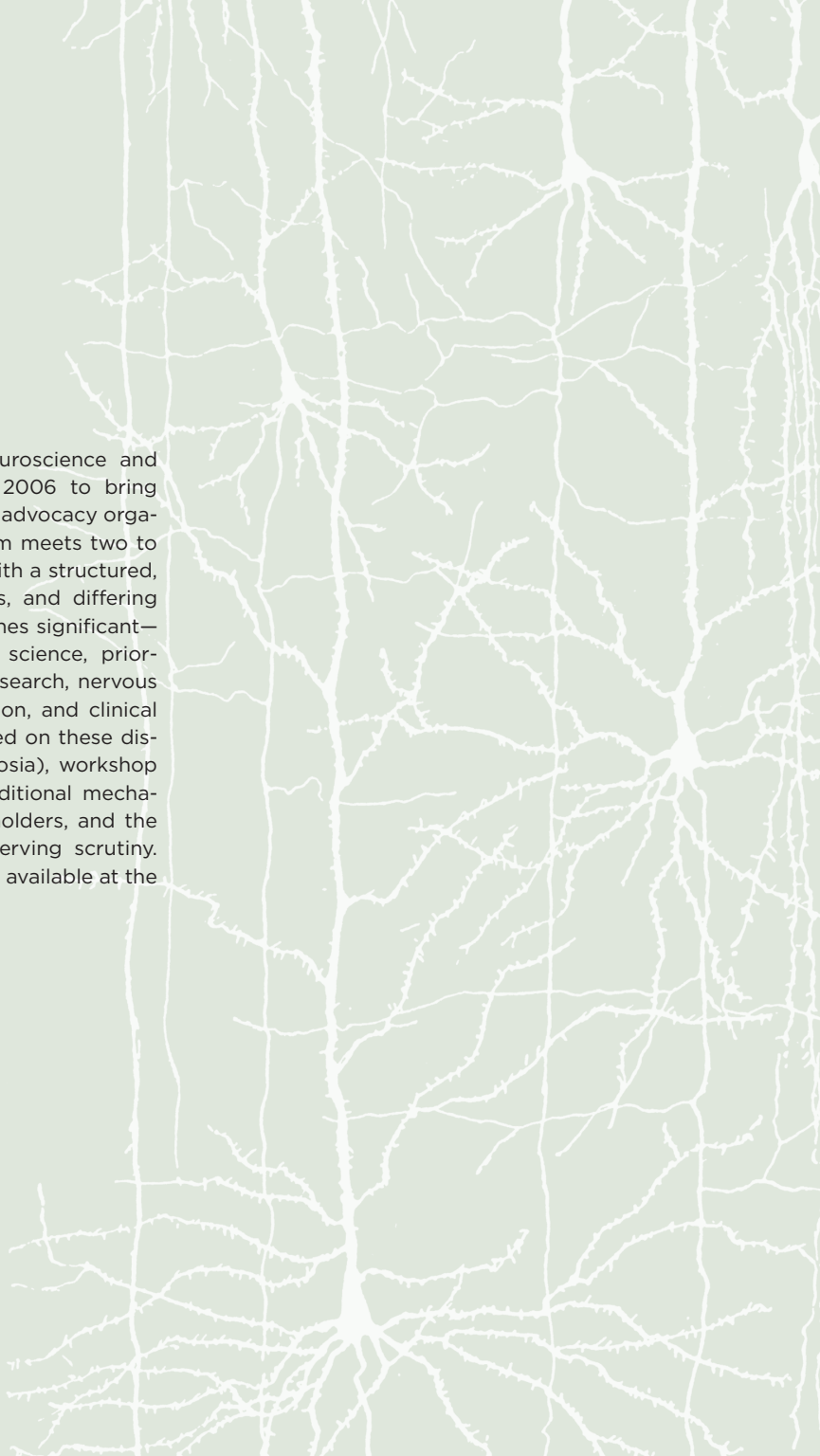
## About the Neuroscience Forum

The Institute of Medicine (IOM) Forum on Neuroscience and Nervous System Disorders was established in 2006 to bring together government, industry, academia, patient advocacy organizations, and other interested parties. The Forum meets two to three times per year and provides its members with a structured, neutral venue for exchanging information, ideas, and differing points of view. At its meetings, the Forum examines significant—and sometimes contentious—issues concerning science, priority setting, and policy related to neuroscience research, nervous system disorders, and the development, regulation, and clinical use of interventions for the nervous system. Based on these discussions, the Forum sponsors workshops (symposia), workshop summaries, and commissioned papers as an additional mechanism for informing its membership, other stakeholders, and the public about emerging issues and matters deserving scrutiny. Information about past and upcoming meetings is available at the Forum's website, www.iom.edu/neuroforum.



## Message from the Chairs

The IOM Forum on Neuroscience and Nervous System Disorders brings together the private sector; federal agencies that serve as research sponsors and regulators; the nonprofit sector, including foundations and groups focused on nervous system disease; and the academic community to consider shared approaches to pressing issues.

Through its meetings and public workshops, the Forum provides an opportunity for its members, other neuroscience leaders, government officials, and members of the public to have candid discussions about emerging, critical issues of common interest. In 2014, rich discussions from multiple perspectives included such diverse topics as improving the access of the research community to large datasets; needed new approaches to training neuroscientists in a world of rapidly advancing technologies, including computation; the path of development for treatments for dry age-related macular degeneration (AMD); access to essential medicines for mental, neurological, and substance abuse disorders in sub-Saharan Africa; and the neuroscience of electronic gaming with emphasis on relevant scientific, ethical, and societal issues ranging from utility in cognitive training to problematic use.

Looking ahead to 2015, the Forum plans an array of activities on topics such as:

- Country-specific opportunities in Ghana and Kenya to improve the health system infrastructure in order to develop sustainable access to mental health care;
- Consideration of approaches to increase private-sector investments in the discovery and development of novel therapeutics to address unmet needs for nervous system disorders;
- Discovery, development, and translation of treatments for cognitive dysfunction in depression; and
- Opportunities, challenges, and ethical questions surrounding therapeutic and non-therapeutic uses of non-invasive neuromodulation of the central nervous system.

We look forward to another productive year for the Forum.

**Steve Hyman and Story Landis**
Chair and Vice-Chair

# Reflecting Back

## Forum Activities in 2014

### Managing and Sharing Large Research Datasets

Neuroscience and allied areas of science and medicine are generating ever larger, richer, and more complex datasets. These datasets have tremendous potential to improve understanding of the nervous system and the biology of disease and to aid in the development of therapeutics. Data collected from such areas as genomics, imaging, and other technologies to examine human brain circuitry would provide extraordinary opportunities for greater understanding if they were more effectively shared. Technological infrastructure and policies, however, have not yet been firmly established to ensure successful management, sharing, and sustainability of databases within the global neuroscience community. The Forum hosted an activity to address challenges and examine potential strategies to facilitate better management and greater sharing of large basic research datasets.

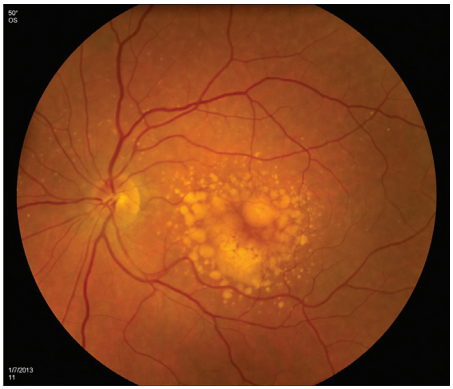
### Training the Next Generation of Neuroscientists

From its beginning, neuroscience has been fundamentally interdisciplinary. As a result of rapid technological advances and the advent of large collaborative projects, however, neuroscience is expanding well beyond its traditional subdisciplines to include engineering, computer science, and applied mathematics. Revolutionary tools, such as optogenetics and genome engineering like CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), are quickly being incorporated into research programs. The rapid proliferation and importance of transformative technologies, however, raises important questions about how best to train the next generation of neuroscientists, not only in the use of specific tools, but also in how best to take advantage of a changing technological landscape. In addition, the advent of new types of data and the growing importance of large datasets will require training in approaches to data standardization and sharing and to appropriate analysis.

Attention to improved scientific practices ranging from experimental design (powering of studies, appropriate blinding) to greater sophistication in statistics is essential. To address these issues, the Forum hosted a workshop that explored future workforce needs and considered the design of training programs. Current and new components of training programs were discussed to identify methods for enhancing data handling and analysis capabilities, increasing scientific rigor, and improving research practices. Finally, the roles of mentors, mentees, training program administrators, and funders in the development and the execution of revised training programs for new and current researchers was explored.

### Developing Treatments for Dry Age-Related Macular Degeneration (AMD)

Age-related macular degeneration (AMD) is the leading cause of blindness in adults over the age of 65 years. Currently, there are no treatments available for the dry form of AMD. Advances in drug discovery and development in dry AMD have been limited by incomplete understanding of the disease, lack of surrogate endpoints, and questions about clinical trial design. Given the pressing need for progress in the field, this workshop brought together key stakeholders from industry, government agencies like the National Institutes of Health and the U.S. Food and Drug Administration, academia, and patient advocacy groups to discuss opportunities for advancing drug development for dry AMD.




Feb 27
2nd meeting

Apr 18
**Autism & Environment Workshop**

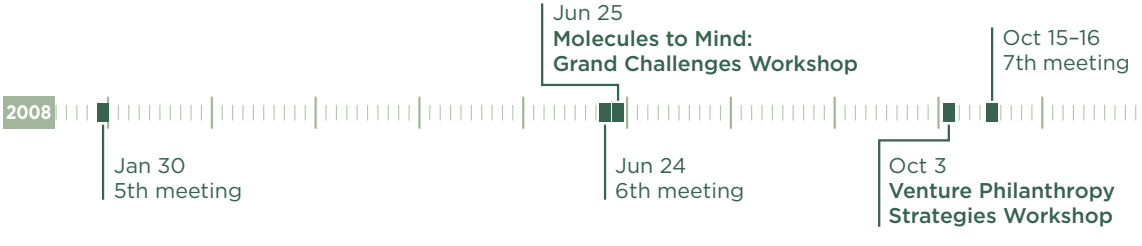
Feb 26
**Biomarkers Workshop**

Jul 30–31
3rd meeting

Oct 24–25
4th meeting

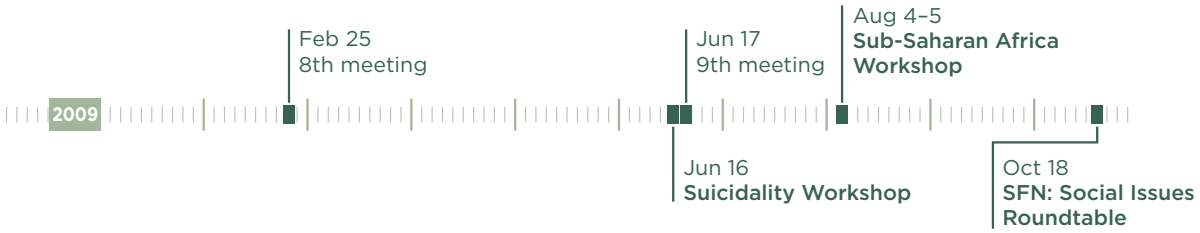
### Improving Access to Essential Medicines for Mental, Neurological, and Substance Use Disorders in Sub-Saharan Africa

Sub-Saharan Africa (SSA) has one of the world's largest treatment gaps for mental, neurological, and substance use (MNS) disorders, causing a substantial burden for the continent's population. Improving access to essential medicines has been identified as a critical and feasibly addressable component of reducing the treatment gap for MNS disorders. To address the need for reliable, sustainable access to safer and more effective medicines, the Forum hosted a meeting that assembled key stakeholders to discuss opportunities for providing access to essential medicines for MNS disorders with a focus on depression, psychotic disorders, and epilepsy. Specifically, participants examined successful models of treatment delivery and examples of effective supply chains for infectious diseases and several noncommunicable diseases in SSA and in low- and middle-income countries outside SSA. Because of the complex and multifaceted nature of this topic, the meeting also focused on determining the specific steps and partnerships needed to make drugs accessible.



### The Neuroscience of Gaming

More than 1.2 billion people worldwide play games (online and via console or mobile device). Many, however, are unaware that programmers often incorporate cognitive and behavioral neuroscience into game design. The use of concepts such as operant conditioning and effective reinforcement schedules has been increasingly integrated into electronic game design to encourage participation. The incorporation of such concepts can enhance both beneficial effects and socially negative outcomes. Several studies have begun to demonstrate the utility of gaming for better engagement and efficacy in education, training, health behaviors, and rehabilitation (e.g., stroke and post-traumatic stress disorder). Excessive gaming, on the other hand, may lead to addictive-like behaviors with physiological effects similar to those of substance use disorders (e.g., craving, narrowing of behavioral choices). New policies to protect gamers from design features that may increase the likelihood of negative outcomes, while encouraging more positive applications from game designers are clearly worth public discussion. Given the high prevalence of gaming in today's society, the Forum hosted a Social Issues Roundtable at the Society for Neuroscience 2014 annual meeting, bringing together key stakeholders who explored the neuroscience of electronic gaming, with emphasis on relevant scientific, ethical, and societal issues.



# Looking Forward

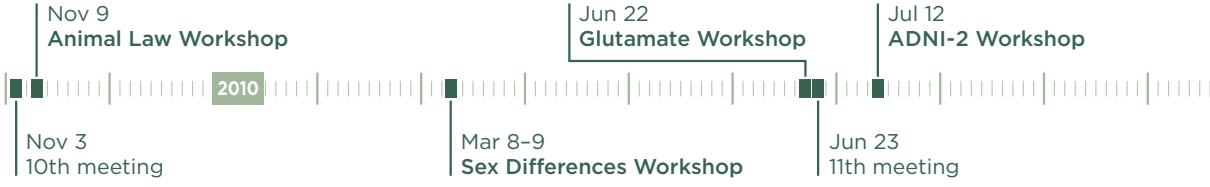
## Forum Activities in 2015

### Providing Sustainable Care for Brain Disorders in Ghana and Kenya

The global burden for mental, neurological, and substance use (MNS) disorders is significant, and the treatment gap is particularly high in sub-Saharan Africa. Less than 1 percent of national health budgets are spent on MNS disorders, which is disproportionately low compared to the burden of these disorders. Competing public health priorities, financial constraints, and poverty are all factors that can negatively affect access to mental health care. Challenges associated with the delivery of care include an inadequate health system infrastructure to support mental health care (e.g., beds and medicines), the lack of national policy frameworks for mental health, and deficient information health systems to monitor and evaluate services. The stigma and lack of community awareness of MNS disorders also negatively affects demand for care and treatment. In addition, more trained health care providers are required to deliver evidence-based treatment in both the hospital and community settings. Recognizing the importance of sustainable mental health care, these workshops will bring together key stakeholders to examine country-specific opportunities in Ghana and Kenya to improve and develop sustainable access to mental health to ensure that the right patients get the right care and treatment at the right time in the right setting.

### Financial Incentives to Address Unmet Medical Needs for Nervous System Disorders

The global burden of nervous system disorders is projected to increase significantly over time and is estimated to cost society more than $6 trillion per year by 2030 (according to the report "The Global Economic Burden of Noncommunicable Diseases" by World Economic Forum and Harvard School of Public Health).




Although there have been recent international initiatives to better understand the human brain, several large pharmaceutical companies have decreased investment or even withdrawn from their neuroscience research programs. The perceived high risk and low probability of success have made the neuroscience sector less attractive than other therapeutic areas for research and development (R&D), despite the large market potential. As a result, patients are often left with few if any options for treatment. Thus, there is a need to consider policy options to increase private-sector investment in R&D for nervous system disorders. With this context, this public workshop will explore opportunities to foster private-sector innovation and support for new investments directed toward the development of novel therapeutics to treat nervous system disorders.

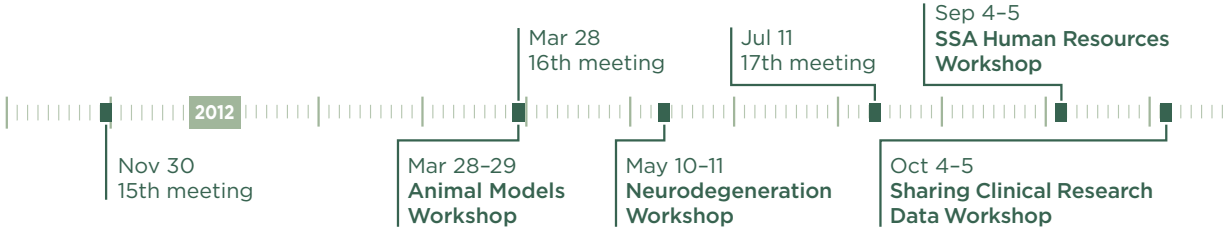
### Enabling Development, Discovery, and Translation for Cognitive Dysfunction in Depression

Depression is a highly prevalent and disabling disorder for which existing treatments (including both medications and psychotherapies) are only partly effective for some patients and ineffective for many. Many patients, who would be considered

responders by the criteria used in clinical trials, continue to have symptoms and difficulties returning to their previous level of function (e.g., study or work). Increasing clinical and epidemiologic evidence suggests that cognitive dysfunction is an underestimated dimension of depression that may well contribute to ongoing symptoms and poor functional outcomes. Currently available treatments have only modest benefits in treating cognitive dysfunction in depression, and some treatments, especially older drugs with anticholinergic properties, may actually worsen cognitive function in some patients. At present, the scientific field is not aligned on the best way to assess cognitive dysfunction in depression, and whether this dimension of illness is dependent on, or independent from, mood symptoms. The workshop will bring together key stakeholders to explore ways to improve the discovery, development, and regulatory path for new treatments addressing this aspect of depression.

### Non-Invasive Neuromodulation of the Central Nervous System

Based on advances in biotechnology and neuroscience, neuromodulation devices are poised to gain clinical importance in the coming years and to be of increasing interest to patients, health care providers and payers, and industry. Emerging evidence suggests that the potential therapeutic and non-therapeutic uses of non-invasive neuromodulation devices for the central nervous system are broad and will continue to expand. Indeed the availability of such devices without prescription has given rise to a growing "do it yourself" movement in which individuals attempt to self-treat symptoms or to enhance their congition or mood states. There are many



open questions and challenges associated with the use of these devices. Currently, there is a need for greater understanding of both the potential benefits and risks, especially with long-term use, which has not been well studied. From a regulatory standpoint, there are scientific and clinical questions that may bear on the approval and labeling of devices. A third area needing consideration is the levels of evidence that might be required for insurance reimbursement. There are also many relevant ethical questions, including the potential for off-label, over-the-counter, or "do it yourself" uses or for enhancement. Given the growing interest in non-invasive neuromodulation devices for the central nervous system, the goal of this workshop is to explore opportunities, challenges, and ethical questions surrounding the development, regulation, and reimbursement related to the use of such devices.

### Assessing the Impact of Applications of Digital Health Records (DHRs) on Alzheimer's Disease Research

Given the opportunities and challenges associated with applying data from DHRs to Alzheimer's disease research, the workshop will bring together key stakeholders to discuss how information contained in DHRs could be used to identify novel surrogate markers and modify clinical trial design in the field. The workshop will explore potential data sharing and data management strategies as well as the infrastructure necessary to identify surrogate outcomes for Alzheimer's disease research. Current computational approaches to health care data will be discussed to identify methods for analyzing digital health data that already exist for patients, for increasing data sharing, and for improving clinical research practices. Finally, the ethical, societal, and legal issues that should be considered in applying DHRs to Alzheimer's disease research will be explored.

# Working Groups

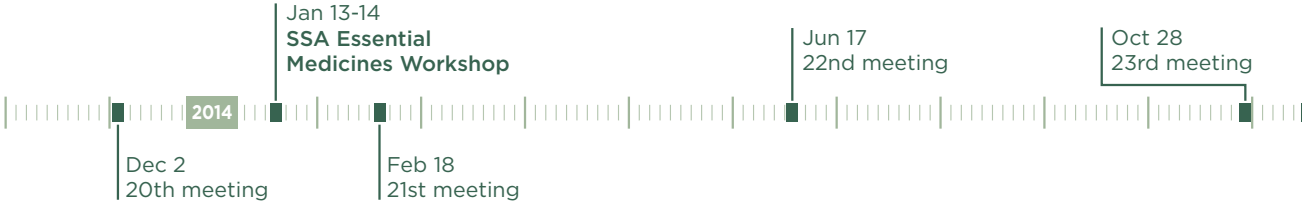
The Forum has created a series of working groups to provide an opportunity for subsets of the broader group to work together on selected topics. Workshop topics often result from these groups and are organized by an independently appointed workshop planning committee.

### Exploring Financial Incentives to Improve Neuroscience Research and Development Innovation for Drug Discovery and Development

The Forum established a working group that will explore potential financial incentives that could spur additional investment from the private sector in translational neuroscience research and development that would focus on novel treatment mechanisms and unmet medical needs. To begin this effort, the Forum convened a working group to develop a set of two or three incentives that could lead to significant reinvestment by large pharmaceutical companies in central nervous system disorders. This analysis includes the cost to society and how much it would cost payers if a therapeutic drug were delayed from transitioning to a generic form. Using the information generated by the working group, the Forum convened a planning committee to organize a workshop on this topic.

### Translational Neuroscience

The translational neuroscience working group was established to identify areas of synergy where public- and private-sector stakeholders can work together to improve the efficiency and effectiveness of drug discovery and development for neurological and mental disorders. The group is currently addressing barriers to repurposing and reusing existing compounds.

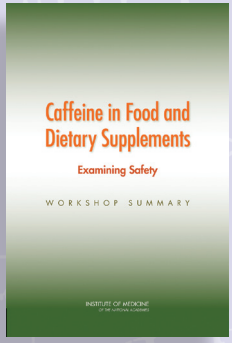


In addition, the working group is discussing strategies to increase communication and information sharing between pharmaceutical and diagnostic developers and academic researchers. The aim would be to inform researchers how they can best contribute to partnerships in a meaningful way with the goal of improving the neuroscience translational therapeutic development pipeline.

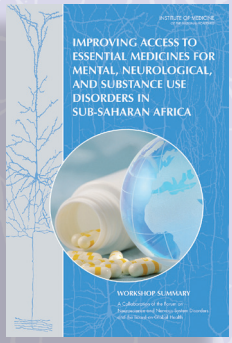
### Mental Health, Neurological, and Substance Use Disorders in Sub-Saharan Africa

In collaboration with the World Health Organization mental health Gap Action Programme (mhGAP), the Forum is continuing to explore additional opportunities to build on the 2009 Mental Health and Neurological Disorders in Sub-Saharan Africa (SSA) workshop. The working group is focused on identifying innovative solutions to enhance care for MNS disorders in SSA. Special attention is being paid to finding solutions to increase human and financial resources to support current and future efforts.

## 2014 Publications




**Caffeine in Food and Dietary Supplements: Examining Safety: Workshop Summary**




**Improving Access to Essential Medicines for Mental, Neurological, and Substance Use Disorders in Sub-Saharan Africa: Workshop Summary**

2015

Nov 15
**Dry AMD Workshop**

Nov 16
**The Neuroscience of Gaming Workshop**

Jan 13-14
**Providing Sustainable Access to Mental Health Care: Kenya Workshop**

Jan 20-21
**Financial Incentives Workshop**

Mar 2-3
**Non-Invasive Neuromodulation Workshop**

Feb 24
**Cognitive Dysfunction in Depression Workshop**

Apr 28-29
**Providing Sustainable Access to Mental Health Care: Ghana Workshop**

Jun 4-5
24th meeting

Jul 18-23
**Assessing the Impact of Applications of Digital Health Records on Alzheimer's Disease**

Nov 10
25th meeting

# Forum Members

(as of December 2014)

**Steve Hyman (Chair)**
Broad Institute of the Massachusetts Institute of Technology and Harvard University

**Story Landis (Vice-Chair)**
Former Director, National Institute of Neurological Disorders and Stroke

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Society for Neuroscience

**Mark Bear**
Massachusetts Institute of Technology

**Stephen Brannan**
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**Katja Brose**
Cell Press

**Daniel Burch**
Pharmaceutical Product Development, Inc.

**Sarah Caddick**
Gatsby Charitable Foundation

**Rosa Canet-Aviles**
Foundation for the National Institutes of Health

**Janet Carbary**
One Mind for Research

**Maria Carrillo**
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**Timothy Coetzee**
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**Daniel Geschwind**
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**Hank Greely**
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**Stuart Hoffman**
Department of Veterans Affairs

**Thomas Insel**
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Pfizer, Global Research and Development

**John Isaac**
Wellcome Trust

**Inez Jabalpurwala**
Brain Canada Foundation

**Daniel Javitt**
Columbia University

**Frances Jensen**
University of Pennsylvania Health System

**George Koob**
National Institute on Alcohol Abuse and Alcoholism

**Walter Koroshetz**
National Institute of Neurological Disorders and Stroke

**Alan Leshner**
American Association for the Advancement of Science

**Husseini Manji**
Johnson & Johnson Pharmaceuticals

**David Michelson**
Merck Research Laboratories

**Richard Mohs**
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**James Olds**
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**Atul Pande**
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**Steven Paul**
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**Todd Sherer**
The Michael J. Fox Foundation for Parkinson's Research

**David Shurtleff**
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# Sponsors

(as of December 2014)

Financial support for the Forum is derived from federal agencies, patient advocacy organizations, industry, and a nonprofit membership society.

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**Brain Canada**
**Department of Veterans Affairs**
**Food and Drug Administration**
**Foundation for the National Institutes of Health**
**Gatsby Charitable Foundation**
**GlaxoSmithKline**
**Johnson & Johnson Pharmaceuticals**
**Lilly Research Laboratories**
**Lundbeck USA**
**Merck Research Laboratories**
**The Michael J. Fox Foundation for Parkinson's Research**
**National Eye Institute**
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**National Institute of Mental Health**
**National Institute of Neurological Disorders and Stroke**
**National Institute on Aging**
**National Institute on Alcohol Abuse and Alcoholism**
**National Institute on Drug Abuse**
**National Institutes of Health Blueprint for Neuroscience Research**
**National Multiple Sclerosis Society**
**National Science Foundation**
**One Mind for Research**
**Orion Bionetworks**
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**Sanofi-Genzyme**
**Society for Neuroscience**
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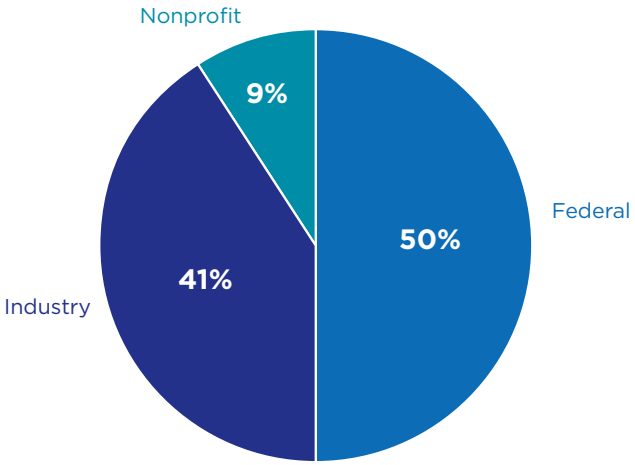
**Wellcome Trust**



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