

Enabling Discovery, Development, and Translation of Treatments for Cognitive Dysfunction in Depression: A Workshop

February 24, 2015

The National Academy of Sciences
2101 Constitution Avenue, Room 120
Washington, DC 20418

Background: It is increasingly recognized that many patients, while fulfilling traditional criteria for response or remission of depression, continue to have subjective complaints and have difficulties returning to their previous level of function (e.g., returning to work). Increasing clinical and epidemiologic evidence suggests that cognitive dysfunction is an underestimated dimension of depression. Such dysfunction could, in part, explain patients' poor response and/or poor functional outcomes. It appears that currently available pharmacological treatments only address cognitive dysfunction in depression in a limited way, and some treatments may even worsen cognition in some patients. Moreover, there is a lack of alignment in the scientific field on the best way to assess cognitive dysfunction and whether this dimension is congruent with, or independent from, mood symptoms. There is also an opportunity in this domain to look beyond the classical definition of major depressive disorder and consider approaches involving neurocircuitry and precision medicine. The goal of the workshop is to bring together key stakeholders to explore ways of speeding improvement of the discovery, development and regulatory path for new treatments addressing this aspect of depression.

Meeting Objectives:

- Examine opportunities to facilitate new target and validation strategies aimed at reinvigorating the development of treatments that address cognition, an under-treated aspect of depression.
- Discuss how lessons from the translational aspects of cognitive dysfunction in other disorders could apply to depression.
- Highlight gaps and limitations of current tools for assessing cognitive dysfunction in depression in clinical trials, and consider how improvements in cognition could relate to functional outcomes.
- Explore potential regulatory challenges, such as recognition of cognitive dysfunction in depression as a public health need and opportunities for treatments.

8:30 a.m. Opening Remarks

THOMAS INSEL, *workshop co-chair*
Director
National Institute of Mental Health

THOMAS LAUGHREN, *workshop co-chair*
Director
Laughren Psychopharm Consulting, LLC

SESSION I: BACKGROUND AND OVERVIEW

Session Objectives: Provide an overview of the unmet medical need of cognitive dysfunction in depression. Discuss lessons learned from developing treatments for cognitive dysfunction in schizophrenia. Examine opportunities to facilitate new target and validation strategies aimed at reinvigorating the development of treatments that address cognition.

8:40 a.m. Opening Remarks

ANDREW NIERENBERG, *session moderator*
Thomas P. Hackett, MD, Endowed Chair in Psychiatry
Massachusetts General Hospital

8:45 a.m. Cognitive Dysfunction in Depression: The Need for Discovery, Development, and Translation in this Domain (20 min talk + 10 min discussion)

BARBARA SAHAKIAN
Professor of Psychiatry
Cambridge University

9:15 a.m. Experimental Design and Approaches: Opportunities to Facilitate New Target and Validation Strategies for Cognitive Dysfunction in Depression (20 min talk + 10 min discussion)

CATHERINE HARMER
Professor of Cognitive Neuroscience
University of Oxford

9:45 a.m. Lessons Learned from Cognitive Dysfunction in Schizophrenia (20 min talk + 10 min discussion)

MICHAEL GREEN
Professor-in-Residence
Department of Psychiatry and Biobehavioral Sciences
Geffen School of Medicine at UCLA

10:15 a.m. BREAK

SESSION II: STATE-OF-THE-SCIENCE FOR TREATING COGNITIVE DYSFUNCTION IN DEPRESSION

Session Objectives: Examine the current state-of-the-science for treating cognitive dysfunction in depression, including what aspects of this dysfunction can be treated with medications, cognitive behavioral therapy, devices, and other treatment modalities. Identify promising future directions.

10:30 a.m. Opening Remarks

AMIT ETKIN, *session moderator*
Assistant Professor of Psychiatry and Behavioral Sciences
Stanford University

- 10:35 a.m. Effects of Non-Pharmacological Treatments on Cognition in Depression
 DIEGO PIZZAGALLI
 Professor of Psychiatry
 Harvard Medical School
- 10:50 a.m. Effects of Pharmacological Treatments on Cognition in Depression
 RICHARD KEEFE
 Professor of Psychiatry and Behavioral Sciences
 Duke University
- 11:05 a.m. Effects of Cognitive Remediation on Cognition in Depression
 CHRISTOPHER BOWIE (*by videoconference*)
 Clinical Psychologist and Associate Professor
 Queen's University
- 11:20 a.m. Discussion among Panelists and Workshop Participants
- 12:00 p.m. LUNCH

SESSION III: DESIGN AND ASSESSMENT CHALLENGES

Session Objectives: Examine opportunities and challenges in studying and assessing treatments for cognitive dysfunction in depression, including combination therapies. Highlight gaps and limitations of current tools for diagnosing and evaluating depression in clinical trials, and consider how the indices could be expanded to include indices of cognitive functioning. Discuss how improved cognition can be measured in short trials and the potential role of proxy measures. Consider acute versus residual treatment.

- 12:45 p.m. Opening Remarks
 MADHUKAR TRIVEDI, *session moderator*
 Betty Jo Hay Distinguished Chair in Mental Health
 UT Southwestern
- 12:50 p.m. Design
 MAURIZIO FAVA
 Director, Clinical Research Program
 Massachusetts General Hospital
- 1:05 p.m. Assessment
 PHILIP HARVEY
 Professor of Psychiatry and Behavioral Sciences
 University of Miami Miller School of Medicine

- 1:20 p.m. Lifespan Issues
 PATRICIA AREAN
 Professor of Psychiatry
 UCSF School of Medicine
- 1:35 p.m. Discussion among Panelists and Workshop Participants
- 2:15 p.m. BREAK

SESSION IV: REGULATORY CHALLENGES AND POTENTIAL SOLUTIONS

Session Objectives: Explore potential regulatory challenges, such as recognition of cognitive dysfunction in depression as a public health need and opportunities for treatments. Examine methods for evaluating cognitive dysfunction in depression. Discuss the evidentiary base that would be needed for approval of treatments for cognitive dysfunction in depression, including combination treatments.

- 2:30 p.m. Opening Remarks
 THOMAS LAUGHREN, *session moderator*
 Director
 Laughren Psychopharm Consulting, LLC
- 2:35 p.m. Food and Drug Administration Perspective: Drugs
 TIFFANY FARCHIONE
 Acting Deputy Director
 Division of Psychiatry Products
 Food and Drug Administration
- 2:45 p.m. Food and Drug Administration Perspective: Devices
 CARLOS PEÑA
 Director, Division of Neurological and Physical Medicine Devices
 Office of Device Evaluation
 Center for Devices and Radiological Health
 Food and Drug Administration
- 2:55 p.m. European Medicines Agency Perspective
 MARIA ISAAC (*by videoconference*)
 Senior Scientific Officer
 European Medicines Agency
- 3:05 p.m. Addressing Regulatory Challenges
 THOMAS LAUGHREN
 Director
 Laughren Psychopharm Consulting, LLC

3:20 p.m. Discussion among Panelists and Workshop Participants

4:00 p.m. BREAK

SESSION V: MOVING FORWARD

Session Objectives: A panel will synthesize and discuss key highlights from the workshop presentations and discussions, including identifying concrete next steps for action and research.

4:15 p.m. Panel Discussion

ANDREW NIERENBERG

Thomas P. Hackett, MD, Endowed Chair in Psychiatry
Massachusetts General Hospital

AMIT ETKIN

Assistant Professor of Psychiatry and Behavioral Sciences
Stanford University

MADHUKAR TRIVEDI

Betty Jo Hay Distinguished Chair in Mental Health
UT Southwestern

THOMAS LAUGHREN

Director
Laughren Psychopharm Consulting, LLC

4:40 p.m. Discussion among Panelists and Workshop Participants

5:15 p.m. Final comments

THOMAS INSEL, *workshop co-chair*

Director
National Institute of Mental Health

THOMAS LAUGHREN, *workshop co-chair*

Director
Laughren Psychopharm Consulting, LLC

5:30 p.m. ADJOURN WORKSHOP
