NIDA Strategic Planning –
Gene x Environment x Development Interactions (GEDI)
Co-Chairs: Naimah Weinberg and Jonathan Pollock
SPB Coordinator: Michele Rankin

Workgroup Webinar
Friday, April 17, 2015
4:00 p.m.

Attendees
Co-Chairs: Naimah Weinberg and Jonathan Pollock; **Scientific Matter Experts/Work Group Panelists**: Hugh Garavan, Eric Johnson, Kenneth Kendler, Daniele Fallin, Bill Iacono, Gustavo Turecki, John Rice, Jane Costello; **Public Guests**: Diana Samek, Lori Whitten; **NIDA staff**: Maureen Boyle, Michele Rankin, Ericka Boone, Emily Einstein, Joni Rutter, Hal Gordon, John Satterlee

Welcome and Overview
Dr. Maureen Boyle opened the meeting, presented an overview of the Strategic Plan process, and introduced the GEDI Workgroup Co-Chairs, Dr. Naimah Weinberg and Dr. Jonathan Pollock.

Dr. Boyle provided a brief background on the initial planning stages of the NIDA Strategic Plan. She explained that Dr. Volkow's idea for a comprehensive and transparent process included release of an RFI in December 2014 to solicit ideas from the field. The RFI outlined NIDA's strategic priorities (basic neuroscience, clinical and translational science, public health, and science infrastructure) and asked for input on how to include these in the updated Strategic Plan.

The comment period closed on January 30, and feedback was synthesized for further review by the workgroups. Two other priority workgroups were formed: Complex Patients and Big Data. Each group will work on its respective area and provide recommendations to NIDA on cross-cutting research priorities and related action items for the next 5 years. Each NIDA Division is also developing its own strategic plan, which will be considered, along with workgroup recommendations, in development of the final plan.

Timeline
The next steps involve:

- Workgroup meetings from now until mid-June:
    - Multiple meetings of the workgroups to discuss relevant issues and formulate priority areas for NIDA research.
    - Draft Strategic Plan recommendations and action items to be submitted by the workgroup by Friday, June 26.
- Draft Strategic Plan released for public comment – Summer 2015.
- Final Plan – Fall 2015.
- Bold Goals Challenge Grant:
    - NIDA will award up to $10K for top ideas (winner selection by August).

Workgroup Charge/Goals

Dr. Boyle said this workgroup is being asked to develop a 3–5-page recommendations document surrounding GEDI as a critical area for inclusion in NIDA's new Strategic Plan. The group will work on identifying strategic research priorities for increasing NIDA's understanding of the interaction between genes, environment, and development as they relate to substance abuse. This will include the identification of measurable objectives for each priority and specifying benchmarks for gauging progress toward each objective. It should also involve the consideration of cross-cutting themes for research projects (e.g., training needs, sex and gender issues) and suggest ways to take action, perhaps by leveraging technology advances or innovations from other fields.

Dr. Boyle explained that WebEx meetings of the GEDI Workgroup would be held biweekly on Tuesdays from 3:00 to 4:00 p.m. The meetings will be recorded and will be open to the public.

Background and Context

Dr. Jonathan Pollock delivered a presentation on NIDA's investment in genetics research for fiscal years 2011–2014, including the distribution of funding by project activity and research area, research successes, and current research opportunities.

The majority of NIDA's FY13 genetics portfolio covered basic & clinical neuroscience and behavioral research (77% of total budget). The total number of funded projects was 334, and they included both intramural and extramural programs of the Institute. Other funded areas included epidemiology, services, & prevention research (9% of budget); intramural research (8%); and pharmacotherapies & medical consequences (6%).

Dr. Pollock said that NIDA's genetics R01 grants were centered on gene discovery, epigenetics, genetic epidemiology, molecular biology, gene function, treatment/biomarkers, pharmacogenetics, statistical genetics, and pharmacology. He explained that NIDA's overall budget shows a 4% decrease over the past 5 years, and a 10% decrease in genetics funding, but that grant opportunities in genetics continue, highlighting a list of several recently completed and ongoing studies.

Dr. Pollock identified several research successes in genome-wide association studies (GWAS), including several on nicotine addiction that have been replicated, as well as a promising study using a mouse model to demonstrate that A118G associated with opioid dependence increases heroin self-administration.

Dr. Pollock discussed some of the challenges involved with GEDI that the workgroup would be discussing, such as the need for quantitative phenotypes; methods for quantifying environmental variables and responses; statistical methods to harmonize and analyze data on gene and environmental factors; animal models for identifying epistasis, pleiotropy, and gene interactions; and translating animal findings to humans.

Dr. Naimah Weinberg pointed out another challenge—to distinguish between correlations and causal factors in SUD—and suggested that studying the interplay of GxExD may help to tease out some causal factors. Dr. Weinberg highlighted the contributions from several recent studies using the GEDI approach, including those that showed sibling transmission as an important

environmental risk factor for SUD, and creative family designs that are contributing to an understanding of the complex relationship between SUD and psychiatric disorders.

Dr. Weinberg talked about gaps and opportunities, asking the group to start thinking about current NIDA research that could be developed further, as well as opportunities for NIDA to pursue. She reiterated the workgroup's charge to help identify and prioritize new areas of research that might cover research gaps; identify resources and training needs; list objectives for each priority; and identify benchmarks to measure progress.

Discussion

Dr. Pollock and Dr. Weinberg directed the workgroup to the list of resources in the slide presentation and to the "proposed recommendations" document and asked members to help generate ideas in the discussion today. They also offered the option of providing input via email for discussion in future meetings. Feedback was not limited to the present framework, and participants were encouraged to suggest alternate frameworks as well as additional approaches and resources to consider.

- Dr. Eric Johnson suggested the group work from the draft document that was distributed to them as a focal point for launching the discussion, but sought clarification on how to identify benchmarks and objectives. Dr. Boyle indicated that they should first try to identify broad priority goals and action items for NIDA to take, and then concentrate on metrics later.
- Based on questions from Dr. Dani Fallin, the group learned that it did not need to rank the priorities identified in its discussions but should concentrate on identifying those that are developmentally relevant at the program level. Dr. Fallin pointed out that we need tools to study issues in a developmental context.
- Dr. Gustavo Turecki and Dr. John Rice expressed interest in NIDA's investment of human vs. animal research in the areas of molecular genetics and epigenetics to gauge the translational potential from basic studies.
- Dr. Hugh Garavan pointed out the need to address training to meet the multidisciplinary challenges of GEDI research. He suggested trials using random assignment to specific interventions as a way to identify causal mechanisms.
- Dr. Kenneth Kendler added that longitudinal studies (vs. cross-sectional) might be more appropriate for inferring causality. He discussed some indepth design approaches to longitudinal design that might lead to developmental and mechanistic perspectives. He said the field is progressing with models of aggregate genetic effects that will form an intermediate research strategy between latent variable models on the one hand and single genetic variants on the other.
- Dr. Johnson and Dr. Rice addressed the need for larger datasets and the need for extremely large samples to study genetics properly. To study interaction, we need known associations. They remarked that the field was facing an imbalance on available genetics data relating to particular substances, as well as gaps in the availability of epigenetics data on brain tissue, and that it would be helpful to prioritize data-sharing on phenotyping and the environmental side.
- Dr. Iacono asked how the workgroup's recommendations would be used by NIDA. Dr. Boyle explained that in the short term, they would likely inform budget requests and that

in the long term, comments will be fed into NIDA's main Strategic Plan. Dr. Boyle also stressed the need to identify *actionable* items in the recommendations document.
- Dr. Jane Costello stressed the need to examine phenotype and environment.

Public Comment Period
No comments were submitted to the group.

Action Items
- Dr. Pollock will disseminate details on animal vs. human research to the workgroup.
- NIDA staff will provide the full list of citations and resources related to the study findings to GEDI panelists.
- The Co-Chairs will send a reminder email to the workgroup asking for written ideas, comments, questions, and suggestions.
- Members of the workgroup will email their feedback to the full workgroup.

Next Meeting
The next webinar is scheduled for Tuesday, April 28, at 3 p.m.

GEDI Workgroup Members

Extramural Workgroup Members

Danielle Dick, Ph.D., Virginia Commonwealth University
Margaret Daniele Fallin, Ph.D., Johns Hopkins Bloomberg School of Public Health
Hugh Garavan, Ph.D., University of Vermont
John Rice, Ph.D., Washington University School of Medicine
E. Jane Costello, Ph.D., Duke University Center of Developmental Epidemiology
William Iacono, Ph.D., University of Minnesota
Kenneth Kendler, M.D., Virginia Commonwealth University
Eric Johnson, Ph.D., RTI International
Gustavo Turecki, M.D., Ph.D., McGill University

NIH Staff

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