Director’s Report to the National Advisory Council on Drug Abuse

May 15, 2018

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National Institute on Drug Abuse

@NIDAnews
Director’s Report to the National Advisory Council on Drug Abuse

• Budget Update

• What’s New @ HHS/NIH?

• Recent NIDA Activities & Events
<table>
<thead>
<tr>
<th></th>
<th>FY 2017 Actuals</th>
<th>FY 2018 Operating Plan</th>
<th>FY 2018 Opioid Funding</th>
<th>FY 2019 President’s Budget</th>
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</thead>
<tbody>
<tr>
<td>NonAIDS</td>
<td>$794,102</td>
<td>$858,106</td>
<td>$250,000</td>
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<tr>
<td>AIDS</td>
<td>$276,711</td>
<td>$268,551</td>
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<td>TOTAL</td>
<td>$1,070,813</td>
<td>$1,126,657</td>
<td>$250,000</td>
<td>$1,137,403</td>
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</tbody>
</table>

\(^1\text{FY 2018 Opioid Funding expires September 30, 2019}\)
National Institute on Drug Abuse Portfolio
FY 2017 Actual

- Division of Neuroscience & Behavior -- 38%
- Division of Epidemiology, Services & Prevention Research -- 28%
- Division of Therapeutics and Medical Consequences -- 15%
- Center for the Clinical Trials Network -- 4%
- RMS -- 6%
- Intramural Research -- 8%
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NIH: Focus on Structure and Function of Brain Circuits

**Goal:** See the circuits in action to understand:

- How the brain moves, plans, executes
- How to monitor/manipulate circuits for improved function
- How disordered brain circuits cause neuro/mental/substance use disorders

**Long-term goal:** Make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention
Overall Support for High Priority Research Areas

345 projects
500+ investigators
$548.3M to date

$ in Millions

2014 2015 2016 2017

110 awards
108 awards
67 awards
58 awards

Data Coordination/Informatics
Neuroethics
Training/Dissemination
Human Imaging/Modulation
Understanding Circuits
Neural Recording/Modulation
Cell/Circuit Tools
Cell Types

58 awards

$0 $50 $100 $150 $200 $250 $300

500+ investigators
$548.3M to date
Figure 2. Awarded and committed BRAIN Initiative funds as of FY2017. Each color represents the initial fiscal year of the corresponding competing awards and associated out-year non-competing obligations. Gray represents anticipated funds for the remainder of the initiative, assuming a “base” budget of $150M (now ~$310) plus funds authorized by the 21st Century Cures Act.²
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29 states have legalized medical marijuana along with D.C., Guam and Puerto Rico

States with MML vary on:
• Allowable conditions and routes of administration.
• Dispensaries/home growth and registries.
• Testing, regulatory requirements.

States with Recreational Laws vary on:
• Marketing, product labeling, distribution (home growth).
• Taxation.

As of Jan. 22, 2018, the Vermont legislature passed adult-use legalization legislation and the governor signed the bill. The measure does NOT set up a regulatory system for sales or production.
THE EIGHT PRINCIPLES

• The NIDA's research mission is understood to be inclusive, flexible, and public health oriented.

• Research must be neutral about actions, laws, and policies set by any jurisdiction regarding cannabis.

• Priority should be given to research that will remain germane under a wide range of policy frameworks.

• Research should focus on behaviors and consequences that are associated with the greatest harms or benefits and the policies that ameliorate or exacerbate those harms.

• Research should consider both short-and long-term effects.

• Research should be sensitive to the realities of cannabis laws and policies.

• Research should be sensitive to the realities of cannabis production, marketing, and use.

• Research should acknowledge that, sometimes, large gaps can emerge between a law or policy as written and its implementation.
NIDA already doing:

- **Measures of Intoxication or Impairment**: SBIR Request for proposals on Digital Markers for Marijuana Intoxication: 4 funded projects.
- **Common measures**: working with CDC and other Federal partners on common surveillance measures to evaluate impact of changing laws.
- **Policy Databases with up to date information on State laws (Medical and Adult use)**
  - NIAAA Alcohol Policy Information System (APIS) now contains information on adult use (recreational) cannabis laws for policy researchers
- **Policy research portfolio**: DESPR has expanded its research on cannabis policy impact

Proposed Future plans:

- **Convene a meeting on measures**: Defining a “standardized dose” is challenging —range of products, routes of use, inability to measure what is used (legal issues prevent our accessing state products).
  - Partner with Canada for they may have more accurate product measures under their new legalization policies. (Already have this for medical cannabis)
- **Expand research on cannabis policy: add as a priority area to Drug Abuse Topics (DAT) of Interest website.** Currently have DAT on cannabis and developing brains (prenatal and adolescent)
- **Expand interest on intersection with opioids for pain treatment, relation to opioid use/OUD**
- **Include in NIDA’s International priorities**—to take advantage of changes occurring in Canada, Uruguay and elsewhere
A system for the Specification of Acute THC Impairment using Validated Algorithms (SATIVA)

SATIVA

- Smartphone Sensor Data Collection Application
  - Onboard Psychomotor Psychometric Task
  - Accelerometer
  - Camera (Front Facing)
  - Camera (Rear Facing)
  - Blood Pressure Hardware Plugin
  - Pulse Plethysmograph Plugin

  Powered by Android’s ResearchStack

- Data Processing and Fusion Engine
  - Pre-Processing and Fusion of Sensor and Task Data
  - Data handling techniques for dealing with real-world data (e.g., filtering, de-noising, time-aligning)

- Impairment Detection Algorithms
  - Dynamic Bayesian Networks
  - Hierarchical Dynamic Bayesian Networks
  - Bayesian Deep Learning

- Laboratory-based, Controlled Evaluation and Validation (McLean Hospital)
  - Phase I Pilot Study: Demonstrating Feasibility (N=10-15)
  - Controlled Administration
  - Driving Simulator

  - Psychophysiological Testing (e.g., Divided Attention, Visual Search, Time Estimation, Stop Signal)
  - Physiological Testing (e.g., Average Heart Rate, Blood Pressure, Pupil Diameter, Pupil Reactivity, Emotion, Blood Oxygen Saturation, Plasma THC Concentration)
Cannabis Impairment Detection Application (CIDA)

The proposal is based on the family of systems developed by Advance Brain Monitoromg which combines battery-powered hardware with a sensor placement system that provides a lightweight, easy-to-apply method to acquire and analyze up to 20 channels of high-quality EEG, ECG and accelerometry.

a) B-Alert X10 EEG system, b) Sleep Profiler, c) Stat X24 EEG System, d) M4 System
ABCD Update

ABCD Enrollment
As of May 10, 2018

Number of Participants


Singletons Twins Total Target

ABCD Study Fast Track Data
DICOM images from ~6,000 participants currently available.

Interim curated data on first 4,500 participants released Feb 2018!

• Basic demographics
• Assessments of:
  o Physical and mental health,
  o Substance use,
  o Culture and environment, and
  o Neurocognition
• Tabulated structural and functional neuroimaging data
• Minimally processed brain images
• Biological data (e.g., pubertal hormone analyses)
• Residential history derived data related to residential density/walkability, crime, area deprivation, population density, and satellite-based pollution measures
FOA will support creative educational activities with a primary focus on courses for skills development that will allow participants to explore the hands-on use of ABCD data, through cooperative or competitive approaches.
Overdose Death Rates

1999

2016

Legend for estimated age-adjusted death rate (per 100,000 population):
- <2
- 2-3.9
- 4-5.9
- 6-8.9
- 8-10
- 10-11.9
- 12-13.9
- 14-15.9
- 16-17.9
- 18-19.9
- 20-21.9
- 22-23.9
- 24-25.9
- 26-27.9
- 28-29.9
- 30+

Evolution of the Opioid Crisis

1. Over prescription of opioid medications led to misuse
2. Addiction to prescription opioids led to heroin
3. Emergence of fentanyl(s), with higher potency and greater profitability in the black market than heroin.

Puja Seth et al., MMWR, Weekly / March 30, 2018 / 67(12);349–358.
NIH OPIOID RESEARCH INITIATIVE

Using Research to End the Opioid Crisis

**PAIN MANAGEMENT**
Safe, more effective strategies

**OPIOID ADDICTION TREATMENT**
New and innovative medications and technologies

**OVERDOSE REVERSAL**
Interventions to reduce mortality and link to treatment
How do Endogenous Opioids Differ From Synthetics?

Non-peptide
- permeant agonist
- Activation site 1
- Activation site 3
- Golgi

opioid peptide
- plasma membrane
- endosomes
- Activation site 2

Stoeber M et al., Neuron 2018
Ligand-specific Spatiotemporal Distinctions in Opioid Receptor Signaling

Stoeber M et al., Neuron 2018
New NIDA FOAs

Exploring Epigenomic or Non-Coding RNA Regulation in the Development, Maintenance, or Treatment of Chronic Pain (R61/R33 Clinical Trial Optional) (PAR-18-742) NIDA & NCCIH


Research that investigates the role of epigenetic or non-coding RNA regulatory pathways in the development, maintenance, or treatment of chronic pain. Expand knowledge that can be exploited to develop non-addictive pain medications or pain biomarkers.
Medication Assisted Treatment (MAT)

DECREASES:
• Opioid use
• Opioid-related overdose deaths
• Criminal activity
• Infectious disease transmission

INCREASES
• Social functioning
• Retention in treatment

MAT is highly underutilized!
Relapse rates are very high (50% in 6 months)

OUD Cascade of Care in USA

Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017
SUBLOCADE™ (Buprenorphine ER), Once-Month Injectable
FDA Approval 11.30.2017

CAM2038: Subcutaneous ER Buprenorphine
Weekly or monthly injection

% urine samples negative for opioids (Weeks 5 to 24)

Comparison CAM2038 versus Daily SL BPN

Heidbreder et al., CPDD 2017
New Targets: Medications to Decrease Withdrawal

FDA committee votes to approve lofexidine for opioid withdrawal

By Ellen Daniel

Symptoms of opioid withdrawal include abdominal cramping, diarrhoea, dilated pupils, goose bumps, nausea and vomiting. Credit: Flikr/U.S. Department of Agriculture

The US Food and Drug Administration (FDA) Psychopharmacologic Drugs Advisory Committee has voted to approve lofexidine hydrochloride to treat symptoms of opioid withdrawal.
PATIENT FOCUSED DRUG DEVELOPMENT
MEETING FOR OPIOID USE DISORDER (OUD)
APRIL 17th, 2018; 10:00 am – 4:00 pm

AGENDA

9:00 – 10:00 am Registration
10:00 – 10:05 am Welcome
   Sara Eggers, PhD
   Office of Strategic Programs (CSP), Center for Drug Evaluation
10:05 – 10:10 am Opening Remarks
   Theresa Mullin, PhD
   Associate Director for Strategic Initiatives, CDER, FDA
10:10 – 10:20 am Background on Opioid Use Disorder and Treatment
   Maryam Alhar, MD
   Division of Anesthesia, Analgesia, and Addiction Products (DAAAP), CDER, FDA
10:30 – 10:50 am The Road from PFD Meeting to Clinical Trial Endpoints
   Elektra Papadopoulou, MD, MPH
   Associate Director, Clinical Outcome Assessments Staff, CORD, FDA
10:55 – 10:55 am Overview of Discussion Format
   Sara Eggers, PhD
   CSP, CDER, FDA
10:55 – 11:05 am Panel #1 Discussion on Topic 1: Health Effects and Daily Impacts
   A panel of individuals and families will provide comments to discuss the
   significant health effects and daily impacts on opioid use disorders
   and other potential problems
   11:05 – 12:00 pm Large-Group Facilitated Discussion on Topic 1
   Individuals and families in the audience will be invited to add to the dialogue
12:00 – 1:00 pm Lunch
1:00 – 1:05 pm Afternoon Welcome
   Sara Eggers, PhD
   CSP, CDER, FDA
1:05 – 1:35 pm Panel #2 Discussion on Topic 2: Current Approaches to Treatment of OUD
   A panel of individuals and families will provide comments to start the discussion on current
   approaches to treating opioid use disorder
   1:35 – 2:00 pm Large-Group Facilitated Discussion: Topic 2
   Individuals and families in the audience will be invited to join the dialogue
2:00 – 2:45 pm Break
2:45 – 3:15 pm Large-Group Facilitated Discussion: Topic 2 Continued
3:15 – 3:45 pm Open Public Comment
3:45 – 4:00 pm Closing Remarks
   Mitra Ahradpour, MD, DABAM
   Deputy Director, Office of Translational Sciences (OTS) CDER, FDA

DISCUSSION QUESTIONS

Topic 1: Health effects and daily impacts of Opioid Use Disorder (OUD)

1. Of all the ways that OUD negatively affects your health and well-being, which effects have the
   most significant impact on your daily life? Examples of negative effects may include:

2. Besides prescription medical treatments, are there other treatments or therapies that you
currently use to address your OUD if so, please describe. How do these treatments
or therapies help address the effects of OUD that are most bothersome to you?

3. Of all treatments, therapies, or other steps that you have taken to address your OUD, what
have you found to be most effective in helping you manage your OUD?

4. What are the biggest factors that you take into account when making decisions about
seeking out or using treatments for OUD?

5. What specific things would you look for in an ideal treatment for OUD?

6. If you had the opportunity to consider participating in a clinical trial studying experimental
treatments for OUD, what factors would you consider when deciding whether or not to participate?

Docket Information: We encourage you to submit your written comments to the docket by June
New NIH Initiative to Address the Crisis: HEAL: Helping to End Addiction Long-term

- Collaborative, cross-cutting research
  - From basic to behavioral – and everything between
  - Innovative partnerships – across agencies, sectors, organizations – will ensure rapid progress
- $500M just added by Congress
  - Adds to $600M current funds = $1.1B for FY18
  - Will propel HEAL
- Advances national priorities for pain, addiction research…
NIH HEAL Initiative: Some Priorities

**Prevention**
- Understand Origins of Chronic Pain
- Develop New Non-Addictive Treatments for Pain
- Build Clinical Trial Network for Chronic Pain
- Enhance Precision Pain Management

**Treatment**
- Improve Therapeutic Approaches to Addiction
- Evaluate Treatments, Consequences of NOWS
- **Optimize Effective Treatments through Pilot Demonstration Projects**
1. Multisite Implementation Research Study
2. CTN Expansion
3. Justice Community Opioid Intervention Network
4. Focused Medications Development
## Priority Areas

### Prevention Research

(Children & Adolescents)  
genetics/epigenetics  
development  
environment  
co-morbidity

### Treatment Interventions

(New Targets & New Strategies)

## HIV and Drugs

Prevention  
Treatment
Predictors of Linkage to HIV Care and Viral Suppression After Release From Jails and Prisons

Time to linkage to care as measured by first HIV RNA viral load drawn after release from prison or jail

New NIDA FOAs

Coordinating Center to Support NIDA Rural Opioid HIV and Comorbidity Initiative (U24 - Clinical Trial Not Allowed) (RFA-DA-19-004)
Issued: March 20, 2018; Application Receipt/Submission Date(s): August 15, 2018.

Fund a single interdisciplinary Coordinating Center to centralize support of the rural opioid initiative administered by NIDA and co-funded by CDC, SAMHSA, and ARC.
NIDA Topics of Special/Continuing Interest (DAT)

**NIDA Topics of Interest (DAT)**

*Important: Please contact the Program Official/Contact(s) before submitting an application.*

NIDA is attempting to limit the number of Program Announcements we issue each year; however, we remain committed to informing applicants about emerging and continuing areas of research interest. The Drug Abuse Topics (DATs) of interest will leverage existing parent funding opportunity announcements to solicit topic-specific applications within areas of emerging interest to the Institute. Note that we continue to encourage investigator-initiated projects in topic areas not listed here, and that applications submitted in response to the Relevant Funding Opportunities are NOT limited to the research and development areas described below.

This website only lists scientific/research topics and contact information and instructions for linking applications to specific topic areas of interest to NIDA (DATs). What is not included are additional application instructions, eligibility restrictions, review criteria, selection criteria, or other items related to the completeness or compliance of an application. These are found in the SF424 application guide.