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

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse
May 9, 2023
<table>
<thead>
<tr>
<th></th>
<th>FY 2022 Final</th>
<th>FY 2023 Enacted</th>
<th>FY 2024 President’s Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base</strong></td>
<td>$1,250,828</td>
<td>$1,308,070</td>
<td>$1,308,070</td>
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<tr>
<td><strong>HEAL</strong></td>
<td>$345,295</td>
<td>$355,295</td>
<td>$355,295</td>
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<tr>
<td><strong>Total</strong></td>
<td>$1,596,123</td>
<td>$1,663,365</td>
<td>$1,663,365</td>
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*NIDA’s FY 23 budget includes a 3.8% general increase as well as a $10m increase for the HEAL program and a $10m increase for research on pain and pain management.*
Building on BICCN, the BRAIN Initiative Cell Atlas Network (BICAN) will map brain cells and circuits across multiple species, with an emphasis on humans.

BRAIN Initiative Connectivity Across Scales (BRAIN CONNECTS) Network will provide a wiring diagram by mapping all the connections in the brain.

The Armamentarium for Precision Brain Cell Access leverages new brain cell census data to build a toolkit to access brain cells based on their molecular identity.
9th Annual BRAIN Initiative Meeting

In-person & Virtual: June 12-13, 2023

Featuring:

✓ Plenary lectures & symposia discussions
✓ Trainee highlights & contest winners
✓ Poster sessions & networking events
  ○ Pre-meeting event: “BRAIN, Neuroscience, and Beyond: Building Our Early Career Community”

All those interested in the U.S. BRAIN Initiative are encouraged to attend and participate.

https://brainmeeting.swoogo.com/2023/home
Adolescent Brain Cognitive Development Study

97.1% Percent Retained

Antipoverty Programs Associated with Reduced Disparities in Brain Development and Mental Health
HEALthy Brain and Child Development Study

- Funded through partnership of NIH Institutes, Centers, and Offices including HEAL
- Longitudinal study of normative neurodevelopment from birth to 9-10 years that will assess impact of in utero exposures to drugs and harmful environments
- Will enroll approximately 7,500 families across the country

Pilot Study initiated in all sites
- 330 parents, 240 children
- 3 timepoints tested

○ Enrollment of study cohort expected in May
○ Child Welfare & Research workshop in development
US State Cannabis Laws

38 States & DC with MML
22 States & DC with Adult Use Laws

Adverse Adolescent Psychosocial Events Among Nonuse, Non-disordered Cannabis Use, and Cannabis Use Disorder
NSDUH Data 2015-2019

NDCU and CUD were significantly associated with adverse psychosocial events in a stepwise gradient manner

Sultan et al., JAMA Netw Open. 2023;6(5):e2311294.
Cannabis-Involved Overdose Deaths

Number of fatalities, by Year

In 2021, 90% of fatalities involving cannabis products also involved opioids or stimulants.

*There is no evidence that cannabis products are being laced with fentanyl.


* Poisoning by, adverse effect of cannabis (derivatives) including synthetic cannabinoids
Provisional* Drug Overdose Deaths 12-months ending in select months

<table>
<thead>
<tr>
<th></th>
<th>ALL DRUGS</th>
<th>HEROIN</th>
<th>NAT &amp; SEMI SYNTHETIC</th>
<th>METHADONE</th>
<th>SYNTHETIC OPIOIDS (mainly illicit fentanyl)</th>
<th>COCAINE</th>
<th>OTHER PSYCHO-STIMULANTS (mainly meth)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/2021*</td>
<td>108,076</td>
<td>9,707</td>
<td>13,938</td>
<td>3,737</td>
<td>71,321</td>
<td>24,487</td>
<td>33,100</td>
</tr>
<tr>
<td>12/2021*</td>
<td>109,179</td>
<td>9,411</td>
<td>13,906</td>
<td>3,765</td>
<td>72,484</td>
<td>25,174</td>
<td>33,637</td>
</tr>
<tr>
<td>11/2022*</td>
<td>108,712</td>
<td>6,143</td>
<td>11,945</td>
<td>3,346</td>
<td>74,507</td>
<td>27,529</td>
<td>34,135</td>
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<tr>
<td><strong>Percent Change</strong></td>
<td><strong>0.58%</strong></td>
<td><strong>-36.7%</strong></td>
<td><strong>-14.3%</strong></td>
<td><strong>-10.5%</strong></td>
<td><strong>4.5%</strong></td>
<td><strong>12.4%</strong></td>
<td><strong>3.1%</strong></td>
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<tr>
<td><strong>11/21-11/22</strong></td>
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*NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months.

Xylazine

- Alpha-2 adrenergic agonist used as a veterinary sedative
- Inhibits release of norepinephrine, decreasing sympathetic activity
- By itself it induces hypoxia as severe as that from fentanyl but longer lasting
- When combined with Fentanyl it blocks the compensatory hyperoxemia observed with fentanyl (also with heroin)
- When combined with Fentanyl and Heroin it appears to extend the duration of their pharmacological effects (analgesia, respiratory depression, reward)
- Toxic doses in humans range from 40 to 2400 mg (0.6-34.3 mg/70 kg)
- Not reversed by naloxone
- Associated with severe tissue injury
Xylazine effects on Brain Oxygenation

Xylazine by itself induces long lasting decreases in oxygenation of the brain

Xylazine + Fentanyl combination induced a similar peak hypoxic response as Fentanyl alone but blocked the compensatory hyperoxic response observed with fentanyl

Choi et al., bioRxiv preprint doi: https://doi.org/10.1101/2023.03.31.535103
Research Needs

- Implementation research of screening interventions for substance misuse and SUD in teenagers
- Research on interventions to prevent drug misuse in teenagers and in the transition into young adulthood
- Treatment of SUD in teenagers including mild, moderate and severe OUD
Trends in mortality ratios by cause among pregnant women in 50 states and DC

National Vital Statistics System: 2018-2021 final mortality data and 2018-2021 final birth data. Mortality ratio=deaths among pregnant women by causes/live births*100,000; AQPC=average quarter percentage change. “Drug overdose” deaths included overdose deaths with unintentional or undetermined intent only. Other non-suicide deaths included deaths caused by COVID-19 infection, myocardial infarction, cancer, etc.
SUD/OUD Prevention Cascade in US

- **Social determinants of health**
- Interventions informed by scientific and technological advances
- Implementation, scale-up and sustainment of prevention services

**INFRASTRUCTURE NEEDED TO DEPLOY AND SUSTAIN PREVENTION**
## Fentanyl OUD (fOUD) and OUD Clinical Research Priorities

<table>
<thead>
<tr>
<th>Research Gaps</th>
<th>Goal</th>
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<tbody>
<tr>
<td>Optimal strategies to treat individuals with fOUD</td>
<td>Determine comparative effectiveness of methadone, sublingual buprenorphine, XR-buprenorphine and NXT-XR</td>
</tr>
<tr>
<td>Induction protocols for treatment of fOUD and comparisons of doses</td>
<td>Determine doses needed to initiate and retain in treatment individuals with fOUD</td>
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<tr>
<td>Improve entry into and retention in MOUD treatment</td>
<td>Expand the number of individuals suffering from OUD that receive MOUD treatment and increase treatment retention</td>
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<tr>
<td>Treatment of mild or subthreshold OUD</td>
<td>Determine the role of NXT-XR or buprenorphine in overdoses in high-risk opioid misusers</td>
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<td>Treatment of adolescents with OUD</td>
<td>Determine the efficacy of the various MOUD and best strategies to increase retention and recovery</td>
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<tr>
<td>Patient-specific optimal medication, doses and length of treatment</td>
<td>Personalize interventions to increase retention and recovery</td>
</tr>
<tr>
<td>Treatment of patients with OUD and co-morbid psychiatric disorders or with co-morbid pain</td>
<td>Improve outcomes on patients with dual diagnoses</td>
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Volkow and Blanco AJP in press
Social Determinants of Health: Impact on Treatment Responses in Clinical Trials
Treatment Research

Identification of the brain networks underlying SUD provide therapeutic targets for neuromodulation

Invasive Neuromodulation Techniques

Deep Brain Stimulation

High Intensity Ultrasound (ablative)

Non Invasive Neuromodulation Techniques

Transcranial Magnetic Stimulation (TMS)

Transcranial Direct Current Stimulation (tDCS)

Low Intensity Ultrasound
Percent change in Persons with a Stimulant Prescription Fill (aged 5–64 years)

Narcan, 4 mg naloxone nasal spray for OTC, nonprescription. To be sold in places like drug stores, convenience stores, grocery stores and gas stations, as well as online.
A Review of the President’s Fiscal Year 2024 Funding Request and Justification for the National Institutes of Health

• The Senate LHHS Subcommittee Hearing was held Thursday, May 4, 2023 at 10am.

• ICDs joining Dr. Tabak included: Drs. Lowy, Hodes, Volkow, & Gordon
THANK YOU!