Adolescent Substance Use: From the Neuron to the Clinic

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Disclosures/Acknowledgements

• Hulvershorn
  – Indiana IFSSA: Division of Mental Health and Addictions
  – NIDA
  – NARSAD, KTGF, IU Health
Outline

1) The influence of in utero drug exposure on fetal development
2) The impacts of substance use disorders
3) Substance diagnoses in teens
4) Epidemiology of adolescent substance use
5) Risk factors & comorbidities
6) Screening & intervention
7) Brief interventions for any provider (MI)
8) Treatment models
In utero Drug Exposure

Research is limited by:

- Polydrug use
- Retrospective report
- Selection Bias

So, we have many studies with flawed designs and rely on animal studies.
3 Hypotheses

1) Drug abuse affects fetal brain development
2) Drug abuse is multigenerational and those epigenetic influences are profound
3) Drug abuse is less influential than the self-regulatory deficits passed down from certain mothers
Hypothesis 1: Drugs Affect Fetal Development

ORIGINAL ARTICLE
Persistent inhibitory circuit defects and disrupted social behaviour following *in utero* exogenous cannabinoid exposure

GA Vargish, KA Pelkey, X Yuan, R Chittajallu, D Collins, C Fang and CJ McBain

Placental transfer of Δ9-tetrahydrocannabinol (THC) during pregnancy has the potential to interfere with endogenous cannabinoid (CB) regulation of fetal nervous system development *in utero*. Here we examined the effect of maternal CB intake on mouse hippocampal interneurons largely focusing on cholecystokinin-expressing interneurons (CCK-INTs), a prominent CB subtype-1 receptor (CB1R) expressing neuronal population throughout development. Maternal treatment with THC or the synthetic CB1R agonist WIN55,212-2 (WIN) produced a significant loss of CCK-INTs in the offspring. Further, residual CCK-INTs in animals prenatally treated with WIN displayed decreased dendritic complexity. Consistent with these anatomical deficits, pups born to CB-treated dams exhibited compromised CCK-INT-mediated feedforward and feedback inhibition. Moreover, pups exposed to WIN *in utero* lacked constitutive CB1R-mediated suppression of inhibition from residual CCK-INTs and displayed altered social behavior. Our findings add to a growing list of potential cell/circuit underpinnings that may underlie cognitive impairments in offspring of mothers that abuse marijuana during pregnancy.

*Molecular Psychiatry* (2017) 22, 56–67; doi:10.1038/mp.2016.17; published online 15 March 2016
Hypothesis 2: Epigenetic Hypothesis

“These transgenerational effects occur in the absence of in utero exposure. It is speculated that 19-THC exposure during female adolescence may affect neural mechanisms that are shaping reward-related behavioral responses in a subsequent generation, as indicated by the shifts in the reward-facilitating effects of commonly used and abused drugs.”

Pitsilis 2017, Frontiers in Pharmacology
Hypothesis 3: Maternal Regulatory Deficits Are More Prominent than the Effects of Drugs of Abuse
Hypothesis 3

RESULTS Of the 1,680,219 offspring included in the analysis, 816,775 (48.67%) were female. At the population level, offspring exposed to moderate and high levels of smoking during pregnancy had greater severe mental illness rates than did unexposed offspring (moderate smoking during pregnancy: hazard ratio [HR], 1.25; 95% CI, 1.19-1.30; high smoking during pregnancy: HR, 1.51; 95% CI, 1.44-1.59). These associations decreased in strength with increasing statistical and methodologic controls for familial confounding. In sibling comparisons with within-family covariates, associations were substantially weaker and nonsignificant (moderate smoking during pregnancy: HR, 1.09; 95% CI, 0.94-1.26; high smoking during pregnancy: HR, 1.14; 95% CI, 0.96-1.35). The pattern of associations was consistent across subsets of severe mental illness disorders and was supported by further sensitivity analyses.
TAKE HOME POINT

• Drugs can’t be good for fetal development, but they may pale in comparison to other obstacles some kids may face

• Comprehensive support for drug abusing moms may be the best plan: enhance communication skills (reconnect with family?), job/education skills, treat mental illness (self-fulfilling relationship choices) and drug abuse; Enhance parenting skills
How should pregnant/postpartum moms be treated for SUDs?

Integrated care:

• Prenatal Care
• Child Care/bring baby
• Parenting skills
• Drug Treatment (including MAT)
THE IMPACTS OF DRUGS OF ABUSE
Impact of Substance Use Disorders

drugabuse.gov
Could we have seen this coming?
Consequences and correlates

In 2000, youths ages 12 to 17 who reported past-year alcohol use (19.6%) were more than twice as likely as youths who did not (8.6%) to be at risk for suicide during this time period.

Girls ages 12 to 16 who are current drinkers are four times more likely than their nondrinking peers to suffer from depression.

Among adolescents who drink alcohol, 38% to 62% report having had problems related to their drinking, such as interference with work, emotional and psychological health problems, the development of tolerance, and the inability to reduce the frequency and quantity of use.

In 2006, 1.4 million youth ages 12 to 17 needed treatment for an alcohol problem. Of this group, only 101,000 of them received any treatment at a specialty facility, leaving an estimated 1.3 million youths who needed but did not receive treatment. (< 8% in treatment)

Of all children under age 14 killed in vehicle crashes in 2006, 23% were killed in alcohol-related crashes.

Cannabis use is associated with earlier and worse psychosis in a subset of people.
Drugs and the adolescent brain
Cortical brain region activations on a working memory task in adolescents with heavy marijuana use vs controls
(Jager et al., JAACAP, June 2010).
Drugs & Alcohol

- Brain development altered in alcohol-abusing teens
  - Reduced prefrontal white and gray matter in adolescent-onset alcohol-use disorder (De Bellis et al., 2005)
  - White matter development impaired in teen binge drinkers (McQueeny et al., 2009)

- Of people who begin drinking before age 14, 47% became dependent at some point, compared with 9% of those who began drinking at age 21 or older.
Why should we care about adolescent substance misuse?

- Those who began drinking or using drugs early in life are more likely to develop substance use disorders.
- The adolescent brain is more sensitive to toxicity from drugs and alcohol: cognitive impairments as well as psychiatric.
- Adolescence is a crucial developmental period with necessary progress through milestones. Substance use derails this progress.
Outline

1) The impact of substance use disorders
2) Substance diagnoses in teens
3) Epidemiology of adolescent substance use
4) Risk factors & comorbidities
5) Screening & intervention
6) Brief interventions for any provider (MI)
7) Treatment models
Warning Signs

• Any prescription or other drug seeking behavior.
• Contact with drug using peers.
• Unsupervised time.
• Need to medicate every symptom (fatigue, anxiety).
• Use of any one drug, alcohol or nicotine.
• Distress at inability to obtain substances.
• Family History of substance use disorders.
How are substance use disorders different in adolescents than adults?

• Less chronic, less refractory
• Fewer withdrawal symptoms
• Can be as severely affected
• Fewer judicial/community resources
• More oversight from authorities (parents, school)
• A greater variety of drugs, use impacted more by availability
DSM-5

- Substance Intoxication
- Substance Withdrawal
- Substance-Induced: Psychotic Disorder, Depressive Disorder, etc.
- Substance Use Disorder: (2/11 over 12 months) Problematic pattern of use leading to clinically significant impairment or distress
- New: Caffeine, Tobacco (not nicotine), gambling
How to Diagnose?

- **Diagnostic Evaluations (2-3 hours)**
  - Standardized Measures and Evaluation for SUDs
    - Kiddie Schedule for Affective Disorders an Schizophrenia (KSADS); Composite International Diagnostic Interview (CIDI); etc.
    - Timeline Follow Back for Drug Use (Sobell & Sobell, 1992)
    - Urine Drug Screens
  - ...and Mental Health Comorbidities
    - KSADS, CIDI, CDISC, etc.
    - High risk sexual behaviors
    - Psychiatric symptom ratings: MASC, CDRS, ADHD-RS
    - Multiple respondents when possible
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Epidemiology

- Nearly 50% of American youth used an illicit drug by the time of high school graduation.

- 7.6% of youth aged 12 to 17 years meet criteria at some point for substance dependence.

Source: MTF, NSDUH
Consumption and Consequences of Alcohol, Tobacco and Drugs in Indiana: 2015

- **ALCOHOL**: 33% of high school students used and 20% engaged in binge drinking in the past 30 days
- **TOBACCO**: 9% of 12-17 year olds currently use — e-cigarettes on the rise (2012: 4% → 2014: 16%)
- **MARIJUANA**: 20% of h.s. students currently use
- **COCAINE**: 5.6% of h.s. students have tried
- **HEROIN**: 2.8% of h.s. students have tried
- **METHAMPHETAMINE**: 4% of h.s. students have tried
- **RX DRUGS**: 5% of 12-17 year olds have misused pain relievers in the past year

Source: IN SEOW, CDC, SAMHSA, Gassman et al., 2015
Gateway Drugs?

- Alcohol
- Tobacco
- Marijuana
Problems in Indiana 2015

- Cannabis is not dangerous?
- Synthetic cannabinoids
- Prescription pills: opiates and benzodiazepines
- Heroin
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Risk Factors

Bronfenbrenner, 1977
Risk Factors

• Early use

• Genetics: 80% of variance explained

• Externalizing disorders: ADHD, CD, ODD

• Internalizing disorders: depression, anxiety
  (O’Neil et al., Clin Psychol Rev, 2011)

• Environmental moderators: peer group (norms, use), childhood stressors, availability of drugs, antisocial activities

• “Neurobehavioral Disinhibition”
Comorbidities (80-90%)

- Externalizing Disorders
  - ADHD, ODD, CD
- Internalizing Disorders
  - Depressive Disorders
  - Anxiety Disorders
- Psychotic Disorders (less common)
- PTSD
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Clinical Approach

• May vary by setting, point-of-entry
• American Academy of Pediatrics (AAP, 2011) recommends all pediatricians provide Screening, Brief Intervention, & Referral to Treatment

• SBIRT model also endorsed by other professional and public health organizations
Screening

• **GOAL:** quickly identify who *may* have (or be at elevated risk for) substance use problems
  - **If positive**...further evaluation and/or intervention
  - **If negative**...reinforce healthy choices and conserve intervention resources
  - Screening is **NOT** diagnostic
Screening

• Best when standardized:
  • Interview
    • HEADSS(S)
    • GAPS: Guidelines for Adolescent Preventive Services
  • Questionnaires
    • CRAFFT: Car, Relax, Alone, Forget, Friends, Trouble
    • S2BI: Gate questions, follow-up
    • BSTAD: adaptation of NIAAA questions, self and friends’ use
    • POSIT: Problem Oriented Screening Instrument for Teachers
    • AUDIT: Alcohol Use Disorders Identification Test
    • CAGE-A: Cut down, Annoyed, Guilty, Eye Opener
    • Bright Futures: Tailored to different ages

Cohen, Reif, Knight, Latimer, 1991; Knight, 1999; Levy et al., 2014; Kelley et al., 2014
### Screening: CRAFFT

<table>
<thead>
<tr>
<th>C</th>
<th>Have you ever ridden in a <strong>CAR</strong> driven by someone (including yourself) who was “high” or had been using alcohol or drugs?</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>Do you ever use alcohol or drugs to <strong>RELAX</strong>, feel better about yourself, or fit in?</td>
</tr>
<tr>
<td>A</td>
<td>Do you ever use alcohol or drugs when you are by yourself, <strong>ALONE</strong>?</td>
</tr>
<tr>
<td>F</td>
<td>Do you ever <strong>FORGET</strong> things you did while using alcohol or drugs?</td>
</tr>
<tr>
<td>F</td>
<td>Do your family or <strong>FRIENDS</strong> ever tell you that you should cut down on your drinking or drug use?</td>
</tr>
<tr>
<td>T</td>
<td>Have you ever gotten into <strong>TROUBLE</strong> while you were using alcohol or drugs?</td>
</tr>
</tbody>
</table>

Source: Knight 1999
## Screening to Brief Intervention (S2BI) Tool

The following questions will ask about your use, if any, of alcohol, tobacco, and other drugs. Please answer every question by checking the box next to your choice.

**Alcohol?**
- Never
- Once or twice
- Monthly
- Weekly or more

**Marijuana?**
- Never
- Once or twice
- Monthly
- Weekly or more

**IN THE PAST YEAR, HOW MANY TIMES HAVE YOU USED:**

**Tobacco?**
- Never
- Once or twice
- Monthly
- Weekly or more

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S2BI Tool developed at Boston Children’s Hospital with support from the National Institute on Drug Abuse. It is best used in conjunction with “The Adolescent SBIRT Toolkit for Providers” mass.gov/maclearinghouse (no charge).

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Levy et al., 2014, *JAMA Pediatrics;* C2BI Toolkit
Screening – S2BI

Prescription drugs that were not prescribed for you (such as pain medication or Adderall)?
- Never
- Once or twice
- Monthly
- Weekly or more

Inhalants (such as nitrous oxide)?
- Never
- Once or twice
- Monthly
- Weekly or more

Illegal drugs (such as cocaine or Ecstasy)?
- Never
- Once or twice
- Monthly
- Weekly or more

Herbs or synthetic drugs (such as salvia, “K2”, or bath salts)?
- Never
- Once or twice
- Monthly
- Weekly or more

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## Table 1. Definition of Substance Use Categories

<table>
<thead>
<tr>
<th>Substance Use Disorder</th>
<th>Full Screen and Brief Assessment Tool</th>
<th>Screen to Brief Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Any past-year substance use, RAFFT score = 0, other assessment questions negative</td>
<td>Once or twice use of any substance</td>
</tr>
<tr>
<td>Mild-moderate</td>
<td>Any past-year substance use, RAFFT score &gt; 1, other assessment questions negative</td>
<td>Monthly use of any substance</td>
</tr>
<tr>
<td>Severe</td>
<td>Any past-year substance use, RAFFT score &gt; 1, other assessment questions positive</td>
<td>Weekly or greater use of any substance</td>
</tr>
</tbody>
</table>

Abbreviation: RAFFT, relax, alone, forget, friends or family, trouble.

Levy et al., 2014, *JAMA Pediatrics*; C2BI Toolkit
In the past year, how many times have you used:
Tobacco? Alcohol? Marijuana? (Ask separately.)

- **No Use**
- **Once or Twice**
- **Monthly Use**
- **Weekly Use**

**Positive Reinforcement**

**Ask Follow Up S2BI Questions:** Prescription drugs, illegal drugs, inhalants, herbs?

**Brief Advice**

**Motivational Intervention:** Assess for problems, advise to quit, make a plan

**Reduce use & risky behavior**

**Reduce use & risky behaviors & refer to treatment**
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**Brief Education and Advice**

- **Q:** What advice can I give?
  **A:** The safest option is to NOT use substances, so you can recommend this option to all of your patients.

- Provide medically accurate, developmentally appropriate education to youth and families

[teens.drugabuse.gov]
Motivational Interviewing

“A collaborative, person-centered form of guiding to elicit and strengthen motivation for change.” – Miller & Rollnick, 2009

- Applicable with adolescents and/or caregivers
- Method or style, not a school or theory
- Assume most adolescents are not ready for change at first
Motivational Interviewing Techniques for Adolescents

• Themes: ACE
  – **Autonomy**
    • Key developmental task
  – **Collaboration**
    • Build a partnership
  – **Evocation**
    • Elicit reasons for and concerns about change

Naar-King & Suarez, 2011
## MI for Adolescents: Responding to Resistance

<table>
<thead>
<tr>
<th>What to Do</th>
<th>What Not to Do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop, Drop, and Roll</td>
<td>Convince, Persist, or Advise</td>
</tr>
<tr>
<td>Use different types of reflections to respond to resistance or change talk</td>
<td>Argue against sustain talk, attempt to correct it, or fall into persuasion</td>
</tr>
<tr>
<td>Respond strategically by emphasizing person control, agreeing with a twist, eliciting pros and cons, or shifting focus</td>
<td>Ignore or avoid the young person’s perspective or continue to reflect when the conversation seems stuck</td>
</tr>
</tbody>
</table>

From Naar-King & Suarez, 2011
Family Check-Up

1. Communication
2. Encouragement
3. Negotiation
4. Setting Limits
5. Supervision

www.drugabuse.gov/family-checkup
Outline

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Evaluation

• Diagnostic Evaluations (2-3 hours)
  – Standardized Measures and Evaluation for SUDs and Mental Health Comorbidities
    • E.g. Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS)
    • High risk sexual behaviors
    • Baseline psychiatric ratings: MASC, CDRS, ADHD-RS
    • Timeline Follow Back for Drug Use
    • Urine Drug Screens
Existing Treatment Models

• Outpatient:
  – **Family Therapy:** Multidimensional Family Therapy, Brief Strategic Family Therapy, Functional Family Therapy, SOFT, Adolescent Community Reinforcement Approach (A-CRA), Multisystemic Therapy
  – **Individual Therapy:** CBT, Motivational Interviewing/Motivational Enhancement Therapy (+/- CBT), Contingency Management
  – **Group Treatments:** 12 step, CBT
  – **Medication Management**

• Inpatient, Partial Hospitalization
• Residential “Rehab”
• Integrated outpatient treatments for co-occurring disorders: ENCOMPASS
## Evidence-Based Treatment Models (Outpatient)

<table>
<thead>
<tr>
<th>Level of Support</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Works well, Well-established</td>
<td>• Group CBT&lt;br&gt;• Individual CBT&lt;br&gt;• Family-based treatment (ecological; MDFT, FFT, EBFT)&lt;br&gt;• Combined MET/CBT&lt;br&gt;• Combined MET/CBT/Family-based treatment (behavioral)</td>
</tr>
<tr>
<td>2: Works, Probably efficacious</td>
<td>• Family-based treatment (behavioral)&lt;br&gt;• Motivational interviewing/MET&lt;br&gt;• Combined family-based treatment (ecological)/Contingency Management&lt;br&gt;• Combined MET/CBT/Family-based treatment (behavioral)/Contingency management</td>
</tr>
<tr>
<td>3: Might work, Possibly efficacious</td>
<td>• Drug counseling/12-step</td>
</tr>
</tbody>
</table>

Hogue, Henderson, Ozechowski, & Robbins, 2014, *JCCAP*
Contingency Management

• Strong data to support decrease in drug use in adults and adolescents
• Approach to behavior change (A-B-C)
  – Can be used by parents alone or in coordination with a therapist
• Point-and-level system or “Prize draws” for positive behaviors:
  – Session attendance
  – Negative UDS
  – Pro-social activities
• Bonus prizes for sustained or early abstinence

Henggeler et al., 2012
ENCOMPASS

• 13 weeks of individual CBT + 3 sessions with family/supports

• **Week 1:** Personal rulers, Supportive People, Functional Analysis of Pro-Social Activities

• **Week 2:** Personal Feedback, Goal Setting, Happiness Scale

• **Week 3 Exploring Use:** Functional Analysis of Drug Use behavior, Expectation of Effects, Consequences of Use

• **Other 13 Modules:**
  • Coping with cravings
  • Communication
  • Managing anger
  • Negative moods
  • Problem solving
  • Realistic refusal skills
  • Support systems
  • School & employment
  • Coping with a slip
  • Seemingly irrelevant decisions
  • HIV prevention
  • Saying goodbye
  • Bringing in the family (3 sessions)
Family involvement is a key ingredient of nearly all adolescent substance use treatment programs.
Goals of family/parenting interventions

- Parent training
- Improve Family Functioning
- Reduce/Eliminate Substance Use
- Increase Problem Solving Skills
- Develop (Nurture Existing) Future Orientation
- Address Ecology of the Problem
Treatment

• **Medication Management**
  – SUDs
    • Small literature for use in adolescents but wealth of adult research in treatment for SUDs

  – Comorbidities
    • Depression and Anxiety have clear pharmacologic targets
    • ADHD: Stimulants (controversial), Bupropion
Medication Treatments for Substance Use Disorders

- **Replacement**
  - Opiates
    - Suboxone
    - Methadone
  - Nicotine

- **Aversive** (rarely used)
  - Alcohol
    - Disulfiram

- **Others**
  - Nicotine
    - Varenicline
    - Bupropion
  - Opiates
  - Alcohol
    - Acamprosate
    - Naltrexone
Components of Comprehensive Drug Abuse Treatment (NIDA, 2014)

- Vocational Services
- Family Services
- Legal Services
- HIV/AIDS Services
- Educational Services
- Medical Services
- Mental Health Services
- Continuing Care
- Recovery Support Programs
- Clinical and Case Management
- Substance Use Monitoring
- Evidence-Based Treatment
- Assessment

Diagram describes the various components and services involved in comprehensive drug abuse treatment.
Existing Models

• Separate treatment programs for substance use problems, mental health, and other medical issues

Sterling et al., 2010, JAACAP; Suarez et al., 2012, Am J Comm Psych
Telemedicine

- Extends patients’ **access**, clinicians’ **reach**
  - School, local clinic, ED, home
  - Cost-effective

- **Acceptable** to teens and families

- **Flexible & multi-modal**
  - Computer, tele-video, SMS texts, apps
  - One-way or two-way information

Belendiuk & Riggs, 2014; Marsch & Dallery, 2012
Telemedicine

• Can be effective in reducing substance use and related problems – more research needed in teens and families

• Can also be used to link or coordinate care teams

• Many special considerations:
  – Legal, ethical, security, credentialing, space, etc.
1. Decatur County Memorial Hospital  
   (Greensburg, IN)

2. IUH White Memorial Hospital  
   (Monticello, IN)

3. Deaconess Riley Children’s Specialty Center  
   (Evansville, IN)

4. The Bowen Center  
   (Albion, IN)

5. Foundations Family Medicine  
   (Austin, IN)

6. IU North  
   (Carmel, IN)

COMING SOON

7. IUH Arnett Hospital  
   (Lafayette, IN)

8. The Hamilton Center  
   (Linton and Bloomfield, IN)
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References (2)

References (3)

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