Psychopathological Antecedents to Substance Use Disorders in Youth

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Bidirectional overlap between ADHD & SUDs and smoking


Is ADHD a Risk Factor for Smoking?

• The neurobiology of ADHD may involve deficits in cholinergic nicotinic receptors
• ADHD individuals may have genetic or acquired deficits in nicotinic cholinergic receptors

Potential Areas of Neurochemical Manipulation: Treatment of ADHD with Cholinergic Agents

ADHD and Nicotinic Receptors

Clinic-referred ADHD boys (n=128) and controls (n=109) ages 6 to 17 years followed prospectively for 4 years

Milberger et al. JAACAP 1997;36:38.
Maternal Smoking During Pregnancy: Results in Children

History of Maternal Smoking (%)

<table>
<thead>
<tr>
<th>History of Maternal Smoking (%)</th>
<th>ADHD (N=140)</th>
<th>Controls (N=120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
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<tr>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>15</td>
<td>5</td>
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<tr>
<td>20</td>
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<td>0</td>
</tr>
<tr>
<td>25</td>
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</tbody>
</table>

P = 0.002

* P = 0.04, controlling for SES, parental ADHD, and parental IQ

ADHD Clinical Global Impression Percent Much or Very Much Improved at Endpoint

<table>
<thead>
<tr>
<th>Percent</th>
<th>ABT-418</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>13%</td>
</tr>
<tr>
<td>10</td>
<td>20%</td>
<td>26%</td>
</tr>
<tr>
<td>20</td>
<td>30%</td>
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<td>30</td>
<td>40%</td>
<td>44%</td>
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<tr>
<td>40</td>
<td>50%</td>
<td>56%</td>
</tr>
<tr>
<td>50</td>
<td>60%</td>
<td>67%</td>
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</table>

P = 0.026


Smoking and Comorbidity

Common Comorbid Diagnoses

Approximate Prevalence Rate in Children With ADHD (%)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Male</th>
<th>Female</th>
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<tr>
<td>Oppositional defiant disorder</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Learning disorders</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>


ADHD and Smoking in Youth

Impact of psychiatric comorbidity with Mood, Conduct or Anxiety Disorder

<table>
<thead>
<tr>
<th>% Smoking</th>
<th>ADHD (+)</th>
<th>ADHD (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>10</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>20</td>
<td>20%</td>
<td>20%</td>
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<td>30%</td>
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<td>40</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td>50</td>
<td>50%</td>
<td>50%</td>
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</tbody>
</table>

p = 0.01

Milberger et al. JACAP 1997;36:38.

ADHD and Smoking in Youth

Impact of psychiatric comorbidity: Number of comorbid diagnoses in ADHD probands

<table>
<thead>
<tr>
<th>Number of Psychiatric Comorbidities</th>
<th>% Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>10%</td>
</tr>
<tr>
<td>2</td>
<td>20%</td>
</tr>
<tr>
<td>3</td>
<td>30%</td>
</tr>
<tr>
<td>4</td>
<td>40%</td>
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</tbody>
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p = 0.03

Milberger et al. JACAP 1997;36:38.
ADHD and Smoking in Youth

Impact of psychiatric comorbidity:
Conduct Disorder

Impact of psychiatric comorbidity:
Major Depression

Impact of psychiatric comorbidity:
Multiple (=2) Anxiety Disorders

Is ADHD a Risk Factor for SUDs?

ADHD & SUDs

Kaplan-Meier Curves for PSUD Onset in ADHD Adults
Rate of SUD in ADHD Probands and Siblings

Biederman et al, JAACAP, 1997

Is ADHD a Risk Factor for Specific Types of SUDs?

Preferred drugs of abuse by ADHD probands vs controls


No pairwise comparisons were significant.

Preferred Drugs of Abuse Among High-Risk Siblings of ADHD Probands


No pairwise comparisons were significant.

Are ADHD-Associated Comorbidities Risk Factors for SUDs?

Conduct Disorder (CD)

SUD in ADHD and Control Probands

OR = 13.4, p=0.02
OR = 5.7, p=0.002

Follow-up Drug Dependence (N=237)

ADHD + CD ADHD Control + CD Control

4 Year Follow-Up Study of ADHD

Follow-up Alcohol Dependence (N=237)

ADHD + CD ADHD - CD Controls

4 Year Follow-Up Study of ADHD

Remission and Symptom Decline in CD

Subjects with Conduct Disorder

Continued to Exhibit CD Sxs at follow-up
Did not exhibit CD Sxs at either follow-up
Lost to follow-up

Remission and Symptom Decline in CD

Substance (Alcohol/Drug) Use and Smoking at Follow-up

Percent

Persistent-CD Desistent-CD Non-CD Persistent-CD Desistent-CD Non-CD

Substance Dependence at Follow-up

Percent

Persistent-CD Desistent-CD Non-CD Persistent-CD Desistent-CD Non-CD

Alcohol

Drugs


Biederman et al 1995

Biederman et al 1996

Biederman, et al. (2000)

Biederman, et al. (2000)
Does ODD share with CD the risk for SUD?

Is Childhood ODD a Precursor to Adolescent CD?

Do Mood Disorders Increase the Risk for SUD?
**SUD in ADHD and Control Probands**

Bipolar Disorder (BPD)

- OR = 3.6, p=0.03
- OR = 3.4, p=0.40

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Non-BPD ADHD</th>
<th>Normal Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD + BPD</td>
<td>10%</td>
<td>15%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>ADHD</td>
<td>5%</td>
<td>10%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>Control + BPD</td>
<td>10%</td>
<td>15%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>Control</td>
<td>5%</td>
<td>10%</td>
<td>5%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**ADHD and Mania**

Baseline SUD

- No pairwise comparisons were significant

<table>
<thead>
<tr>
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<th>Follow-up</th>
<th>Non- BPD ADHD</th>
<th>Normal Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPD + ADHD</td>
<td>1%</td>
<td>2%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>BPD + ADHD</td>
<td>2%</td>
<td>3%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Non- BPD ADHD</td>
<td>1%</td>
<td>2%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Normal Control</td>
<td>0%</td>
<td>0%</td>
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</tbody>
</table>

**Towards Defining A Dysphoric Subtype of CD**

Diagnostic Overlap Between CD and BPD

- N=116
- N=110
- N=6

**Kaplan-Meir Survival Estimates in Relatives>14 Yrs, Stratified by Diagnosis**

**Alcohol Dependence**

- Test statistics, p values
  - CD: Z = 2.3, p = .023
  - BPD: Z = 2.4, p = .016
  - Interaction: Z = -0.2, p = .838

**Drug Dependence**

- Test statistics, p values
  - CD: Z = 1.4, p = .176
  - BPD: Z = 3.6, p<.001
  - Interaction: Z = 0.5, p = .600

**Kaplan-Meir Survival Estimates in Relatives>14 Yrs, Stratified by Diagnosis**
ADHD and SUDs in Adults

ADHD and Smoking in Adults

SUD in ADHD Adults:
Age at Onset and offset of SUD

SUD in ADHD Adults:
Subtypes of SUD

SUD in ADHD Adults:
Type of Drugs used in Subjects with Drug A/D
Is ADHD Pharmacotherapy a Risk Factor for Subsequent SUDs?

**Myth** - Stimulant Medication Causes Substance Abuse
**Is ADHD Pharmacotherapy a Risk Factor For Subsequent Substance Abuse?**

**Conclusions**

- The bulk of studies indicate that in ADHD youth treated with medication (typically stimulants), there is a reduction in the risk of substance abuse.
- These data are particularly robust when treated and untreated groups are matched at baseline for severity of illness.
- These data are among the strongest within Child Psychiatry indicating the preventive influence of treatment on the development of substance abuse.

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**Myth - Stimulant Medication Causes Substance Abuse**

- **Fact** – Stimulant treatment lowers the risk of ADHD patients abusing alcohol and drugs

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**ADHD + SUDs:**

- ADHD is a risk factor for cigarette smoking and SUDs
- Comorbidity increases smoking and SUDs risks
- Pharmacotherapy for ADHD reduces the risk of SUD in ADHD youth (association less clear with smoking)
- ADHD and comorbid disorders onset in childhood whereas smoking and SUDs onset in adolescence:
  - Opportunity for prevention and early intervention strategies