MATERNAL SUBSTANCE ABUSE, CHILD DEVELOPMENT AND DRUG ENDANGERED CHILDREN

Claire D. Coles, Ph.D.

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Dr. Coles’ Affiliations

- Fetal Alcohol Center, at the Marcus Center of Children’s Health Care of Atlanta

- Departments of Psychiatry and Behavioral Sciences and Pediatrics, Emory University School of Medicine
MANY, DIFFERENT, DEVELOPMENTAL AND BEHAVIOR PROBLEMS ARE NOTED IN CHILDREN AND ADOLESCENTS WHOSE PARENTS ABUSE DRUGS AND ALCOHOL
Why are we concerned about the effects of substance use on neurodevelopment?

- Prevalence of Substance Use by Pregnant Women
- Teratogenic effects of exposure
- Relationship between Substance Use and Postnatal Environmental problems
- Behavior and Developmental Problems noted in Children of Substance Abusers
Alcohol and Drugs in PREGNANCY: Mother
Why the Concern for Prenatal Drug Exposure?

- 1 - 5% in U.S. have tried cocaine
- 10% of U.S. are alcoholics
- 20% of women smoke in pregnancy
- 40% of women report some alcohol use during pregnancy
- 60 - 80% of DFCS referrals in GA involve substance abuse; 78% nationwide
- Estimates range from 0.6 to 31% prenatally exposed children
Why the Concern for Prenatal Drug Exposure, continued

- Exposure higher in some SES groups already at risk
- Public belief that cocaine, methamphetamine and other drug exposure causes birth defects and developmental problems
Reality?

- The majority of women who use alcohol/drugs in pregnancy, use more than one drug.
- Cigarettes and alcohol the most common.
- Next are marijuana and prescription drugs.
- Cocaine, maybe Methamphetamines, are next.
- Finally Opiates, like Heroin.
- Genetic loading? Antisocial personality?
- And then there is the postnatal environment!
Lifetime Prevalence (%) of Substance Use Reported by Young Women (18-25)

SAMHSA, National Survey on Drug Use and Health, 2002
Drug Use During Pregnancy

Percent of Women Using Drugs During Pregnancy by Racial and Ethnic Groups, 1992

- Cigarettes
- Alcohol
- Cocaine
- Marijuana
- Any illicit drug

Legend:
- Hispanic
- Whites
- Afr-Amer

Notes:
- NIDA
- J/F 1995
FACTORS INFLUENCING DRUG USE

A. **EXTERNAL**
   - Isolation
   - Poverty
   - Violent Crime
   - Drug Related Lifestyle
   - Unstable Family / Social Environment
   - Inadequate Social Services
   - Solitary Caregiver or Provider

B. **INTERNAL**
   - Poor Coping Skills
   - Depression
   - Boredom
   - Anger
ENVIRONMENTAL FACTORS: Social Problems Associated With Substance Abuse

- Poverty
- Violent crime
- Parent’s drug-related life style
- Parent’s poor physical and mental health
- Disorganized / dysfunctional families
- Lack of stable social environment
- Inadequate medical services
- Inadequate social services
MEDICAL PROBLEMS COMMONLY ASSOCIATED WITH ALCOHOLISM

Liver:
- Alcoholic steatosis (fatty liver)
- Alcoholic hepatitis and fibrosis
- Cirrhosis

Cardiovascular Injury
- Alcoholic cardiomyopathy
- Hypertension
- Hemorrhagic strokes
MEDICAL PROBLEMS COMMONLY ASSOCIATED WITH ALCOHOLISM

Neurological disorders:
  Wernicke - Korsakoff syndrome
  Alcoholic dementia
  Organic mental disorder

Pancreatitis

Immune system impairment:
  Cancers of mouth and upper respiratory tract
  Liver cancer

PSYCHIATRIC CONDITIONS OFTEN CO-MORBID WITH ALCOHOL / DRUG ABUSE

Personality Disorders:
- Antisocial Personality Disorder
- Borderline Personality Disorder

Psychotic Conditions

Anxiety Disorders

Conduct Disorder

Posttraumatic Stress Disorder

Sexual Dysfunction
Figure 1: Survival Curve for Drinkers and Nondrinkers

41 (7%) of the 583 women were deceased, 6 controls and 35 alcohol users, with alcohol users significantly more likely to die, $X^2(1) = 7.59$, $p<.006$. 

% Alcohol
Control

Years between Childbirth and Mother's Death
ALCOHOLISM IN WOMEN VS. MEN
Difference in Signs Associated with Alcohol Abuse

- Fewer reports of academic / work difficulties
- Less antisocial behavior
- Fewer legal problems
- Fewer DUI’s, auto accidents
- More physical problems
- Spouse/partner leaves more often
- More suicide attempts
- More depression
- More neurological damage

Roman, 1988; Tamerin et al., 1986
ALCOHOLISM IN WOMEN
Effects on Reproductive Function

- Amenorrhea or severe oligomenorrhea
- Dysmenorrhea
- Anovulation/luteal phase dysfunction
- Increased premenstrual discomfort
- Spontaneous abortion
- Increased gynecological problems
- Fetal alcohol effects
- Sexual disorder

Mello, 1986
Obstetrical Complications for Which Drug Abusing Women Are at Increased Risk

- Impaired Fertility
- Spontaneous Abortion
- Poor Maternal Weight Gain
- Intrauterine Growth Retardation (IURG)
- Intrauterine Death
- Placental Insufficiency
- Retroplacental Hemorrhage
- Abruptio Placenta
- Septic Thrombophlebitis
- Uterine Irritability
- Preterm Labor & Delivery
- Premature Rupture of Membranes (PROM)
- Amnionitis
- Precipitous Labor
- Emergency Caesarian Section
- Increased Anesthesia Administration
- Forceps Delivery
- Fetal Distress
- Postpartum Hemorrhage
- Maternal Mortality
**BARRIERS TO TREATMENT**

- **Economic Barriers**
  - lack of health insurance
  - lack of transportation
  - lack of caretakers for children

- **Limited Availability of Treatment Services**
  - lack of women-oriented treatment models

- **Individual Barriers**
  - Maternal psychopathology
  - Family dysfunction
IDENTIFYING WOMEN AT RISK

Self Report Measures

- Quantity / frequency indices
- Forced choice ordinal scales
- Time sampling
- Diary
- Open-ended response format
How do we measure Drug Use?

  - Did you drink/use drugs in pregnancy?
  - How often did you use “crack”?
  - How many cigarettes do you smoke a day?
  - How many joints do you smoke?
  - How many drinks do you have on each occasion when you drink?
How did we measure Drug Use?

- Urine (EMIT) Screens
  - During prenatal care
  - At delivery
  - Postpartum
  - Infants in the nursery
Alcohol and Drugs in PREGNANCY: Child
POSSIBLE MECHANISMS OF DRUGS/ALCOHOL IN PREGNANCY:
Teratogenic (Single Factor) Model

Coles, 1995,
SOME POSSIBLE MECHANISMS OF EFFECTS OF DRUGS/ALCOHOL IN PREGNANCY:
Toxic (interactive) Model

OUTCOMES
- Reduced fertility
- Fetal wastage
- Preterm birth
- Birth defects
- Growth retardation
- Behavior effects

SECONDARY OUTCOMES
- Medical & behavioral problems
- SIDS

Coles, 1995
MULTI-FACTOR MODEL

Prenatal Environment
Social Factors
Legal Issues
Prenatal Care
Substance Use & Abuse
Maternal Characteristics
Genetics

OUTCOMES
• Reduced fertility
• Fetal wastage
• Preterm birth
• Birth defects
• Growth Retardation

SECONDARY OUTCOMES
• Developmental & Medical Effects
• SIDS

POSTNATAL ENVIRONMENT
Maternal Status/ Legal issues/ Social Factors/ Nutrition/ Substance Use Abuse/ Education / Social Services/et cetera

Coles, 1995
MODEL OF ENVIRONMENTAL INFLUENCE

Greater Society

Family

Social Supports

Child
TYPE OF DRUG EXPOSURE: Critical Periods of Development

Embryonic period (in weeks):
- 3
- 4
- 5
- 6
- 7

Fetal period (in weeks):
- 8
- 9
- 16
- 20-36
- 38
- 40

Major morphological abnormalities
- Central Nervous System
- Heart
- Eyes
- Limbs
- Digestive System
- Palate
- Ears
- External Genitalia
- Development and Descent of Thyroid

Physiological defects and minor morphological abnormalities

Adapted from The Developing Human by K. L. Moore, 1993
PERINATAL COMPLICATIONS
SEEN IN DRUG EXPOSED NEONATES

- Preterm birth, with associated problems
  - Respiratory distress
  - Intraventricular hemorrhage (IVH)
  - Necrotizing endocolitis (NEC)
- Asphyxia Neonatorum
- Meconium staining
- Meconium aspiration
PERINATAL COMPLICATION SEEN IN DRUG EXPOSED NEONATES

- Pneumonia
- Hypoglycemia
- Hypocalcemia
- Tachypnea
- Apnea
- Respiratory alkalosis
- Hyperbilirubinemia
- Respiratory distress syndrome (RDS)
ENVIRONMENTAL FACTORS: Effects of Substance Abuse on Caretaking / SES

- Death of parent
- Loss of custody
- Depressed mother
- Neglect / Abandonment
- Abuse
- Inconsistent parenting
- Failure of attachment
- Failure to use social / medical services
AGENCIES INVOLVED WITH EXPOSED CHILDREN

PRENATAL
- WIC
- Health Centers
- Prenatal Clinics
- Physicians/Midwives
- A&D Programs

INFANCY/PRESCHOOL
- WIC
- Hospitals
- Health Centers/Well Baby Clinics
- High Risk Nurses
- Courts
- Social Services Agencies
- Child Protective Services
- County Welfare Agencies

SCHOOL AGE
- Courts
- Schools
- Special Education Programs
- Hospital & Health Centers
- County Welfare Agencies

Educational Programs
- Treatment Programs
- Parenting Programs
Alcohol and Drug Affected children may have problems in the following areas:

- Physical/Health/Motor
- Developmental/Cognitive
- Behavioral/Social
- Academic/Vocational
What are the effects of various drugs?

- **Alcohol**
  - Global cognitive deficits
  - Specific neurodevelopmental impact
  - Academic deficits

- **Cocaine**
  - Arousal regulation
  - Emotional development
  - Executive Functioning

- **Smoking/Nicotine**
  - Auditory perception
  - Language development
  - Conduct Disorders
Alcohol
Prenatal Alcohol Exposure

- Fetal Alcohol Syndrome (FAS)
- Fetal Alcohol Spectrum Disorders (FASD)
THE TIP OF THE ICEBERG
FETAL ALCOHOL Spectrum Disorders

- FAS: 1 per 1000
- Partial FAS: 5 per 1000
- Alcohol-related Birth Defects: 1 per 100
- Alcohol-related Neurobehavorial Effects

73,000 Alcohol-Affected Georgia Citizens, 0 to 21 years
How is FAS Diagnosed?

- Prenatal Alcohol Exposure
- Face
- Growth
- Brain
Facial Features

- Microcephaly
- Short palpebral fissure
- Thin upper vermilion
- Absent philtrum
- Hypoplastic midface
- Low nasal bridge
Effect of Alcohol Exposure on Birth Weight (N = 368)
(Neuro) Behavioral Outcomes Examined in FASD

- General Cognitive/Learning Skills (IQ)
- Executive Functioning Skills
  - Attentional regulation
  - Memory, Planning and organization
- Motor skills
- Visual/spatial skills
- Academic Achievement
- Adaptive Behavior
- Social Behavior
- Mental Health/Behavioral Disorders
FAS Neurocognitive Deficits

FAS is associated with a clinically significant level of general intellectual impairment.

- IQ range: 40-110; X=70’s across many studies of children with FAS
- Deficits related to neurological damage
- Additional clear, but unacknowledged, environmental component to functional deficits
Effects on Educational Functioning

- Global functioning - global limitations on learning abilities
- Arousal regulation/Attention
- Executive Functioning Skills - metacognition
- Visual/Spatial Skills
- Memory (or metamemory and strategy use)
- Speed of processing
- Specific deficits in math
- Depression
Is there a “Pattern” of Learning and Behavior that affects Education?

- Although hard to find against this complicated background, patterns are emerging.
- Cognitive: Both Global and Specific deficits
- Behavior: “Arousal Dysregulation”.
- Early deficits in motor and visual/motor
- Commonly find secondary disabilities in achievement, behavior.
Clinical Presentations 0 to 5 years

- Significantly **Developmental Delayed** with complex medical histories. Asthma.
- Behavioral disturbances with **mild delays** and significant histories of abuse/neglect.
- **Arousal dysregulation** beginning with sleep problems progressing to behavior problems.
- Need for **PT, OT, Speech** and social work services. More motor than other areas.
Clinical Presentations: School Age

- **Mild Intellectual Disabilities** (IQ=50 to 69) with significant physical findings. Occasionally lower.
- **Borderline IQs** with history of foster care and specific learning deficits. Frequent **behavior problems**.
- International adoption with **emotional** (attachment) problems and **specific language disabilities**. IQ varies.
- **Nonverbal learning disabilities**. V/P split with significantly higher language than performance scores.
ADHD and FASD

- Many (many) children with FASD are diagnosed with ADHD.
- Questionable diagnosis due to history of exposure, arousal dysregulation, parenting problems, custody issues.
- In clinical observation, medications do not seem to improve outcomes. Little systematic research on this.
Effects of Disadvantage on Development in Alcohol and Control Samples*

![Graph showing the effects of disadvantage on development in alcohol and control samples. The graph compares norms, SES controls, and alcohol groups across various age points from 6 months to 15 years.](image-url)

*Various N’s*
However, it is also widely reported that prenatal alcohol exposure is associated with later criminal behavior. But most studies didn’t controlled for environmental factors.

Predicting Adolescent Delinquency (N=250)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Std Beta</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life Stress</td>
<td>.363</td>
<td>6.6</td>
<td>.000</td>
</tr>
<tr>
<td>Child Drug Use</td>
<td>.265</td>
<td>4.4</td>
<td>.000</td>
</tr>
<tr>
<td>Parenting: Supervision</td>
<td>-.222</td>
<td>-3.7</td>
<td>.000</td>
</tr>
<tr>
<td>Prenatal Exposure</td>
<td>.01</td>
<td>.16</td>
<td>.96,ns</td>
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Specific Deficits:

- e.g., Math Disabilities
  - Math skills more impaired than language
  - Probably related to visual/spatial deficits
  - Probably related to executive functioning problems
  - Can be observed in preschool period and persists through adulthood
Cortical regions exhibiting PAE effects

<table>
<thead>
<tr>
<th>A. General PAE Group Effect</th>
<th>B. Specific PAE Group Effect</th>
<th>C. Control vs. Non-Dysmorphic</th>
<th>D. Group By Gender Interaction</th>
</tr>
</thead>
</table>

- SFr: Superiorfrontal
- RMF: Rostralmiddlefrontal
- CMF: Caudalmiddlefrontal
- PTr: Parstriangularis
- POR: Parsorbitalis
- LOF: Lateralorbitofrontal
- PrC: Precentral
- PoC: Postcentral
- SuM: Supramarginal
- SPA: Superiorparietal
- STE: Superiortemporal
- ITE: Inferiortemporal
- LOC: Lateraloccipital
- CAC: Caudalanteriorcingulate
- PCu: Precuneus
- Cun: Cuneus
- PCA: Pericalcarine
- Lin: Lingual
- Fus: Fusiform
- PHI: Parahippocampal
- RAC: Rostralanteriorcingulate
- IPA: Inferiorparietal
- POP: Parsopercularis.

Sub-cortical regions exhibiting PAE effects

Why study corpus callosum (CC)?

- Agenesis of CC found at higher rate in FAS patients
- Previous studies have identified CC abnormalities (e.g., Riley et al., 1995, Johnson et al., 1996, Swayze et al, 1997, Sowell et al, 2001, Bookstein et al. 2001)
- Large, white matter tract often associated with efficiency of information processing
Segmentation of the corpus callosum (A), in which some portions (1, 4 and 5) exhibited the general PAE effect (B). 1: Anterior, 2: Mid-Anterior, 3: Central, 4: Mid-Posterior, 5: Posterior.

Interhemispheric Transfer of Information

- **Authors:**
  - P. Santhanam¹, X. Hu¹, S.J. Peltier¹, Z. Li¹, C.D. Coles², M.E. Lynch²

- **Experimental Design:**
  - 7 dysmorphic PAE, 7 non-dysmorphic PAE, 7 Controls: 20-24 yrs old from longitudinal cohort
  - PAE: identified by reported alcohol consumption by mother during pregnancy
Results: ‘Same’ Condition

Left hand response to Same side stimulation (LS)

Right hand response to Same side stimulation (RS)

No significant difference seen between groups in the ‘same’ condition
Results: ‘Opposite’

<table>
<thead>
<tr>
<th>Left hand response to Opposite side stimulation (LO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
</tr>
<tr>
<td>Non-Dys PAE</td>
</tr>
<tr>
<td>Dys PAE</td>
</tr>
</tbody>
</table>

Significant difference between Dys-PAE and Control groups in primary motor (arrows) and premotor areas

<table>
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<tr>
<th>Right hand response to Opposite side stimulation (RO)</th>
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</thead>
<tbody>
<tr>
<td>Controls</td>
</tr>
<tr>
<td>Non-Dys PAE</td>
</tr>
<tr>
<td>Dys PAE</td>
</tr>
</tbody>
</table>

Significant difference between Dys-PAE and Control groups in premotor area
Using TBSS for DTI analysis, voxel-wise statistics on the skeletonized FA data reveal subregions of the **cingulum** with significantly lower FA values in both PAE groups versus control subjects.

Skeletonized FA difference between Control and Non-Dysmorphic PAE groups (green=skeleton, purple=anatomically defined ROI, pink=region of significant difference). Similar differences were seen between control and dysmorphic PAE groups. Santhanam, et al, 2009, in preparation.
Caudate
Pallidum
Putamen
Amygdala
Hippocampus
Trial by Group

$F(4,553)=2.3$, $p<.006$

Con vs Dys, $p<.03$

vs EtOH, $<.08$
Verbal Selective Reminding - Total Recall (N=82)

Trial by Group

F(4,539)=1.65, p=.06

Con vs Dys, p<.01

vs EtOH, NS
Mediation Model

- **Assumptions:**
  1. Memory function is affected by prenatal alcohol exposure
  2. Memory deficits are the result of alterations in brain associated with prenatal alcohol exposure
  3. Regions of brain showing volumetric reductions in alcohol affected individuals will be found to mediate memory performance.
Alternate Hypotheses

- **Direct effect**
  - IV must be related to DV; IV must be related to Mediator; Mediator must be related to DV.

- **Mediated effect**
  - If mediated, adding Mediator to equation must significantly reduced IV-DV correlation.
Hippocampus Mediates effects of Alcohol Exposure

Hippocampal Volume

Dysmorphia Score

Spatial Learning Slope

\[ b = -56.6, \text{SEb} = .14.62, \beta = .38, p < .000 \]

\[ b = -.03, \text{SE}_{b} = .02, \beta = -.18, p < .10, \text{ns} \]

\[ b = .000, \text{SE}_{b} = .00, \beta = .26, p < .017 \]
Overall Conclusions: Alcohol

- Evidence for persistent, global deficits even when SES and post natal environment accounted for.
- In addition to global deficits, there may be specific cognitive problems in the following areas: Motor functioning, visual spatial skills, math, memory.
- MRI (and fMRI) suggest neurological basis for behavioral findings.
Cocaine
Weight over first 8 years

- Cocaine
- Control
- EBD

Child’s Age:
- Birth
- 1 year
- 2 years
- 8 years
Mental Development Standard Scores and Cocaine Exposure

![Bar chart showing BSID MDI and DAS scores over time for different groups: Cocaine, Control, and EBD. The chart uses standard score categories from 0 to 120.]
CBCL Summary T-Scores at 8 Years

* p < .000
Slope of Skin Conductance Level During Stressors

Conclusions

- The BD group demonstrated elevated heart rate across all conditions but no differences in change in HR as a function of stress
- The BD group demonstrated a pattern of “hypo-responsiveness to stressors”
- The cocaine group demonstrated a pattern of “hyper-responsiveness to stressors”
Linda Mayes’ Neurochemical Regulatory Switch Hypothesis

- Cocaine alters reuptake of monoamines (Norepinephrine, dopamine, & serotonin)
- Neural regions involved in gating regulation of arousal by mesolimbic systems and prefrontal cortex involving executive mediation of arousal disrupted to that set point of the neurochemical regulatory switch is altered making cocaine-exposed children vulnerable to hyperarousal responses
Bilateral Amygdala area (brain images) comparing activation between Cocaine exposed and Controls (bar graphs). Activation level is the produce of mean regression coefficient (representing the fMRI signal amplitude) and number of activated voxels in the ROI (representing the activation volume). With “NEU0” value as the baseline (zero). The error bars represent standard error.

Cocaine exposed adolescents do not show the usual balance between cognitive and emotional arousal.

Left dorsal lateral prefrontal area (brain images) and the activation amount comparison between groups (bar graphs). As in the previous slide, there is an interaction between Condition (Neuo.Neg) and Exposure Group.
Cocaine does not have the same teratogenic effect as alcohol

- No effects on growth
- No effects on cognition
- What about behavior?
- It may affect psychophysiology (that is, arousal and attention).
- Psychophysiology may interaction with environmental factors to produce developmental psychopathology.
MATERNAL SMOKING: DEVELOPMENTAL CONSEQUENCES

- Behavior Disturbances
- Language Development
- Medical Consequences
Medical Consequences

- Lower Birthweight
  - SGA
  - Increased weight as older children and adults
- Sudden Infant Death Syndrome (SIDS)
- Respiratory problems in infancy
- Asthma or aggravation of asthma symptoms
- Otitis Media
Studies of Behavior Problems Following Maternal Tobacco Use During Gestation

- Reports of ADHD
- Criminal Behavior in Young Adults (Brennan, Grekin, & Mednick, 1999, Maternal smoking during pregnancy and adult male criminal outcomes. Arch Gen Psychia 56, 215.)
Auditory Processing and Language Development

Previous Links Between Maternal Smoking and Language Development

- Early teratology studies found deficits in auditory habituation items of the Brazelton
- Fried found deficits in language development among toddlers and preschoolers
- Deficits in phonemic and phonetic processing in Middle Childhood
- Fried: Suggested that prenatal tobacco smoke caused an auditory processing deficits
Emory Language Development Study

Proposed looking at auditory processing skills and language development in children of smokers between 6-months and 2-years Using:

- **Bayley Scales of Infant Development, 2\textsuperscript{nd}, 3\textsuperscript{rd} Ed**
- **Sequence Inventory of Communication Development (SCID)**
- **Natural Language Protocol for assessing phonetic expression (tapes to Georgia State) (15 \& 24 mos)**
- **Parent report of language development (MacArthur CDI)**
- **ABERs and Information Processing Paradigm**
Early Language: % showing language delays on BSID Language Facet

* Linear trend, $p<.05$
CID/Words and Gestures: Number of Words Said and Understood

* Linear trend, p<.006
Effects of Multiple Risk Factors

- Poverty
- Disability
- Prenatal exposure
- Behavior Disorder
- Family Dysfunction
- Poor Schools
- Inadequate Medical Care
- Other drug Use
- Genetics
- Bias
Conclusions

- Parental Substance Abuse, perhaps, particularly abuse by mothers, affects child development.
- Effects are seen across a broad range, including motor, cognitive, behavioral, social and academic functioning.
- It is clear that there are teratogenic effects (direct effects of the substances); however, many problems are the results of environmental and social factors, as well.
- Prevention and treatment are both necessary.