Long Term Impact of Maternal Substance Abuse on Babies

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No Disclosures

Common Drugs of Abuse

- Tobacco/Nicotine
- Cannabis
- Alcohol
- Opiates
- Cocaine
- Methamphetamine

22 weeks gestation

32 weeks gestation

36 weeks gestation

adult

Dependence, Withdrawal, Tolerance and Addiction

- **Dependence** occurs as a result of physiological adaptations to chronic exposure to a drug. It is often a part of addiction, but they are not equivalent.
- Those who are dependent on a medication will experience **withdrawal** (unpleasant physical symptoms) when they abruptly reduce or stop use of the drug.

Dependence, Withdrawal, Tolerance and Addiction

- **Withdrawal** symptoms can be mild to severe (depending on the drug) and can usually be managed medically or avoided by slowly tapering down the drug dosage

Dependence, Withdrawal, Tolerance and Addiction

- **Tolerance**, or the need to take higher doses of a medication to get the same effect, often accompanies dependence.
- **Addiction** involves other changes to brain circuitry and is distinguished by compulsive drug seeking and use despite negative consequences.

Teratogen

An agent or factor that causes malformations of an embryo.

Plasticity

"Brain plasticity refers to the ability of the brain to persistently change its structure and function according to genetic code in response to environmental changes."

Maquet, Smith, Stickgold

Plasticity

- The brain is shaped by the environment is experiences
- Gene expression is influenced by the environment

Long Term Impact of Maternal Substance Abuse on Babies

- In utero effects on fetal development
- Environmental effects on infant-childhood development
  - Family structure
  - Socio-economic status

In Utero

- Maternal health: comorbidities, mental health, complications of pregnancy
- Hostile in utero environment
- Toxic metabolites impact brain development
- Altered gene expression in the brain

Home Environment

- Life style: chaos, support, isolation, poverty
- IQ/verbal abilities
- Psychopathology
- Will the environment exacerbate or mitigate the behavioral disorders that arise from the in-utero CNS injury?

Tobacco/Nicotine
Cannabis
Alcohol
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Cocaine
Methamphetamine

Tobacco

- Nicotine (1 of 4000+ compounds cigarette smoke)
- Nicotine levels: fetal compartments > maternal serum
- Preterm birth
- Low birth weight
- Abruption
- Increase risk of SIDS x5

Tobacco

- Deficits in self-regulation (soothe/calm self)
- Lower IQ
- MRI: reduced cortical gray matter/parenchyma vol
- ADHD
- Conduct disorders
- Depression/anxiety (childhood - adolescence: substance abuse)
- Aggression
- Impulsivity

Tobacco

- Gene expression
  - Smoking exposure during the prenatal period was directly associated with differential expression of 14 genes; in contrast, during adulthood, despite a much larger sample size, only two genes showed significant differential expression.

Tobacco

- Gene expression Semick et al, *Molecular Psychiatry 2018*
  - 1,315 genes showed significantly different exposure effects between maternal smoking during pregnancy and direct exposure in adulthood
  - these differences were largely driven by prenatal differences that were enriched for pathways previously implicated in addiction and synaptic function.

Tobacco

- US 2017
- 4,000,000 births
- 1 in 14 women smoked during pregnancy (7%)
- 280,000 newborns exposed

Cannabis

- Mild withdrawal symptoms
- Delayed state regulation
- Reading, spelling difficulty
- Executive function impairment: problem solving, memory planning impulsivity, attention

Cannabis

- Increased depressive symptoms
- Increase risk of tobacco/cannabis use
- fMRI altered neural functioning

Alcohol

- Teratogen with irreversible CNS effects
- Fetal elimination rate 3-4% of maternal rate
- Toxic metabolite acetaldehyde product of maternal and fetal metabolism
- Heterogeneity in symptom severity and presentation

Alcohol

- Fetal Alcohol Syndrome (FAS) 15/1000 in USA (2017)
- Low IQ
- Impaired executive function
- Memory process and attention
- ADHD: hyperactivity and impulsivity
- Speech/language difficulties

Alcohol

- Secondary conditions
  - Mental health disorders: conduct disorder, depressive disorder, oppositional defiant disorder
  - Difficulties in school including withdrawal/suspension
  - Involvement with justice system, deviant sexual behavior, substance abuse
  - Employment challenges (rampant work place drug screens)

Alcohol

- Prenatal Alcohol Exposure and Childhood Behavior at Age 6 to 7 Years; I. Dose-Response Effect (Sood et al; Pediatrics 2001; August)
  - Maternal alcohol consumption even at low levels was adversely related to child behavior
  - A dose-response relationship was identified, effect observed at average levels even as low as 1 drink/week
  - Children with any exposure were 3.2 times as likely to have Delinquent behavior scores in the clinical range

Alcohol

- The Association Between Prenatal Alcohol Exposusre and Behavior at 22 Years of Age (Day et al; Alcohol Clin Exp Res 2013 Jul)
  - Prenatal alcohol exposure (PAE) effects are dose dependent and significant at each trimester
  - Binge drinking did not predict more problems then nonbinge drinking
  - PAE, even at low to moderate levels extends into young adult

Alcohol

- No gold standard for treatment of FASD

  Singal et al. BMJ Open: 2018;8:e013775
- Treatment pharmacologic and behavioral as dictated by symptoms

Opiates

- Increase stillbirths
- Risk of certain heart defects and spina bifida with 1st trimester exposure
- Prematurity
- Decreased Birth Weight, length, head circumference
- NAS
- SIDS
- Strabismus

Opiates

- Conflicting outcomes long term:
  - Delayed cognitive function at 3 years; Wilson et al., 1979
  - No cognitive delay 6-13 years; duCubas & Field, 1993
  - At 1 year infants prenatally exposed to opiates are at risk for mild psychomotor developmental impairment
    - » Eur J Pediatrics 1998 Bunikowski et at al
  - At 5.5 years infants of drug dependent mothers their care givers need extra support in order to improve early communication and cognitive development
    - » Acta Paediatric 1994, van Daar et al

Opiates

- Appears to be a pattern liking prenatal exposure to behavioral problems, including
  - Anxiety/Feelings of rejection
  - Aggression
  - ADHD disruptive/inattentive behavior

Opiates

- Most research based on heroine usage (usually intermittent/inconsistent) versus prescription opiate (more consistent)
- Limited outcomes research after treatment with methadone or buprenorphine
- Long term effects of opiate exposure in NICU?

Sympathomimetic

- CNS stimulants
- Vasoactive: vasoconstriction
- Elevate heart rate
- Decrease placental blood flow
- Abruption
- Preterm labor

Cocaine

- IUGR/SGA
- Microcephaly
- Symptoms present 48-72 hours
- Neonatal CNS: irritability, tremors, excess suck, episodes apnea or tachypnea
- Cerebral infarctions

Cocaine

- Early studies limited by confounding variables: such as psychosocial factors, prenatal exposure to other drugs, prematurity, IUGR
- Mythology of “Crack Baby”

Cocaine

- Childhood
  - Slower head & wt trajectories from 1-10 years
  - Lower nonverbal perceptual reasoning
  - Attention problems; poor school performance
  - Disruptive behaviors/rule breaking; lack of self-regulation
  - Structural changes of brain with MRI

Cocaine

- Singer et al (J Peds 2008)
  - "There were persistent teratologic effects of CE on specific cognitive functions…"
- Ackerman et al (Pediatrics 2010)
  - Environmental variables play a key role in moderating effects of PCE; with covariate control, PCE had a significant negative associations with sustained attention and behavioral self regulation

Cocaine

- Li K et al (Human Brain Mapping 2013)
  - "In vivo neuroimaging studies revealed that several brain networks are altered in prenatal cocaine exposure (PCE) affected adolescent brains."

Methamphetamine

- Infant, Developmental, Environmental and Lifestyle Study (IDEAL) 2014 Diaz et al
  - Large scale, well control study of prenatal methamphetamine
  - 412 mother-infant pairs (204 methamp exposed/208 unexposed
  - 151 children exposed/141 comparisons at 7.5 years
- After adjusting for covariates prenatal exposure was associated with increase cognitive problems

Methamphetamine

- Infant, Developmental, Environmental and Lifestyle Study (IDEAL) 2015 Smith et al
  - A neonatal abstinence syndrome was not observed
  - Somatic growth was significantly decreased
  - Increased emotional reactivity in young children

Methamphetamine

- Infant, Developmental, Environmental and Lifestyle Study (IDEAL) 2015 Smith et al
  - Heavy exposure was linked with poorer inhibitory control in children
  - **Responsive home environments lowered risk for behavior issues**

Methamphetamine

- Follow Up IDEAL 2016 Eze et al
  - At 7.5 years, prenatal methamphetamine exposure (PME) is associated with behavior problems; early adversity may be a strong determinant of behavioral outcomes
  - No difference in cognition at 5.5 years

Maternal Interventions

- Placement: Home vs Family vs Foster
- Intensive home-based services
- Mental health treatment
- Substance use treatment

Child Interventions

- Specific individual therapy
  - Speech/language
  - Occupational
  - Behavioral
- Early intervention/enrichment
- Ongoing cognitive & behavioral assessments

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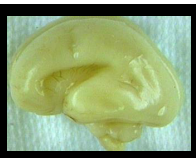

In nature there are neither punishments nor rewards -- there are consequences.

Ingersoll