Neurobehavioral Effects of Prenatal Alcohol Exposure: 
A Developmental Perspective

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Objectives
1. To review the effects of intrauterine alcohol exposure on the developing brain
2. To identify the neurobehavioral vulnerabilities of children with prenatal alcohol exposure at different developmental stages
3. To identify the factors in the caregiving environment that can optimize outcomes and promote resilience in children with FASD.

1. The Effect of Alcohol on the Developing Brain

Pathways to Developmental Risk
Biology or Environment?

Pathways to Developmental Risk
Or… Genes and Environment?


Adapted from Wachs, 1994

Education
Poverty/Mental Illness/Trauma
Maternal Depression
Violence
Intervention
Neonatal Risk (congenital)
Genotype
Maternal Biological Processes (pregnancy, nutrition)
Environmental Stresses
CNS Integrity
Individual Differences (temperament)
Environmental Supports
Infection
Intervention
Multifactorial Influences on Child Development

Brain Regions Affected by Prenatal Alcohol Exposure

Neural Pathways Affected in FASD

The Umbrella of FASD

Neurobehavioral Phenotype of FASD

Revised IOM Criteria (2005)

Evidence of a complex pattern of behavioral or cognitive abnormalities:

- Inconsistent with developmental level
- Cannot be explained by genetic predisposition, family background or environment alone
- Includes marked impairment in the performance of complex tasks in numerous cognitive and behavioral domains:
Neurobehavioral Deficits in FASD

- Complex problem solving
  - Planning
  - Judgment
  - Abstraction
  - Metacognition
  - Arithmetic tasks
- Higher level receptive and expressive language deficits
- Disordered behavior
  - Attention / impulsivity
  - Emotional lability / Self regulation
- Motor dysfunction
- Poor academic performance
- Deficient social interactions

Criteria: Neurobehavioral Deficits

- p-FAS or ARND
  - Neurocognitive Impairment (≥1)
    - Global intellectual impairment
    - Specific Impairment in Learning
    - Impairment in Executive Function
    - Measureable Impairment in Memory
    - Measureable impairment in Visual - Spatial skills
  - Self-Regulation (≥1)
    - Impaired mood / behavioral regulation
    - Attention deficit
    - Impulse Control
  - Adaptive Functioning (≥2)
    - Communication deficit
    - Social Impairment
    - Daily Living Skills Impairment
    - Motor Impairment

Neurobehavioral Deficits

Neurocognitive Impairment

- Global Intellectual Impairment
  - > 2 SD below the mean
  - IQ < 70 (Mental Retardation)
- Specific Impairment in Learning
  - Math/ computational skills
  - Uneven profile of cognitive skills
  - Poor academic achievement
  - Discrepancy between verbal and nonverbal skills
  - Slow information processing

Neurobehavioral Deficits

Self-Regulation / Adaptive Deficits

Self-Regulation Deficits
- Impaired mood / behavioral regulation
- Attention deficit / hyperactivity
- Impulse Control

Adaptive Function Deficits
- Communication deficits
  - Pragmatic difficulties
- Social Impairment
  - Problems in social perception
  - Poor capacity for abstraction
  - Deficits in Metacognition
- Daily Living Skills Impairment
  - Motor Impairment
    - Delayed motor milestones
    - Clumsiness
    - Poor dexterity
    - Balance problems

Neurodevelopmental Deficits of FASD:

Developmental Emergence: School Age Sx.

- Cognitive impairment / LD
- Motor Problems / Incoordination
- Social Skills Deficit
- Memory Deficits
- Executive Dysfunction
- Attention / Poor Impulse Control
- Behavior Problems
- Language Deficits

Alcohol Exposure

Experimental Criteria, CO-FASD
2. Neurobehavioral Vulnerabilities of FASD Throughout the Lifespan

Neurodevelopmental Deficits of FASD:
Developmental Emergence

- Generalized (nonspecific) brain deficits in infancy
- Increased specificity of developmental symptoms as development progresses

Brain Development: Infancy

Age-related Changes in Normal Brain Organization
- DTI images of white matter maturation over time (FA)
  - Higher values greater organization
- Subcortical structures myelinate before cortical regions
- Sensory pathways myelinate first, then motor pathways; higher cortical functions myelinate last
- Maturation of limbic system

Neurobehavioral Deficits: Infancy

- Poor feeders: poor sucking skills, distracted / fatigued while sucking
- Tremulousness / Increased jitteriness
- Weak reflexes: persistent startle
- Poorer habituation/ disordered state regulation
  - Lower levels of arousal
  - Poorer performance on operant learning paradigms
- Delayed motor development
- Delayed mental development
Neurobehavioral Deficits: *Infancy*

**Effect of Maternal EtOH Consumption on Infant Development (13 months)**
- Dose dependent response
- ↓ MDI with ↑ maternal alcohol consumption
- Significant impairment seen with >0.5 oz AA/ day (>6 drinks/ occasion)

\[ F (1, 369) = 5.81, p<0.025 \]


**Neurobehavioral Deficits: *Infancy***

**Deficits in Emotional Regulation / Infant Withdrawal**
- Prenatal EtOH exposure associated with increased infant emotional withdrawal
  - Decreased infant affective function
  - Increased emotional withdrawal associated with
    - Severity of diagnosis : FAS > p-FAS >ARND
    - Lower IQ at 9 years
    - Affective disturbance

*Molteno, Jacobson, et al. 2013*

**Infant Emotional Withdrawal**

**Deficits in Pain regulation**
- Differences in physiological measures of stress reactivity in EtOH exposed infants
  - ↓ HR response
  - No RSA variability
  - Decreased salivary cortisol response to heel stick
  - Blunted HPA activity

*Oberlander, Jacobson, et al. Alcoholism  Clinical & Experimental Research 2010*

**Brain Development: *Preschool***

**Normal Brain Development – Preschool**
- ↑ Cortical surface area
  - Expansion of prefrontal cortex, temporal association areas
- Varying changes in Cortical Volume
  - ↑ volume of dorsal motor and premotor frontal cortex
  - ↑ volume of temporal and frontal lobes


**Neurobehavioral Deficits: *Preschool***

**Neurobehavioral Effects of PAE**
- **Motor function**
  - Gross Motor: problems with balance / gait,
  - Fine motor: tremor, visuospatial deficits
- **Language**
  - Language processing deficits
  - Lower performance and verbal IQ compared to controls (but still within normal range)
  - Greater intellectual deficits in children with FAS
- **Hyperactivity /Attention**
  - Increased errors of commission/ omission
  - Increased impulsivity
- **Sensory / Sleep Deficits**

Neurobehavioral Deficits: *Preschool*

**Deficits in Motor Function**
- **Gross Motor Function**
  - Balance /coordination problems
  - "Clumsiness"
- **Fine Motor function**
  - Difficulty with writing/ drawing
  - Poor dexterity
  - Visuo-spatial deficits
  - Impaired visuo-motor integration


**Dose dependent effects on GM and FM development:** FAS> Exposed > Nonexposed


**Language Deficits**
- Delayed auditory processing
  - Central auditory delay
  - Deficits in word processing/ word recognition
  - Associated with difficulties with language acquisition
  - Not associated with severity of diagnosis (i.e. FAS/ p-FAS/ ARND)


**Speech and Language deficits**
- Deficits in naming / word recognition
- Receptive / expressive language delays
- Deficits in word comprehension
- Grammatical errors
- Articulation deficits
- Deficits in pragmatics/ semantics
  - Deficits in social cognition
  - Deficits in using language for social communication

Mattson, 2011; 2013

**Attention / Hyperactivity**
- Difficulty encoding information
- Difficulty with shifting attention
- Difficulty completing tasks
- Impairment in visual and auditory attention
- Difficulty with sustained attention

**Neurobehavioral Deficits: Preschool**

Sleep and Sensory Characteristics

- Sleep
  - Increased bedtime resistance
  - Shortened sleep duration
  - Increased sleep anxiety
  - Increased night awakenings
  - Parasomnias

- Sensory Processing
  - Significant difficulty modulating sensory input
  - Sensation seeking / active

**Brain Development: School Age**

Normal Brain Development: School Age

- Increased cerebral volume
  - Increased white matter volume: parietal/temporal regions
  - Increased development of corpus callosum, hippocampus
- Increased connections to PFC

**Brain Development: School Age**

Brain Development: PAE

- Decreased Intracranial volume
- Decreased Brain Plasticity
  - Less white matter volume increase
  - Greater volume decreases in Temporal lobe
- Parietal lobe abnormalities:
  - Decreased cortical volume
  - White matter abnormalities

**Neurobehavioral Deficits: School Age**

Deficits in Higher Order Cognitive Functions

- Intellectual Functioning
  - ↓ IQ
  - Learning disabilities
  - Math deficits (numerical operations/global mathematics skills)

- Executive Function
  - ↓ Working memory
  - ↓ Verbal Fluency
  - ↓ Planning / Sequencing / organization

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Mattson 2011, 2013
Coles, 2010
Neurobehavioral Deficits: School Age

Deficits in Language/ Learning / Memory
• Difficulty encoding/consolidating new information
• Deficits in higher order language processing
• Deficits in social cognition
  – Inappropriate social initiations/ social interactions
  – Inappropriate sexual behaviors


Deficits in Spatial Orientation / Visual Perception
• Deficits in spatial processing
• Difficulties with handwriting
• Poor visuo-motor integration


Brain Development: Adolescence

Brain Development: Adolescence
• Increased myelination of WM especially in prefrontal cortex
• Increased structural volume within basal ganglia:
  – Increased connections between prefrontal and subcortical regions (BG) are important for developing cognitive control.


Neurobehavioral Deficits: Adolescence

Deficits in Higher Order Learning / Executive Function/ Memory / Processing Speed
• Working Memory
• Attention Deficits
  – Deficits in sustained attention: Visual >Auditory
• Executive Function
• Information Processing
• Learning problems (mathematics)
• Judgment
• Metacognition

Neurobehavioral Deficits: Adolescence – Attention Deficits

• Adolescents with PAE have more attention deficits that non AE-controls, and meet criteria for ADHD
• ADHD profile for PAE differ from ADHD (non AE):
  • Inattention deficits similar to non-AE ADHD, but AE demonstrate less hyperactivity than non-AE ADHD
Neurodevelopmental Deficits of FASD: Developmental Emergence

• In the absence of microcephaly (FOC ≤10%), significant CNS impairment is often difficult to quantify in infancy
• ** Significant CNS deficits (delays >1-1.5 SD below the mean in multiple areas) are often not demonstrated in young children

Encourage close developmental surveillance and followup… developmental deficits emerge over the lifespan

Optimizing Outcomes in FASD: Promoting Resilience

3. Optimizing Outcomes in FASD: Promoting Resilience

Optimizing Outcomes in FASD

• Promoting Early Diagnosis
  – “The FAS diagnosis and the diagnostic process…are part of a continuum of care that identifies and facilitates appropriate health care, education, and community services.”

• Diagnosis is recommended prior to age 6 to help a child with FAS(D) reach his developmental potential

Fetal Alcohol Syndrome: guidelines for referral and diagnosis. (2005). Department of Health and Human Services, p. 22-23

Optimizing Outcomes in FASD

• Promoting Early Diagnosis
  – Targeting high risk populations:
    – The CHILD as the point of entry
      • Children of substance abusing mothers
      • Children in foster care
      • Children who are internationally adopted

The incidence of FAS is 10X higher for children in the foster care system

Optimizing Outcomes in FASD

• Promoting Prevention
  • The mother has information to prevent FAS in future births
  • The MOTHER as a point of entry:
    GOAL: Identify woman who are drinking during pregnancy, and provide them with intervention services
    • Children who are born to women who STOP drinking in their pregnancy have better outcomes than those who CONTINUE to drink in pregnancy
Optimizing Outcomes in FASD

- Promoting Intervention: Protective factors
  - Stable and nurturing caregiving environment during the school years
  - Absence of exposure to violence
  - Minimal number of placement / caregiver changes
  - Eligibility for social and educational services

Genotype
Biosocial Processes (nutrition)
Teratogens (EtOH, Drugs)
Molecular - Biological Processes (DNA - RNA Transcription)
CNS Integrity
Neonatal Risk (prematurity)
Environmental Stressors
Individual Differences (Temperament)
Maternal Depression
Violence Caregiving Inconsistency

How do caregiving relationships influence social-emotional development?

⇒ Lessons from attachment theory

What is Attachment?

- Described by John Bowlby in 1969
- A bond, tie or enduring relationship between a young child and his caregiver
- Occurs by 12 months of age to primary caregiver, regardless of quality of care
- Quality of the attachment relationship varies with the history of the infant’s caregiving experiences, and reflects the history of caregiving sensitivity (Brazel, 1980)
  - Secure vs. Insecure Attachment
Evolution of Attachment

- Infancy in mammals is characterized as a period of helplessness and vulnerability
- Infant is completely dependent on his caregiver for care and protection
- The attachment system evolved as a behavioral system to promote infant’s proximity to the caregiver

When Do We See Attachment Behaviors?

- Attachment system is activated when the infant is in a state of arousal (distress)
  - Absence/distance from caregiver
  - Caregiver departs
  - Unfamiliar situations
  - Illness
  - Hunger
  - Cold
  - Pain

Ainsworth, 1978

Attachment Behaviors Promote Proximity

- Attachment behaviors are the infant's way of signaling the caregiver (protector) to come closer to the infant
  - Looking
  - Vocalizing
  - Crying/ Calling
  - Following
  - Clinging

⇒ Proximity Seeking and Contact Maintenance Behaviors

Caregiver Responsiveness Influences Attachment Classification

Infant is distressed, signals caregiver
Caregiver responds inconsistently to signals
Infant learns that when he signals for his caregiver, his needs will be not be met, or will be met inconsistently

SECURE pattern of attachment results

Caregiver Responsiveness Influences Attachment Classification

Infant is distressed, signals caregiver
Caregiver responds consistently to signals
Infant learns that when he signals for his caregiver, his needs will be met

INSECURE pattern of attachment results

Secure Attachment
Attachment and R Brain Development

- The quality of early experience impacts maturation of the limbic system (Schore, 1994, 2001)
- Early adverse attachment experiences result in brain organizations that are ineffective in regulating emotion and coping with stress. (Crittenden, 1988; Schore, 1997)

Promoting Resilience

NATURE THROUGH NURTURE

The Neurobiology of Resilience: The Role of Caregiving

- Low licking mothers
  - Low licking offspring
  - High cortisol levels
  - Low anxiety
  - High licking grooming

- High licking mothers
  - High licking offspring
  - Low cortisol levels
  - High anxiety
  - Low licking grooming

The Neurobiology of Relationship Stress Reactivity of Children in Foster Care

- Salivary cortisol obtained from a sample of children in foster care and a comparison group
- Children in foster care demonstrated less decline in levels across the day compared with non-foster care group
  - Conditions associated with foster care interfere with children’s ability to regulate neuroendocrine functioning.
### The Neurobiology of Relationship
**Stress Reactivity of Children After Intervention**

- Relational intervention provided to children in foster care
- Cortisol reactivity was measured before and after stressor
- Cortisol reactivity in intervention group similar to non foster care group

→ Improved stress reactivity with relational intervention

### Promoting Resilience in Foster Care: Promoting Relationships

- Intervention designed to help children in foster care develop regulatory capacity
- Intervention helps caregivers:
  1. Provide an environment to help child develop increased regulatory capacity
  2. Reinterpret child’s alienating cues
  3. Provide consistent nurturing care

→ Improved stress reactivity with relational intervention

### Promoting Resilience
**Intervention Goals**

1. Provide an environment to help child develop increased regulatory capacity

2. Reinterpret child’s alienating cues

3. Provide consistent nurturing care

### (Almost) Everything I Need to Know About Being a Parent in 25 Words or less

**Always**: be BIGGER, STRONGER, WISER, and KIND.

- **Whenever possible**: follow your child’s need.
- **Whenever necessary**: take charge.

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### What we hope for in parent-child relationships

“This is my favorite place - inside your hug.”

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**Thank you!**

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