Neuropsychology of Fetal Alcohol Syndrome: Methods and Findings

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OBJECTIVES

• Identify neuropsychological (information processing deficits) associated with FASDs

• Become familiar with brain imaging findings in individuals with FASDs

• Identify disabilities that arise in the day to day functioning of individuals with FASDs

• Develop a sense of what’s available and how to approach interventions for individuals impacted by FASDs.
Transgenerational Findings
—recent animal model findings

• Impact on information processing neural networks in not only alcohol impacted children, but has currently been shown to last for three generations.

• Increased risk for alcoholism, also currently shown for three generations.
FASDs considered both a birth defect and a developmental disability

• Birth defect: a physical or biochemical abnormality that is present at birth and that may be inherited or the result of environmental influence.

• Developmental Disability: Significant long-term problems. They may be physical, such as blindness. They may affect mental ability, such as learning disorders. Or the problem can be both physical and mental. The problems are usually life-long, and can affect everyday living. Often there is no cure, but treatment can help the symptoms.

Neuropsychology of FASDs
Fetal Alcohol Spectrum Disorder

- Amount/dose
- Timing
- Prenatal environment (care, nutrition)
- Genetics
- Subsequent postnatal environment
Binge Exposure

- Binge-like alcohol exposure during the brain growth spurt may be as devastating as chronic exposure through pregnancy.

- Binge:
  - double the usual amount ingested
  - >3 ounces of absolute alcohol (≈ to 3 shots of 80-proof whiskey)
  - Current standard (CDC): four or more drinks at one time.
• 501 parent–children dyads in a Michigan-based university hospital.
• Children assessed at ages 6 to 7 years of age.
• Alcohol use during pregnancy:
  • 25 % denied
  • 64% Low levels of alcohol use
  • 13% Moderate/heavy use
• The table emphasizes the complexity of factors involved.

• Sood et al 2001
The effect was observed at average levels of exposure of as low as 1 drink per week.

Children with any prenatal alcohol exposure were 3.2 times as likely to have Delinquent behavior scores in the clinical range compared with non-exposed children.

Prenatal alcohol exposure remained a significant predictor of behavior after adjusting for covariates.

Sood et al, 2001

- Though not self-fulfilling. Substantial variability.
- Sood et al., 2001
### TABLE 7

Child Behavior Check List (CBCL/ 6-18) outcomes (see Figure 2) among the 516 patients administered a CBCL when they were between 6 and 18 years of age.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FASD Diagnostic Subgroups</th>
<th>Statistics ANOVA</th>
<th>Duncan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 154</td>
<td>N = 394</td>
<td>N = 722</td>
</tr>
<tr>
<td>Problems: T-score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internalizing</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>63.4(10.1)</td>
</tr>
<tr>
<td>Externalizing</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>69.1(9.9)</td>
</tr>
<tr>
<td>Total</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>71.4(8.9)</td>
</tr>
<tr>
<td>Syndrome Scales: T-score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious/Depressed</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>63.0(11.3)</td>
</tr>
<tr>
<td>Withdrawn/Depressed</td>
<td>N = 50</td>
<td>Mean (SD)</td>
<td>62.4(8.6)</td>
</tr>
<tr>
<td>Somatic Complaints</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>60.0(9.3)</td>
</tr>
<tr>
<td>Social Problems</td>
<td>N = 50</td>
<td>Mean (SD)</td>
<td>72.0(12.0)</td>
</tr>
<tr>
<td>Thought Problems</td>
<td>N = 50</td>
<td>Mean (SD)</td>
<td>70.7(10.7)</td>
</tr>
<tr>
<td>Attention Problems</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>75.5(11.9)</td>
</tr>
<tr>
<td>Rule-Breaking Behavior</td>
<td>N = 51</td>
<td>Mean (SD)</td>
<td>87.9(8.9)</td>
</tr>
<tr>
<td>Aggressive Behavior</td>
<td>N = 50</td>
<td>Mean (SD)</td>
<td>70.2(13.1)</td>
</tr>
</tbody>
</table>

Washington: Astley 2010
FIG. 2  Child Behavior Check List\textsuperscript{24} (CBCL/ 6-18) Syndrome Scales (see Table 7) among the 516 patients administered a CBCL when they were between 6 and 18 years of age. All abbreviations are defined in Table 7.

Washington: Astley 2010
TABLE 11  Mental health disorders reported in the medical records of the 1,064 patients 5 or more years of age at the time of the FASD diagnostic evaluation across the four study groups.

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 154</td>
<td>N = 394</td>
<td>N = 722</td>
<td>N = 130</td>
<td>N = 1400</td>
<td>Chi (p)</td>
</tr>
<tr>
<td>Mental Health Disorders: N (valid%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One or more disorders</td>
<td>73</td>
<td>71.6</td>
<td>180</td>
<td>84.1</td>
<td>293</td>
<td>74.0</td>
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<tr>
<td>ADD/ADHD</td>
<td>53</td>
<td>59.6</td>
<td>161</td>
<td>59.8</td>
<td>233</td>
<td>55.2</td>
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<tr>
<td>Adjustment Disorder</td>
<td>4</td>
<td>2.6</td>
<td>8</td>
<td>2.0</td>
<td>29</td>
<td>4.0</td>
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<tr>
<td>Antisocial Disorder</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Anxiety Disorder</td>
<td>2</td>
<td>1.3</td>
<td>10</td>
<td>2.5</td>
<td>8</td>
<td>1.1</td>
</tr>
<tr>
<td>Reactive Attachment Disorder</td>
<td>6</td>
<td>3.9</td>
<td>19</td>
<td>4.8</td>
<td>27</td>
<td>3.7</td>
</tr>
<tr>
<td>Bipolar/Manic Depression</td>
<td>4</td>
<td>2.6</td>
<td>10</td>
<td>2.5</td>
<td>13</td>
<td>1.8</td>
</tr>
<tr>
<td>Conduct Disorder</td>
<td>2</td>
<td>1.3</td>
<td>16</td>
<td>4.1</td>
<td>24</td>
<td>3.3</td>
</tr>
<tr>
<td>Depression</td>
<td>7</td>
<td>4.5</td>
<td>23</td>
<td>5.8</td>
<td>32</td>
<td>4.4</td>
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<tr>
<td>Dysthmic Disorder</td>
<td>3</td>
<td>1.9</td>
<td>7</td>
<td>1.8</td>
<td>23</td>
<td>3.2</td>
</tr>
<tr>
<td>Obsessive Compulsive Disorder</td>
<td>1</td>
<td>0.6</td>
<td>6</td>
<td>1.5</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Oppositional Defiant Disorder</td>
<td>8</td>
<td>5.2</td>
<td>39</td>
<td>9.9</td>
<td>72</td>
<td>10.0</td>
</tr>
<tr>
<td>Post Traumatic Stress Disorder</td>
<td>10</td>
<td>6.5</td>
<td>32</td>
<td>8.1</td>
<td>49</td>
<td>6.8</td>
</tr>
<tr>
<td>Suicidal</td>
<td>2</td>
<td>1.3</td>
<td>3</td>
<td>0.8</td>
<td>5</td>
<td>0.7</td>
</tr>
</tbody>
</table>


Neuropsychology of FASDs
Neurocognitive (The Holy Grail)

- Executive Function
  - Abstraction/judgment problems
  - Lack of control over emotions
  - Impulsivity
  - Inappropriate/immature social behaviors
  - Difficulty learning from consequences

- Attention (hallmark)
- Visual Spatial/Visual Motor
- Learning and Memory
- Motor
- Achievement (Arithmetic/Inability to manage money)
- Adaptive (Greater than expected day to day deficits given their IQ)
How Researchers Look at the Brain

**Neuropsychological Testing**
- Tests of information processing
- **Structural MRI findings**
  - smaller total brain volume
  - smaller volume of both the white and grey matter in specific cortical regions.
  - consistent findings of alterations in the shape and volume of the corpus callosum, as well as smaller volume in the basal ganglia and hippocampi.

**Functional MRI**
- reduced functional connectivity between cortical and deep grey matter structures.

**Proton magnetic resonance spectroscopy**
- altered neurometabolic profiles in the frontal and parietal cortex, thalamus and dentate nuclei.

**Diffusion tensor imaging**
- lower fractional anisotropy in the corpus callosum.

Donald et al., 2015
### Executive Function Deficits in FASDs and ADHD

**Kingdon et al, 2016**

#### FASD compared to no diagnosis

**Dysmorphic FASD**
- Large deficits in planning, fluency, set-shifting, and working memory
- Moderate deficits in vigilance and inhibition

**Non-dysmorphic FASD**
- Large deficits in planning, fluency and set shifting
- Moderate deficits in working memory
- Nonsignificant difference vigilance and inhibition

#### FASD compared to ADHD

- Moderate to small deficits in fluency, planning, and set-shifting
- Small deficits on working memory
- No differences were found on measures of attentional vigilance or response inhibition

- Great deal of neuropsychological variability within ADHD groups
- Fewer than half of children with ADHD exhibiting significant impairment on any specific executive function task
- FASD does not produce an identical cognitive profile to ADHD.
• Large IQ impairments in
  • FASD versus healthy controls – 20 IQ points
  • FASD versus children with ADHD – 16 IQ points
• Children with FASD evidenced greater executive functioning impairments than healthy controls and ADHD groups, even among studies where groups were matched on intellectual functioning

Also ....
Kingdon et al, 2016

• Full-scale intelligence scores for FASD groups included in the current meta-analysis ranged from 64 to 99, with an average of 84 for both dysmorphic and nondysmorphic groups.
Drawing (VMI) data

- Attention
- Vigilance
- Impulsivity
- Maturation
- Form
- Visual Motor
- Planning
- Organization

Uecker and Nadel, 1996
16 Object Spatial Localization/Distortion

Uecker and Nadel, 1996
Willoughby et al. (2008). Effects of prenatal alcohol exposure on hippocampal volume, verbal learning, and verbal and spatial recall in late childhood.
Verbal Learning and Memory

• The California Verbal Learning Test-Children’s Version

• Children with FASD
  • learn the CVLT-C word lists more slowly than non-exposed children
  • recall fewer words
  • are less accurate at discriminating between target and distractor words on recognition trials
  • use less semantic clustering

• Semantic Clustering reflects organization, specifically providing some insight on grouping, chunking, or categorizing abilities.
• Whole Brain
• Frontal Lobe
• Parietal region
• Corpus Callosum
• Cerebellum
• Basal Ganglia
• Hippocampus

Brain areas variable between individuals.

Figure from: http://people.uwec.edu/piercech/fas/fas...htm
Dramatic changes in intra-neocortical connections between the frontal, somatosensory and visual cortex in mice born to mothers who consumed ethanol during pregnancy. The changes were especially severe in the frontal cortex, which regulates motor skill learning, decision-making, planning, judgment, attention, risk-taking, executive function and sociality.

The alcohol-exposed children performed significantly worse than their peers in all academic areas, with particular weaknesses found in math performance.

Math reasoning < numerical operations < spelling and word reading.

Over half of the alcohol-exposed group (58.2%) demonstrated low achievement on 1 or more academic domains.

Brain imaging revealed several brain surface area clusters linked to math and spelling performance (parietal, occipital and temporal lobe areas).

44 boys, 23 girls eight to 16 years of age: 67 children with heavy prenatal alcohol exposure () and 61 children who were not prenatally exposed to alcohol (33 boys, 28 girls).


Adaptive Function

Primary Disabilities
(CNS mediated neurocognitive abilities and neuromaturation)

Secondary Disabilities
(AKA: Day to Day Life)
This model suggests individuals who are vulnerable (have PRIMARY DISABILITIES) and are exposed to stress, will develop problems (SECONDARY DISABILITIES).

PROTECTIVE FACTORS
- Stable, nurturant, good quality home during critical / important parts of life (experience-dependent/expectant) or majority of life
- Relationship / Bonding
- Remain safe from violence
- Apply for and have appropriate aide (social services)
- Early identification
Secondary Disabilities
Rate increases drastically in adolescence

• School disruption (61%)
• Trouble with the Law (60%)
• Confinement experience (50%)
• Inappropriate sexual behaviors (49%)
• Drug/alcohol problems (35%)
• Mental Health diagnoses affecting adaptive function (94%)
  • At least one mental health episode
• Dysfunctional family interactions

Streissguth et al. Longitudinal study at the University of Washington
- In Sweden, a national register–based study of 79 adults with an FAS diagnosis, at a mean age of 32.
  - Compared to 3160 comparison individuals matched on age, gender, and place of birth.
  - Outcomes for men and women were similar

<table>
<thead>
<tr>
<th></th>
<th>FAS</th>
<th>Non-FAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>State Care as children</td>
<td>81%</td>
<td>4%</td>
</tr>
<tr>
<td>Special Education</td>
<td>25%</td>
<td>2%</td>
</tr>
<tr>
<td>Unemployed</td>
<td>51%</td>
<td>15%</td>
</tr>
<tr>
<td>Disability Pension</td>
<td>31%</td>
<td>3%</td>
</tr>
<tr>
<td>Psychiatric Hospitalization:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---- Alcohol Abuse</td>
<td>9%</td>
<td>2%</td>
</tr>
<tr>
<td>---- Psychiatric Disorders</td>
<td>33%</td>
<td>5%</td>
</tr>
<tr>
<td>Prescribed Psychotropic Drugs</td>
<td>57%</td>
<td>27%</td>
</tr>
<tr>
<td>(Gender)</td>
<td>63% men</td>
<td>37% women</td>
</tr>
</tbody>
</table>
Won’t or Can’t?

• At the interpersonal level, people often misinterpret the primary disabilities of individuals with FASD as willful behavior (e.g., “won't” vs. “can't”).
  • May lead to inappropriate interventions or punishments
  • Result is that the individual with the FASD feels frustrated and discouraged
  • May use maladaptive behaviors to cope with the stress and frustration of not being understood or supported

• Importance of neuropsychology
  • Can frame and assist in understanding social, emotional and behavioral challenges from the information processing perspective
WHY?: Impact on the brain's reward circuitry

• After the prenatal brain is exposed to alcohol, the endocannibinoids have a different effect on certain dopamine neurons which are involved in addicted behaviors.

• The dopamine neurons in the brain become more sensitive to a drug of abuse's effect. So, later in life, a person needs much less drug use to become addicted.

• But not just addiction. Decision making in general.

• Ventral Tegmentum: Reward evaluation. The value of the immediate reward may be overrepresented. Implications for a number of behaviors.


Interventions

No FASD specific interventions, though we have a foot in the door.
Traditional interaction approaches used by parents, teachers and other adults might not be effective for children with an FASD.

Guiding principles include:

<table>
<thead>
<tr>
<th>Guiding Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentrate on the child's strengths and talents</td>
</tr>
<tr>
<td>Accept the child's limitations/Positive Parenting/Differential reinforcement of positive behavior</td>
</tr>
<tr>
<td>Be consistent with everything (discipline, school, behaviors)</td>
</tr>
<tr>
<td>Use concrete language and examples</td>
</tr>
<tr>
<td>Use stable routines that do not change daily</td>
</tr>
<tr>
<td>Keep it simple</td>
</tr>
<tr>
<td>Be specific—say exactly what one intends (and follow through)</td>
</tr>
<tr>
<td>Structure your child's world to provide a foundation for daily living</td>
</tr>
<tr>
<td>Use positive reinforcement often (praise, incentives)</td>
</tr>
<tr>
<td>Supervise: friends, visits, and routines</td>
</tr>
<tr>
<td>Repeat, repeat, repeat</td>
</tr>
</tbody>
</table>
### Summary of FASD Intervention Areas

- Social
- **Family/School Communication Strategies: Positive Behavioral Support**
- Math
- Executive Function
- Adaptive, Vocational and Life Skill
Bruin Buddies:

96 children 6 – 12 years completed the study.
Vineland Social Composite z < 1.0; verbal IQ > 70

• Parent assisted children’s friendship training
  • Target areas: understanding social cues, indiscriminant social behavior, communicating in social contexts
  • Skills taught: a) social network formation with the aid of b) informational interchange with peers leading to a common ground activity, c) entry into a group of children already in play, d) in home play dates, and conflict avoidance and negotiation.
  • Results was improvement at home as a result of treatment, though not in the classroom. More work was suggested.

Georgia: Socioeconomic Habilitation using the Math Interactive Learning Experience

56 children 3 – 10 years of age. Consistent caregiver for 6 months before and after the study.

• Objective: to improve behavioral and mathematic functioning of alcohol affected children.
  • 6 weeks of math tutoring
    • Active learning approach using “plan-do-review” methodology
  • Caregivers received instruction in supporting math learning and weekly home assignments to compliment individualized tutoring sessions
  • Education to the teachers about alcohol related neurodevelopmental problems

• Participants did make gains in math and behavior as assessed via pre- and post- testing with CBCL.
Behavior Consultation Intervention (WA)

52 children 5 – 11 years of age.

• Objective: To develop a program, Families Moving Forward, for families with children with FASDs
  • Positive behavior support techniques
    • (In WA state, 82% of FASD children had disruptive behaviors)
    • That the families tend to be highly stressed is not helpful.
  • Quality of caregiving a specific target
    • Parents of FASDs very diverse group of birth, kinship, foster and adoptive
• The program: 9 – 11 months, with at least 16 every-other weekend 90 min sessions. Program was designed with flexibility in mind.
Parent-Child Interaction Therapy

46 children 3 – 7 years of age.

• Objective: reduce behavior and parenting stress.

• PCIT provides a live coached practice of behavioral parenting skills
  • Enhance parent-child relationship; increase appropriate social skills; reduce inappropriate behaviors; promote positive discipline.
  • 14 weeks 90-min sessions

• Approx 50% attrition rate

• There was improvement, but no significant difference between PCIT and Parent Support and Management group.
Positive Behavior Support

• Emerged from a combination of applied behavioral analysis, the inclusion movement, and person-centered planning.
• The PBS approach primarily focuses on adapting the environment to enhance the individual’s quality of life. The reduction of problem behaviors is a secondary goal.

• 1) lifespan perspective,
• 2) emphasis on prevention,
• 3) a comprehensive lifestyle change and quality of life,
• 5) systems change and multicomponent intervention,
• 5) stakeholder participation (i.e., collaborative vs. expert-driven stance)

• Recommended services for young adults with FASD focus on life skills development and vocational services. Support groups and counseling have also been found to promote positive adjustment and mental health. In particular, the benefits of group services and activities include promoting social skills, positive self-esteem, and a sense of belonging. Knowing the diagnosis is cited as important in providing interventions. A case manager specializing in or having a depth of knowledge about FASD has been found to be helpful.

Petrenko et al. 2014
Neurocognitive habilitation for children with FASDs (Children’s Research Triangle)

78 children, 40 received the intervention. Specific ages not given.

- Recipients: Children with FASDs who had been adopted or who were in foster care.
  - These children do not have the protective factors of
    - Being raised in a stable nurturing home
    - Diagnosis before age 6; receiving early intervention
    - No sexual or physical abuse history
    - Not changing households every few years

- Core components: education and support to family
  - Also executive function
    - Alert program (car engine as a metaphor): 12 weekly 75-min sessions
    - Tools for memory, cause and effect reasoning, sequencing, planning, problem solving

- Results were promising.
How does your engine run? (Executive Function)

• The Alert Program for Self-Regulation
  • Beneficial neuroanatomical changes following treatment for their core deficit in executive functioning.
    • Increases in cortical gray matter in children with FASD, in regions involved with
      • response inhibition,
      • outcome monitoring,
      • and emotion regulation

Higher Level Organization

Children with FASD demonstrate a capacity to learn new skills, though do so through explicit instruction rather than through observation and abstracting rules, skills and ongoing knowledge as we typically expect.

• Organizational strategies across the board, especially as related to skills that mature. These are higher level executive functions. Development of these can't be taken for granted.

• Executive Functions can make it or break it!!
  • Contribute to decision making and problem solving.
Medication for ADHD symptoms in FASDs?

- Although it has been estimated that 50 – 90% of individuals with FASD have ADHD,
- Stimulants have had differential outcomes.
  - May reduce activity, but not improve attention
  - Results may be unpredictable, and even lead to poorer outcomes.
  - May increase spontaneous motor behavior later in life.
  - Clinical trial for Strattera underway.
  - In general, not a great response to methylphenidate
One commonly documented strength among individuals with FASDs is that they tend to work well with animals. AAT is delivered by a professional service provider, such as a recreation therapist, and is designed to promote improvements in physical, emotional, social, or cognitive functioning. Animals used in AAT can include cats, rabbits, birds, fish, and perhaps most commonly, horses and dogs.

Enhancing knowledge Pre-Pregnancy

• Transgenerational effects
• Prompts the question: Is FAS heritable?
• (for example, impact on reward circuitry)

Pregnant rats received the equivalent of one glass of wine, four days in a row, at gestational days 17-20, the equivalent of the second trimester in humans. Juvenile male and female offspring were then tested for water or alcohol consumption. Adolescent males were tested for sensitivity to alcohol by injecting them with a high-alcohol dose, which made them unresponsive (drunk on their back), and measuring the time it took them to recover their senses (back on their four paws). The results suggest that if a mother drinks during pregnancy, even just a little bit, she increases the risk that her progeny will become alcoholic.

"Our findings show that in the rat, when a mother consumes the equivalent of one glass of wine four times during the pregnancy, her offspring and grand-offspring, up to the third generation, show increased alcohol preference and less sensitivity to alcohol," said Cameron. "Thus, the offspring are more likely to develop alcoholism.


The Future

• Neuroplastic Interventions: white matter development could be more resistant to the long-lasting effects of prenatal alcohol exposure and/or be more amenable to plasticity relating to environmental factors
  • Exercise
    • Shown to impact brain structure involved in learning and memory
    • Has been used as an intervention for ADHD, anxiety, PTSD, depression and other conditions
  • Mindfulness/Meditation
    • attention
    • Impulse Control
    • Awareness of Emotions
    • Social Compassion
  
• ALERT program
  • Attention
  • Impulse Control
  • Awareness of Emotions
  • Social Compassion
## Summary of FASD Intervention Areas

- Social
- Family/School Communication Strategies: Positive Behavioral Support
- Math
- Executive Function
- Adaptive, Vocational and Life Skill

Web Resources (Handout)

• FAS Community Resource Center:  http://www.come-over.to/FASCRC/
• National Organization on Fetal Alcohol Syndrome:  http://www.nofas.org/
References (selected)


References (selected)


• Streissguth AP, Barr HM, Kogan J, Bookstein FL. Final report: Understanding the occurrence of secondary disabilities in clients with fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE) University of Washington Publication Services; Seattle, WA:


