Why is Brain Imaging Important?

- Clinical brain scans can tell us if there is frank brain damage in an individual child exposed to alcohol - but this is not very common.
- Research studies, involving detailed analysis of groups of people with FAS can inform us about how the brain is affected by prenatal alcohol exposure.
Change in cerebral size

Mattson et al., 1994
The cerebellum, little brain

Examples deleted because of copyright issues
Change in cerebellum size

Corpus Callosum  Cerebellum

Cerebrum

Cerebellum

NDFASD  FAS

$\ p \leq 0.001$

Mattson et al., 1994
Cerebellar size and shape

Preliminary data not published yet.
Cerebellum

- Reduced cerebellar volumes, at least in children with FAS
- Reduction in the size of the vermis
  - Primarily in the anterior regions (I-V)
- Alteration in shape
- Similar to animal studies
- May be related to balance, verbal learning deficits, and attentional problems
The Corpus Callosum

Examples deleted because of copyright issues

- Connects the left and right halves of the brain
- Allows them to work together and put information together
Corpus callosum abnormalities

Mattson, et al., 1994; Mattson & Riley, 1995; Riley et al., 1995
Reductions in Corpus Callosum Area
Brain Mapping

Gray Matter Density Increase

White Matter Density Decrease

Sowell et al., 2001
Corpus Callosum

- Agenesis of the corpus callosum
  - prenatal alcohol exposure is perhaps the most common cause of this condition

- Reduced in size and displaced
  - specific to genu and splenium - similar to ADHD children
  - may be related to difficulty in dealing with complex stimuli and situations
The frontal lobes, making logical decisions

Examples deleted because of copyright issues
The frontal subcortical circuit

- Frontal Cortex
- Striatum (caudate & putamen)
- Thalamus
- Globus Pallidus (part of lenticular nucleus)

Bar chart showing % of Control for Caudate and Accumbens, with significance markers.
Frontal lobes and basal ganglia – Executive function deficits

- Frontal lobes are too thin and small
- Basal ganglia reduced in volume
  - Primarily due to a reduction in the size of the caudate
- Concordant with animal data
- May be related to deficits in spatial memory, perseverative tendencies, attentional problems, and importantly executive functioning
State of the art imaging – MRS, MEG and fMRI

Figure deleted because data have not yet been published
MRS Data

Figure deleted because data have not yet been published

N-acetylaspartate to choline ratio indicates neuronal dysfunction (fewer neurons) and/or altered glial cell metabolism in the FASD group.

N-acetylaspartate to creatine ratio may indicate a compensational effort in mitochondrial metabolism.
Summary of MRI Findings

- Reductions in overall brain size and in certain brain structures, e.g. the cerebellum, basal ganglia, and corpus callosum
- Too much grey matter and lesser amounts of white matter in some areas
- Distortions in shape of brain
- Changes in energy metabolism
Prenatal exposure to alcohol, at least in high doses, can cause permanent changes in the brain

- These changes in brain may cause or contribute to many of the behavioral problems seen in individuals exposed to alcohol.
- These changes in brain are not due to poor postnatal environments, being in foster care, or a host of other possibilities.
- Knowing what brain areas are involved might enable us to develop better treatment strategies.
So What Do We Need?

Picture deleted because of copyright issues
Prenatal exposure to alcohol can result in a variety of behavioral dysfunctions, even in the absence of obvious physical effects.
Behavioral profile of FAS

- Reduced IQ
- Learning deficits including habituation
- Increased activity and reactivity
- Perseverative
- Attentional and inhibitory deficits
- Poor fine and gross motor skills
- Developmental delays
- Feeding deficits
- Hearing abnormalities
Sample text: General Intellectual Performance

Mattson, S.N., 1997. FAS is the leading known cause of mental retardation in the western world, but the majority are not retarded.
Boston Naming Test

- Picture deleted because of copyright issues
Peabody Picture Vocabulary Test

- Picture deleted because of copyright issues
Language Test Performance

<table>
<thead>
<tr>
<th>Language Measure</th>
<th>PPVT-R</th>
<th>BNT</th>
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<tbody>
<tr>
<td>Standard score</td>
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<td>50</td>
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<tr>
<td>Raw score</td>
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<td>30</td>
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</table>

NC  FAS  NDFASD

* indicates significant difference
Grooved Pegboard Test

- Picture deleted because of copyright issues
Fine-Motor Skill: Grooved Pegboard Test

Time (sec.)

Hand

Dominant

Nondominant

NC
FAS
NDFASD

*
Assessment of Balance
Body Sway Tracings

<table>
<thead>
<tr>
<th>Condition</th>
<th>Control</th>
<th>Alcohol</th>
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<tbody>
<tr>
<td>1</td>
<td></td>
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</tbody>
</table>
“We wondered how a child could get A’s in school and not have the sense to understand that when she is rude to friends they might get mad at her.”

-Hilary O’Loughlin
(Iceberg, 1995)
The frontal lobes, making logical decisions

Frontal Cortex

Striatum (caudate & putamen)

Thalamus

Globus Pallidus (part of lenticular nucleus)
Executive Functioning

Cognitive functions involved in planning and guiding behavior in order to achieve a goal in an efficient manner.

- The ability to organize and plan
- Focus and maintain attention
- Be able to store memories and retrieve them
- Issues related to affect and inhibition, e.g. preventing anger from getting out of control
Executive function deficits

Pictures deleted because of copyright issues
Inhibition and attention

Picture deleted because of copyright issues
Inhibition and attention

Picture deleted because of copyright issues
Executive Functioning
Tower of California Test

Move only one piece at a time using one hand and never place a big piece on top of a little piece.
Twenty Questions

Picture deleted because of copyright issues
Reaction time and decision making

Picture deleted because of copyright issues

Premotor RT (ms)

0 200 400 600

Simple Complex

RT Condition
Relationship between brain areas and behavioral changes

The Corpus Callosum, Cooperation Between the Hemispheres and “Innocent Delinquency”
Left brain/Right brain
The Corpus Callosum

Left Brain
• Language
• Math
• Logic

Right Brain
• Spatial abilities
• Face recognition
• Visual imagery
• Music
What each half of the brain sees

Stimuli

Controls

Alcohol-exposed

Alcohol-exposed
Mental Health and Behavior

Picture deleted because of copyright issues
Why is FAS Important to Mental Health Providers

- Over 90% of individuals with FASD have received mental health treatment
- 60% of individuals with FASD over the age of 11 have experienced school disruption
- FAS is the leading preventable cause of mental retardation
- Attention problems are a hallmark feature and FASD may often be classified as ADHD
Secondary Disabilities

Individuals with FAS/FAE have a range of secondary disabilities – disabilities that the individual is not born with, and which could be ameliorated with appropriate interventions.

Picture deleted because of copyright issues

Streissguth, et al., 1996
The Sociomoral Reflection Measure - Short Form (SRM-SF)

Figure deleted because data are not published yet
Social Problem Solving Skills in Adolescents

Figure deleted because data are not published yet
Parent-rated Executive Functioning In Adolescents

Figure deleted because data are not published yet
Protective Factors

- Diagnosis before age 6
- Nurturing, stable home, good quality of home
- Never experiencing violence
- Being diagnosed FAS rather than FAE
Summary of Neuropsychological Findings

- Heavy prenatal alcohol exposure is associated with a wide range of neurobehavioral deficits.

- Children with and without physical features of the fetal alcohol syndrome display qualitatively similar deficits.

- A specific pattern of relative strengths and weaknesses may exist or there may be several patterns.

- Identification of children with heavy prenatal alcohol exposure is critical.
  - Research has shown that early identification leads to interventions, services and improved outcomes.
Points to ponder

- Currently, almost 2.9 million school-aged children in the US are classified as having specific learning disabilities (SLD) and receive some kind of special education support.
  
  *How many are related to prenatal alcohol exposure?*

- According to epidemiological data, approximately 4% to 6% of the U.S. population has ADHD.
  
  *How many are related to prenatal alcohol exposure?*
International consortium on FASD

- Involves a cross-cultural assessment of FASD.
- Coordinates basic, behavioral and clinical investigators in a multidisciplinary research project.
- First step is to develop a diagnostic schema for the full range of effects from prenatal exposure to large or moderate amounts of alcohol can be determined.
- Utilize international samples to accomplish these goals.
- Funded by NIAAA - Faye Calhoun, Ken Warren, Deidre Roach
Sites

- Moscow  Large number of cases all living in same environment with matched IQ controls and access to large numbers in birthing hospitals (prenatal care)
- South Africa  Large number of cases living in intact families, with high levels of binge exposure, interventions being tested
- Finland  Number of young adult cases with excellent imaging capabilities
- Italy  Different patterns of drinking
- Ukraine  Access to large number of exposed neonates
- San Diego
- Plains Indians
- Seattle
- Collaborations with investigators from Detroit and Atlanta
Dysmorphology Core

- Use traditional dysmorphology exam
- All diagnosis done by K.L. Jones or one of his collaborators using a standardized assessment
  - K.L. Jones
  - Luther Robinson
  - Eugene Hoyme
- A system of reliability checks
DYSMORPHOLOGY CORE PHYSICAL EXAMINATION FORM

1. Identification Number ___________
2. Examiner: [ ] Pediatrician
   [ ] Expert
3. Examiner last name: ___________
4. Date of Examination _____ / _____ / _____
   (dd / mm / yy)
5. Patient’s Name ___________
   (first) _______________________
   (last) _______________________
6. Patient’s Gender: [ ] Male
   [ ] Female
7. Birth Date _____ / _____ / _____
   (dd / mm / yy)
8. Number of completed weeks of gestation ___________
   (weeks)
   If child is:
   <1 year old
   ≥1 year old
9. Was child born prior to 37 weeks of gestation?
   [ ] Yes
   [ ] No
10. Current Age
    [ ] Yes
    [ ] No
    (months) ___________ (weeks) ___________
11. Gestational weeks at exam ___________
    (g.weeks)
12. Adjusted Age ___________ (months) ___________ (weeks)
- classic dysmorphology exams will only provide information about individuals with FAS, and not about individuals with nondysmorphic FASD

  • Looking for 3 facial features
FAS and PFAS measurements

Figures deleted because of copyright issues
Computerized Assisted Diagnosis of FAS

Picture deleted because of copyright issues
Behavioral Assessment

- Use common behavioral assessment instruments across sites
  - Common findings across these disparate sites should be those due to alcohol
  - Discrepancies are due to cultural factors
    - Modification of alcohol related effects by cultural factors
The Future:
A World Free of Fetal Alcohol Syndrome