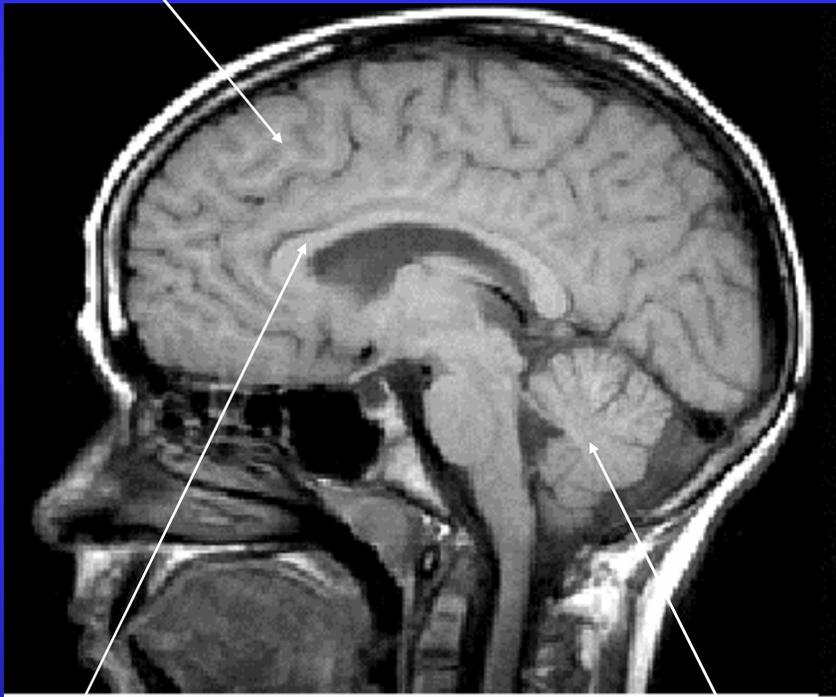


Why is Brain Imaging Important?

- 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

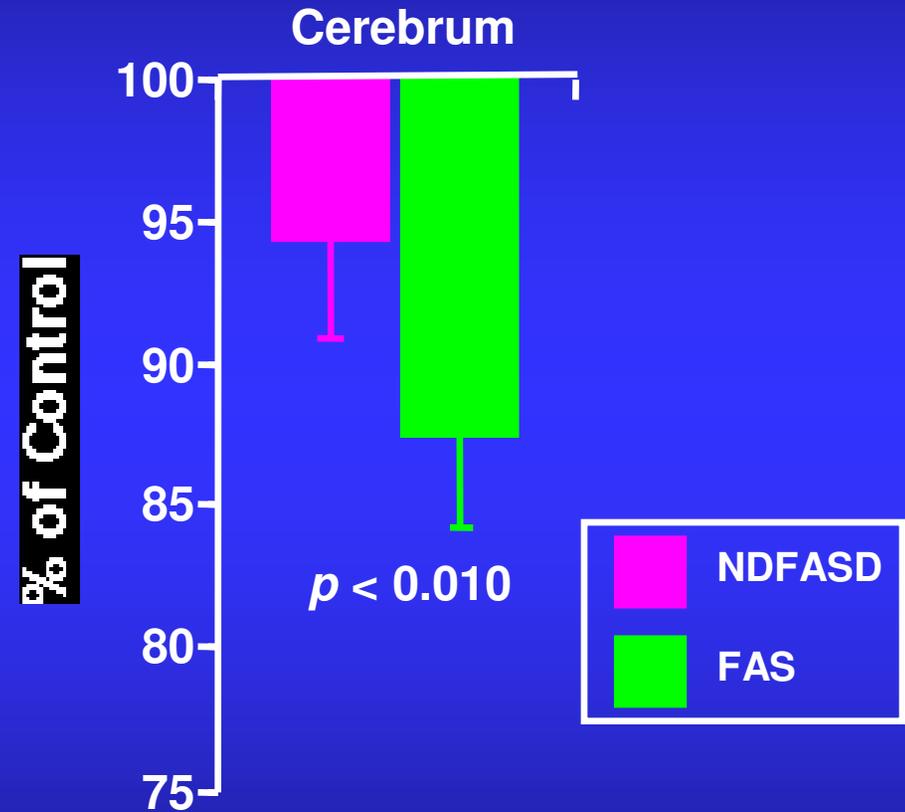
Change in cerebral size

Cerebrum



Corpus Callosum

Cerebellum

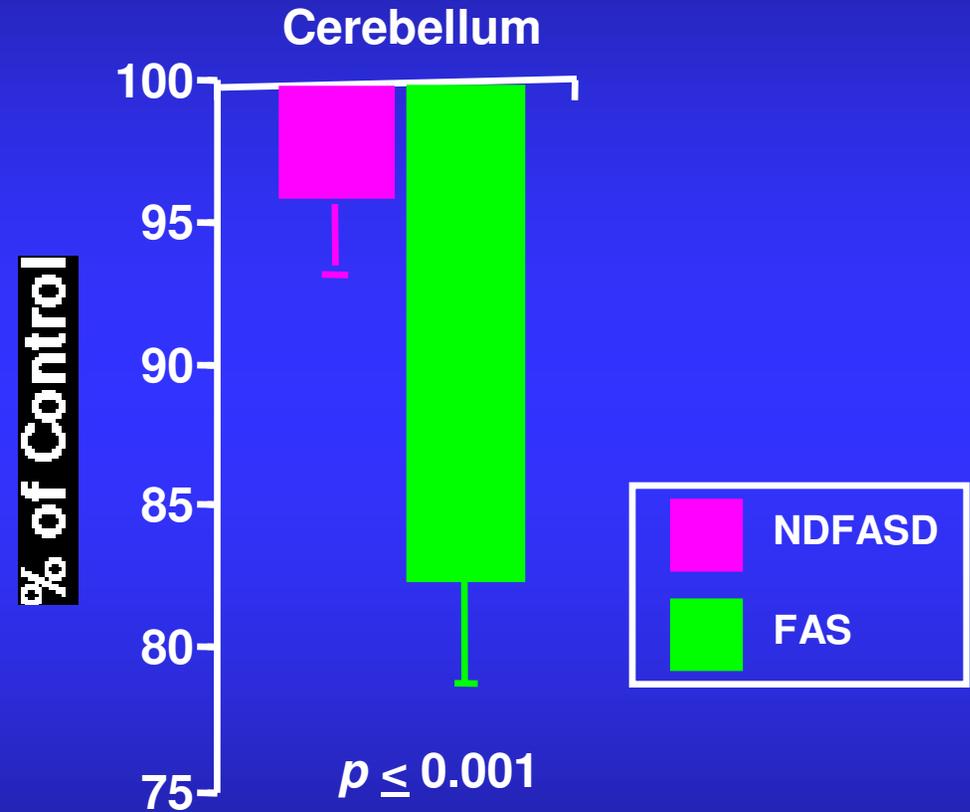
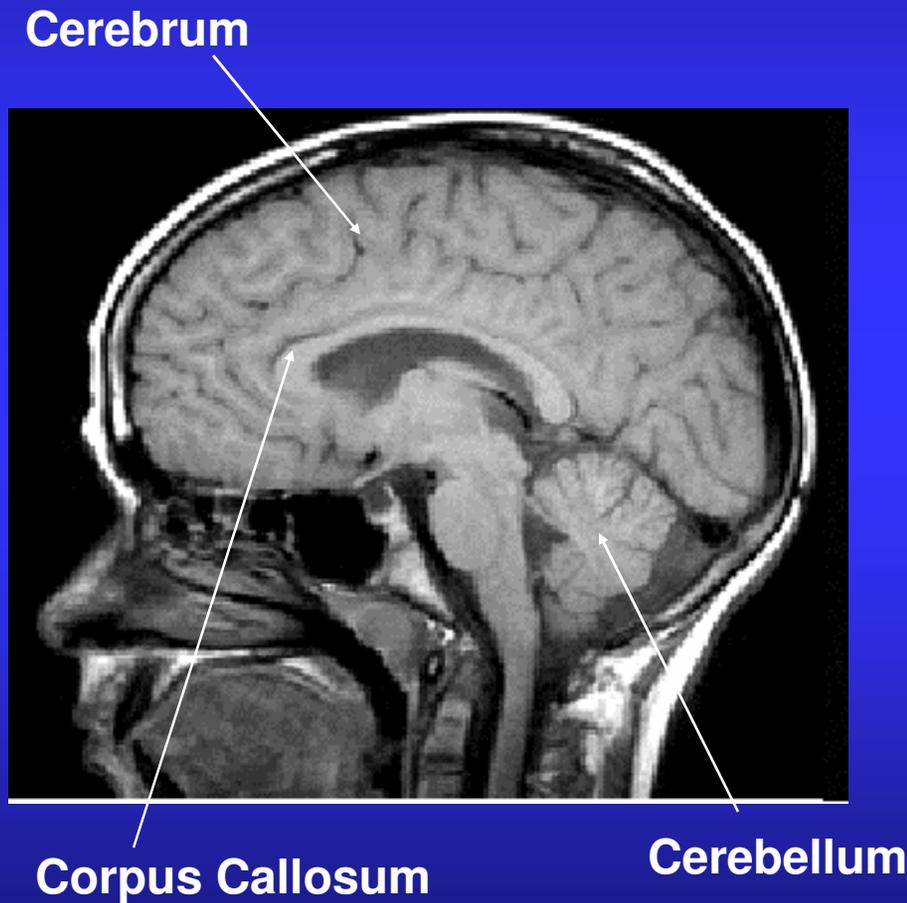


Mattson et al., 1994

The cerebellum, little brain

Examples deleted because
of copyright issues

Change in cerebellum size



Mattson et al., 1994

Cerebellar size and shape

Preliminary data not published yet.

Cerebellum

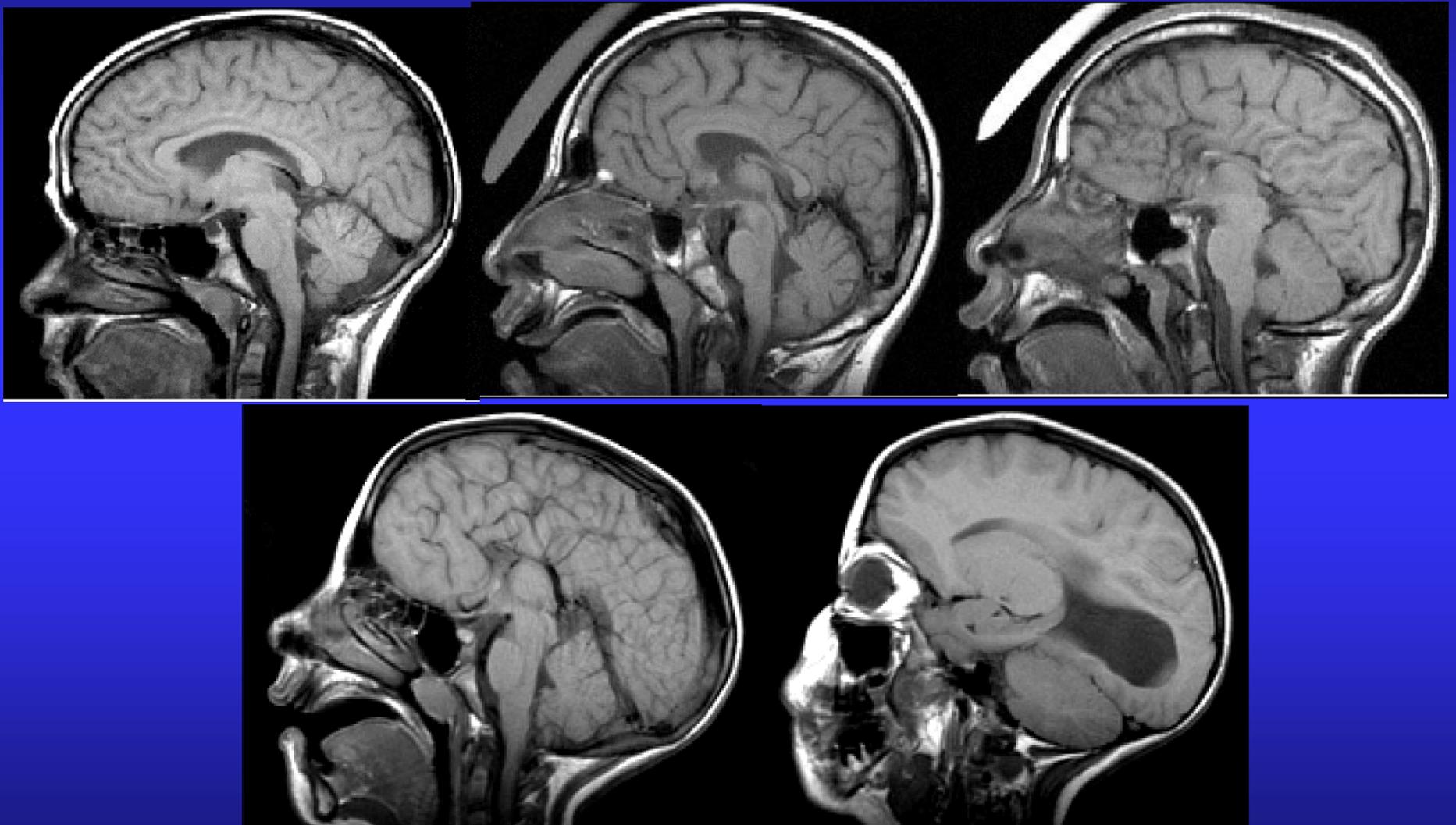
- Reduced cerebellar volumes, at least in children with FAS
- Reduction in the size of the vermis
 - Primarily in the anterior regions (I-V)
- Alteration in shape
- Similar to animal studies
- May be related to balance, verbal learning deficits, and attentional problems

The Corpus Callosum

Examples deleted because
of copyright issues

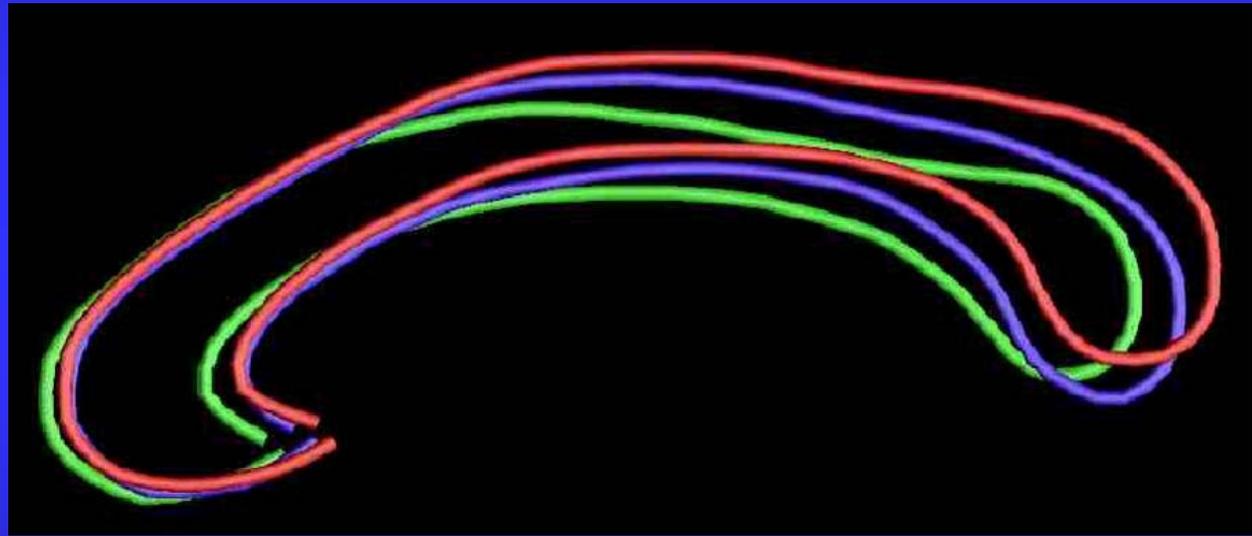
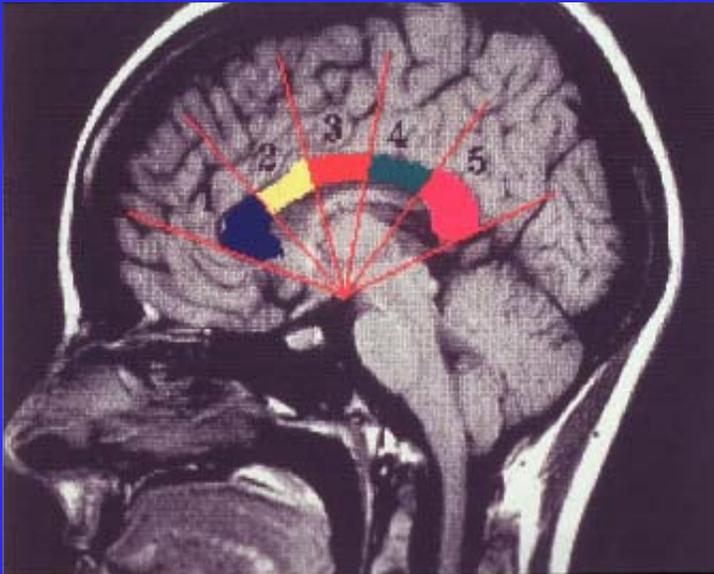
- Connects the left and right halves of the brain
- Allows them to work together and put information together

Corpus callosum abnormalities



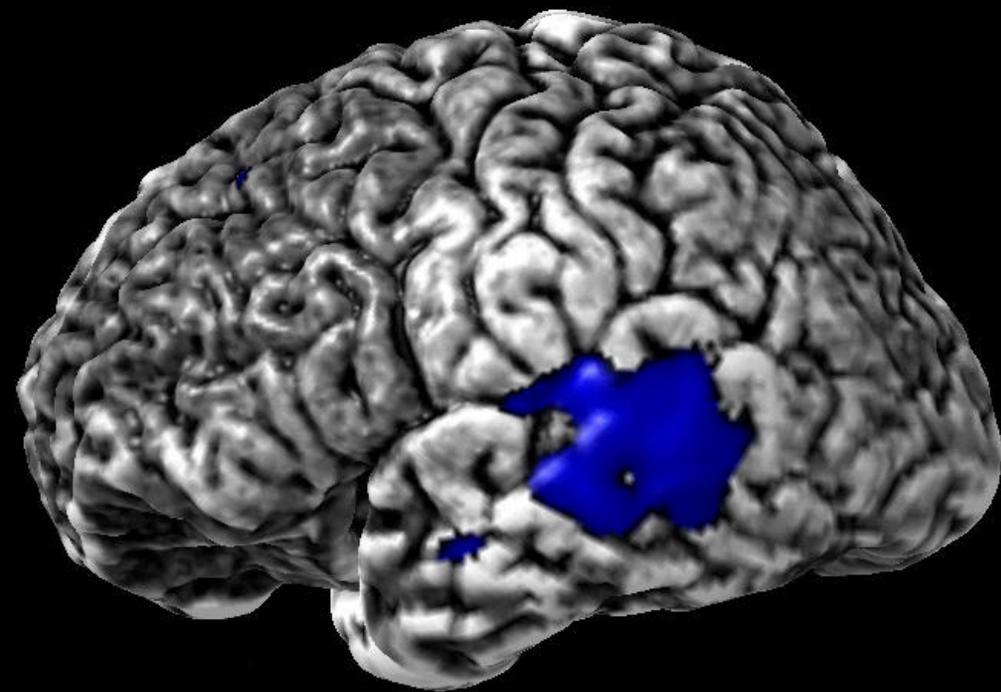
Mattson, et al., 1994; Mattson & Riley, 1995; Riley et al., 1995

Reductions in Corpus Callosum Area

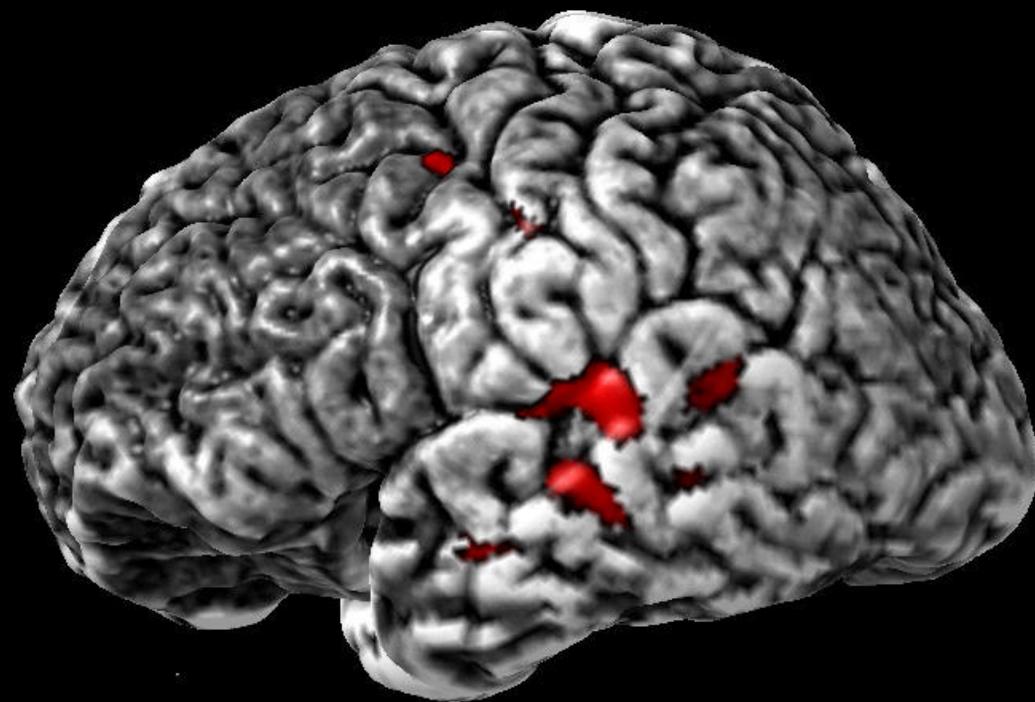


■ CON ■ NDFASD ■ FAS

Brain Mapping



Gray Matter Density Increase



White Matter Density Decrease

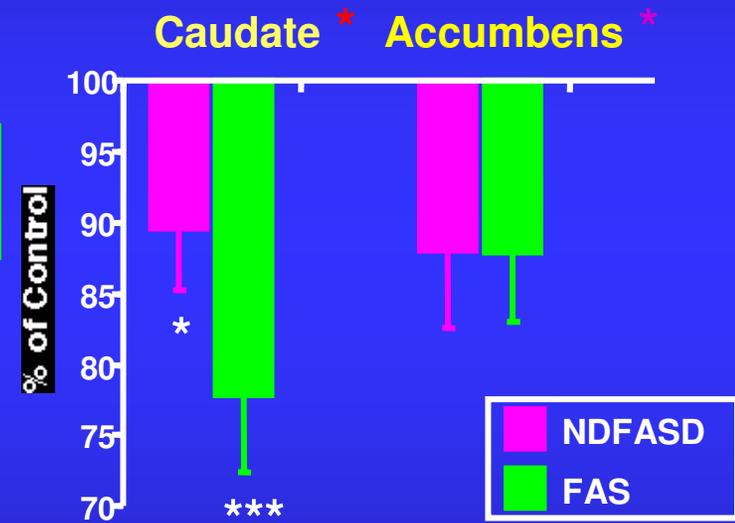
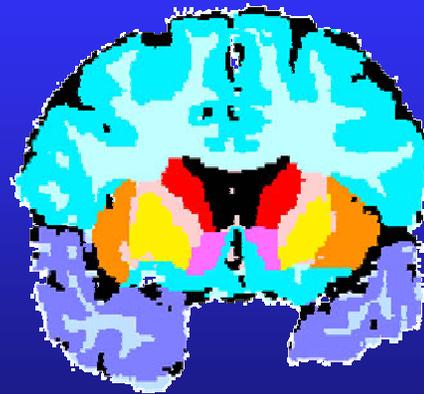
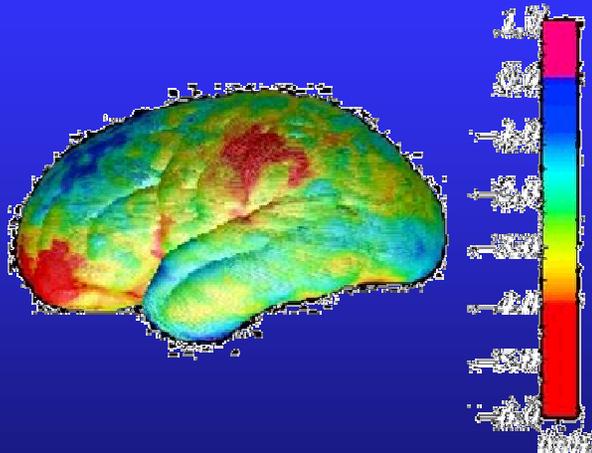
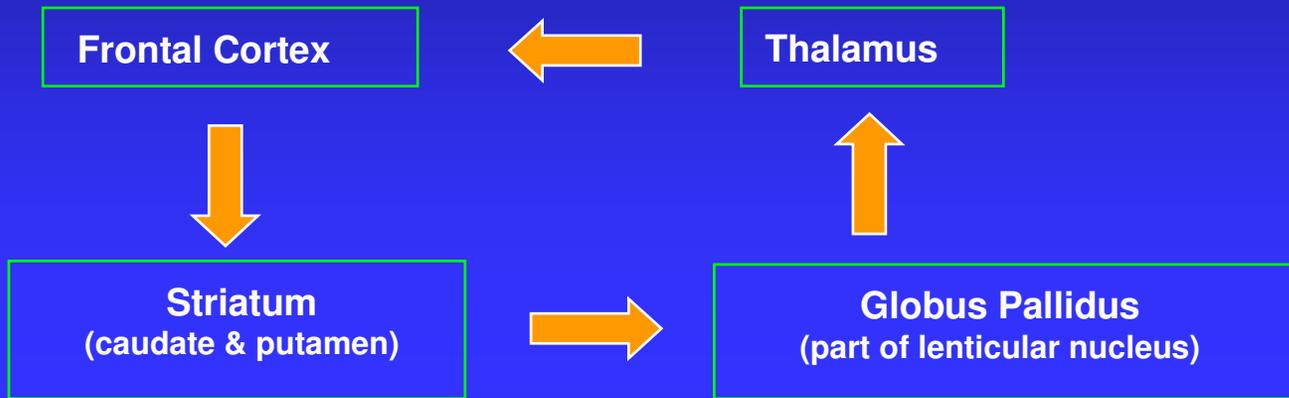
Corpus Callosum

- 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 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?

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copyright issues

Take home message number 2

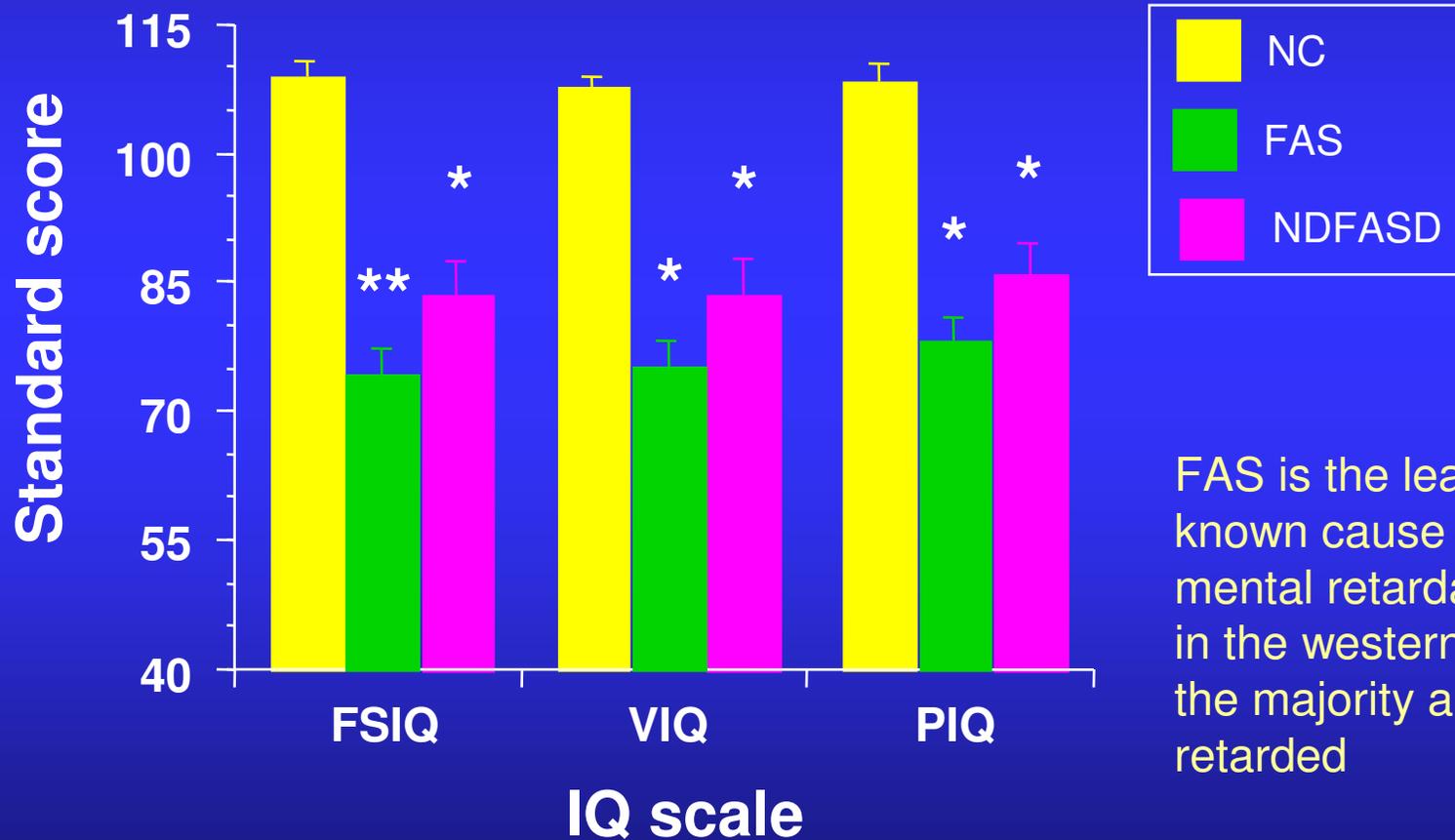
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of copyright issues

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

General Intellectual Performance



FAS is the leading known cause of mental retardation in the western world, but the majority are not retarded

Mattson, S.N., 1997.

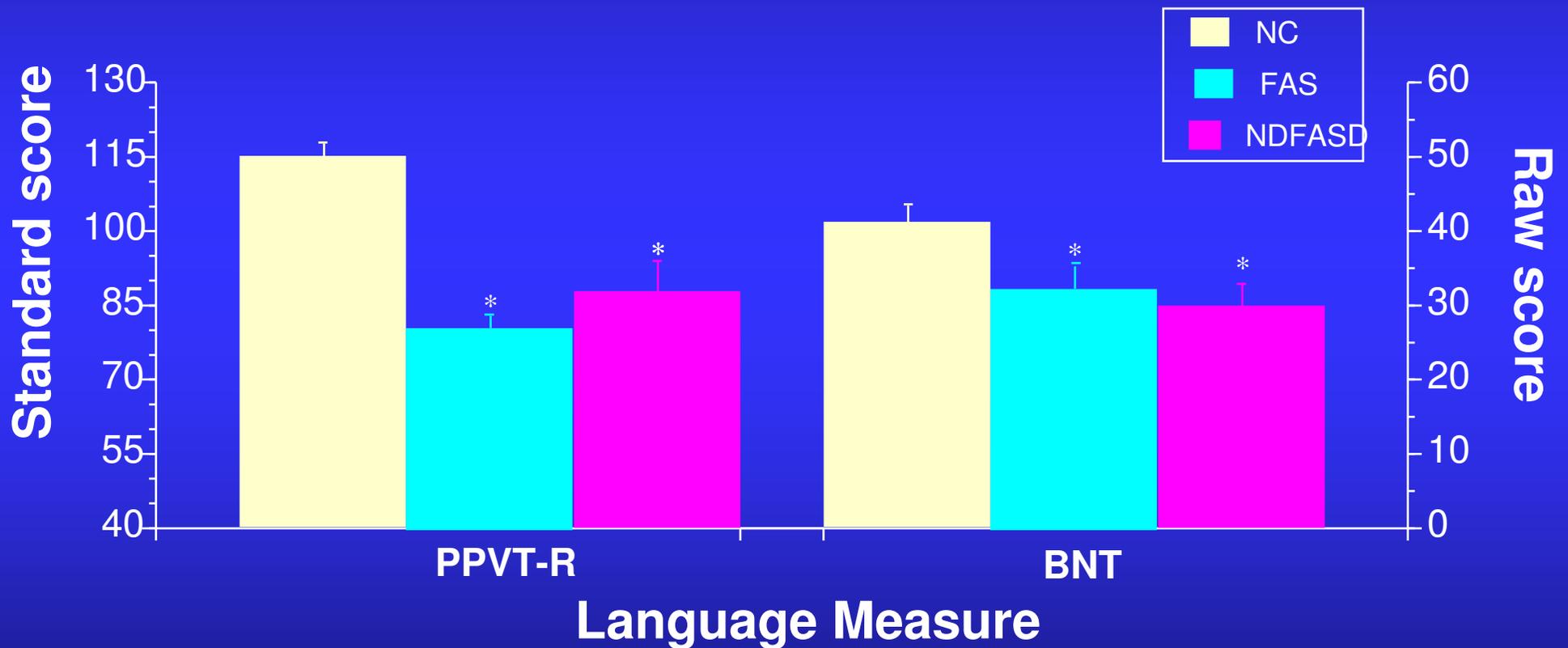
Boston Naming Test

- Picture deleted because of copyright issues

Peabody Picture Vocabulary Test

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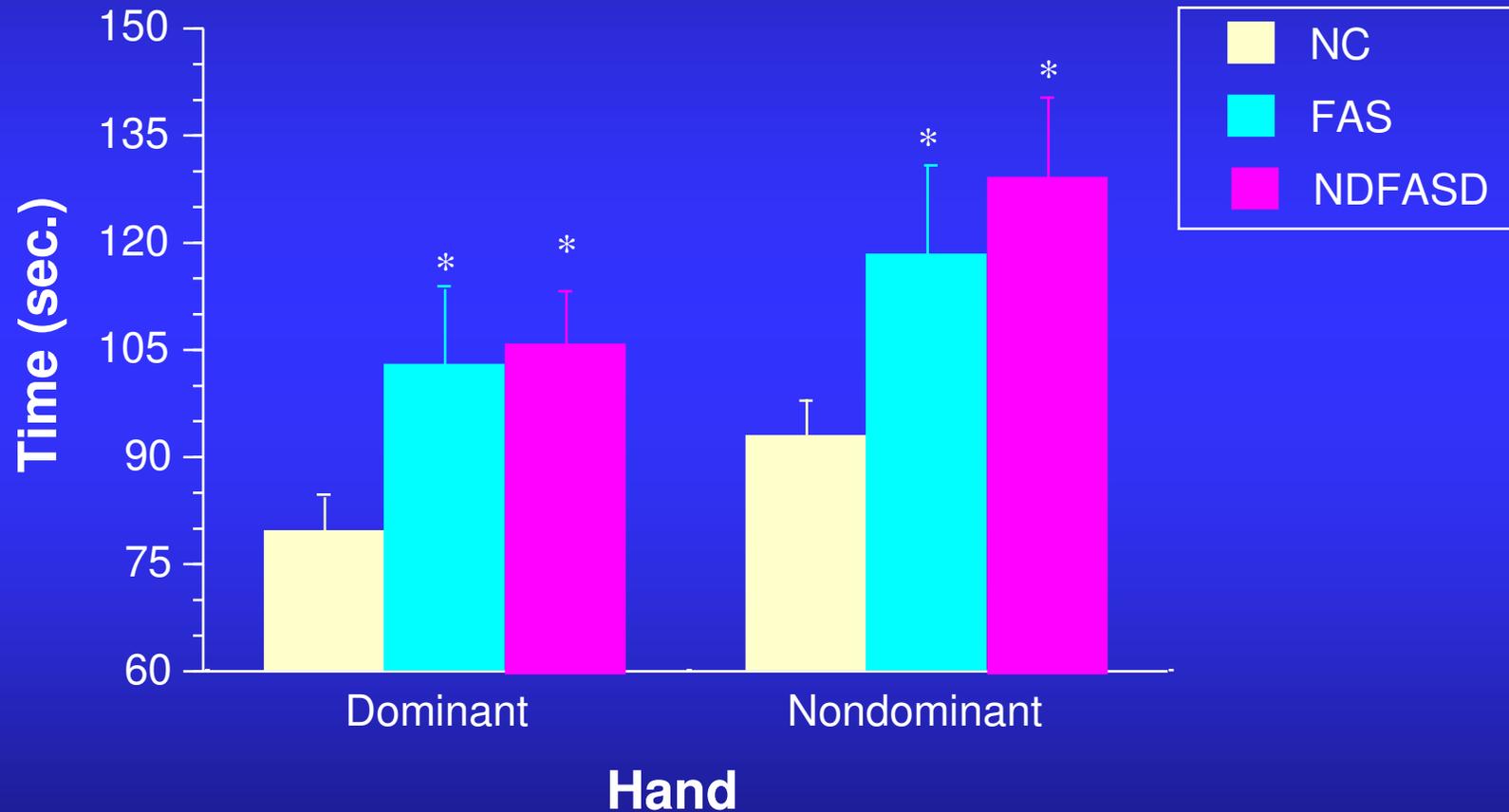
Language Test Performance



Grooved Pegboard Test

- Picture deleted because of copyright issues

Fine-Motor Skill: Grooved Pegboard Test



Assessment of Balance



Body Sway Tracings

Control Alcohol

Condition 1



Condition 2



Condition 3



Condition 4



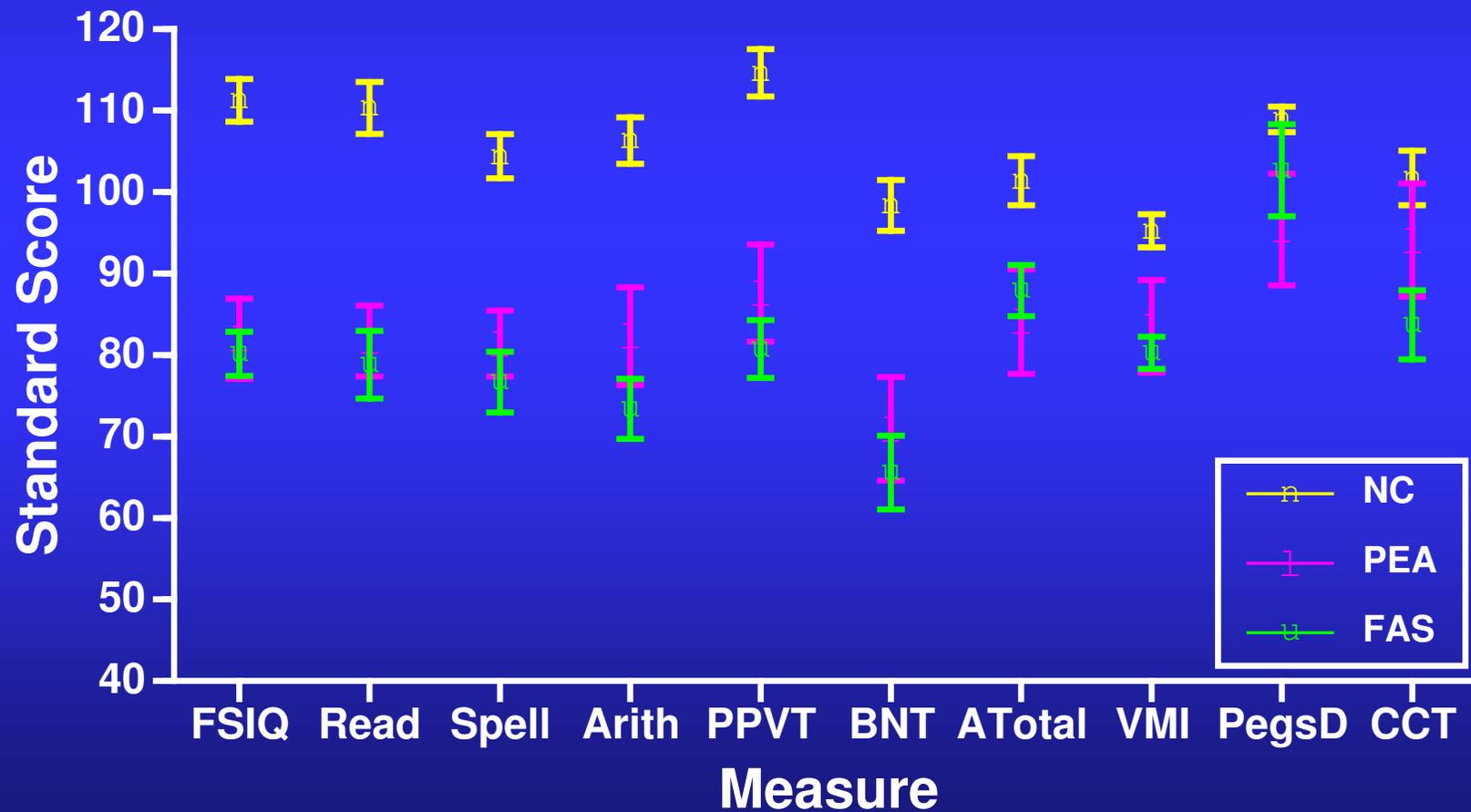
Condition 5



Condition 6



Neuropsychological Performance

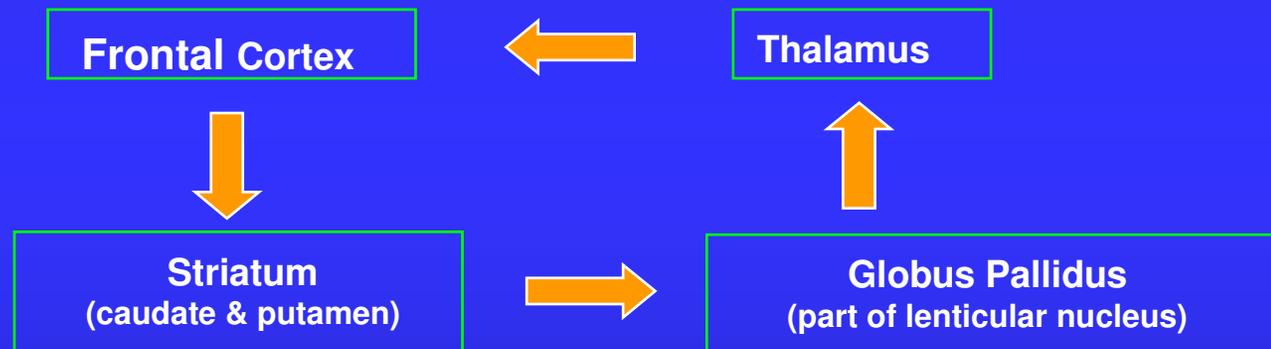


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of copyright issues

“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



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

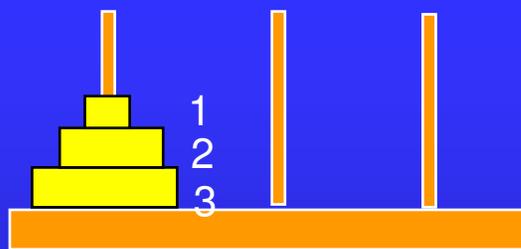
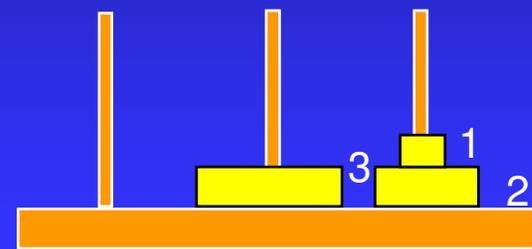
Inhibition and attention

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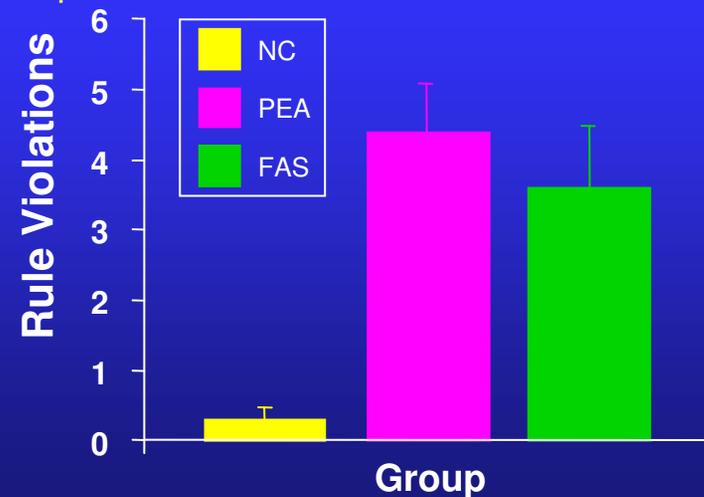
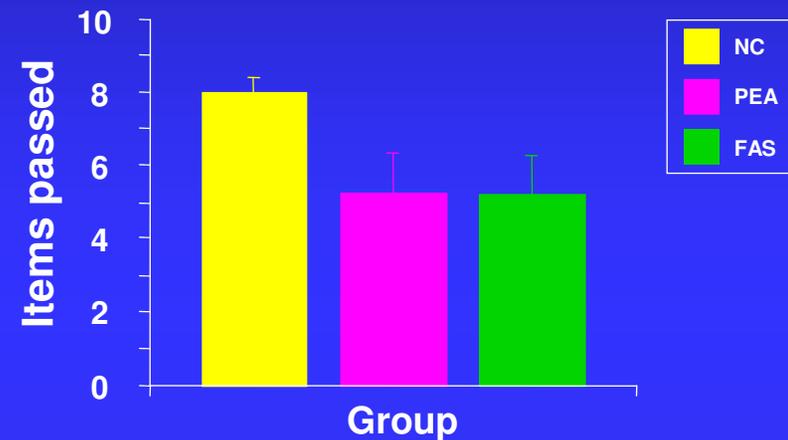
Inhibition and attention

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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

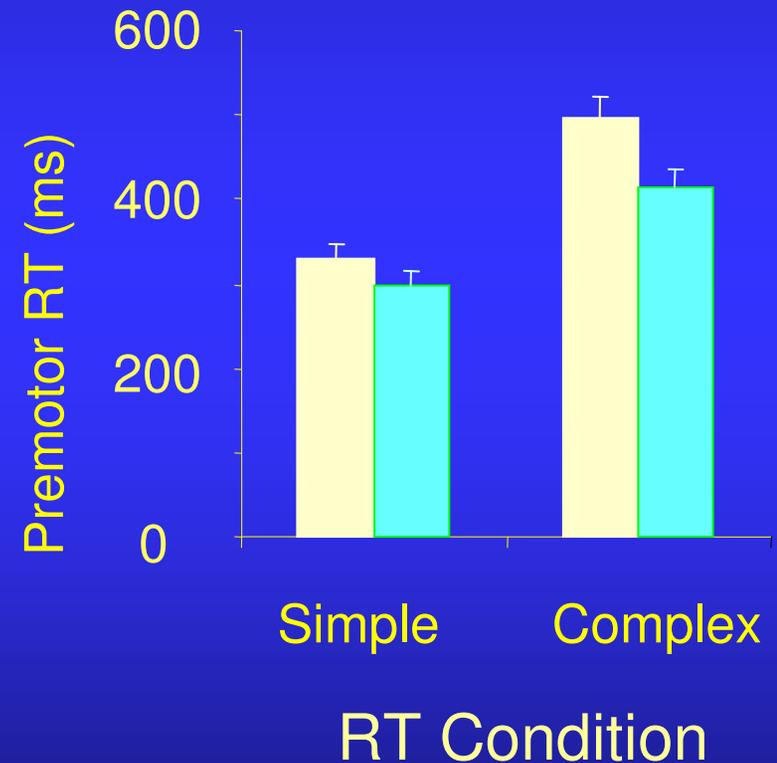


Twenty Questions

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Reaction time and decision making

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of copyright issues



Relationship between brain areas and behavioral changes

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of copyright issues

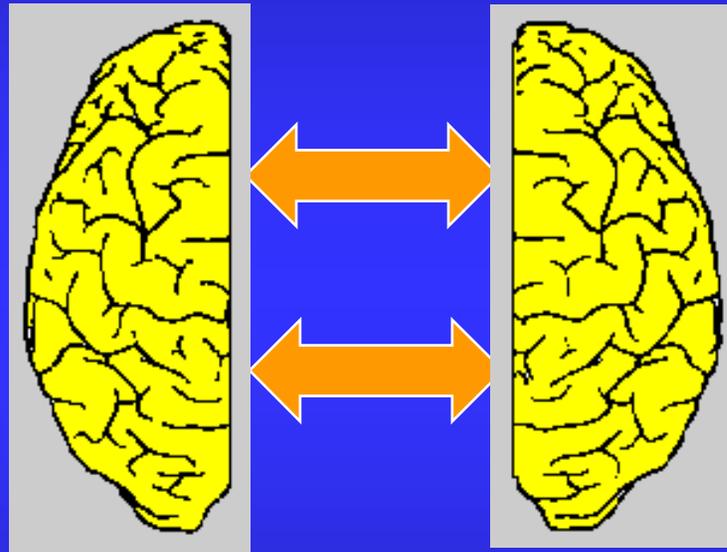
The Corpus
Callosum,
Cooperation Between
the Hemispheres
and
“Innocent
Delinquency”

Left brain/Right brain

The Corpus Callosum

Left Brain

- Language
- Math
- Logic

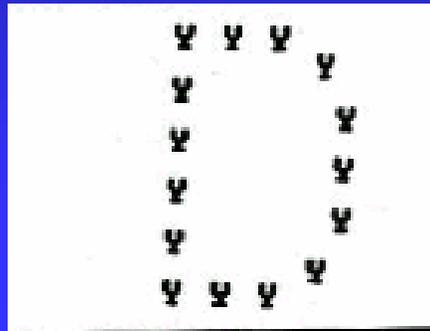


Right Brain

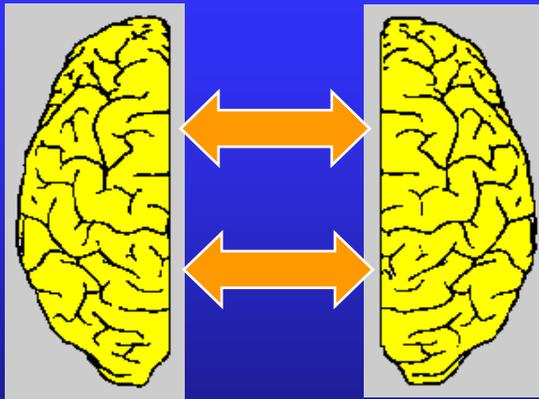
- Spatial abilities
- Face recognition
- Visual imagery
- Music

YELLOW	BLUE	ORANGE
BLACK	RED	GREEN

What each half of the brain sees



Y Y Y
Y Y Y
Y Y Y

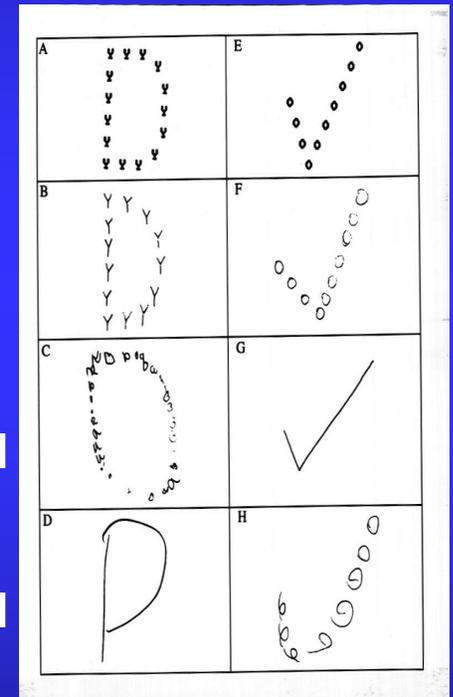


Stimuli

Controls

Alcohol-exposed

Alcohol-exposed



Mental Health and Behavior

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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.

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of copyright issues

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 3. Examiner last name: _____
 Expert

4. Date of Examination ____/____/____
(dd / mm / yy)

5. Patient's Name _____ 6. Patient's Gender: Male
(first) (last) Female

7. Birth Date ____/____/____ 8. Number of completed weeks of gestation _____
(dd / mm / yy) (weeks)

If child is:
 <1 year old
 ≥1 year old

9. Was child born prior to 37 weeks of gestation?

13. Current Age: Years _____ Months _____

Yes

No

10. Current Age _____
(months) (weeks)

Examined prior to EDC

Examined after EDC

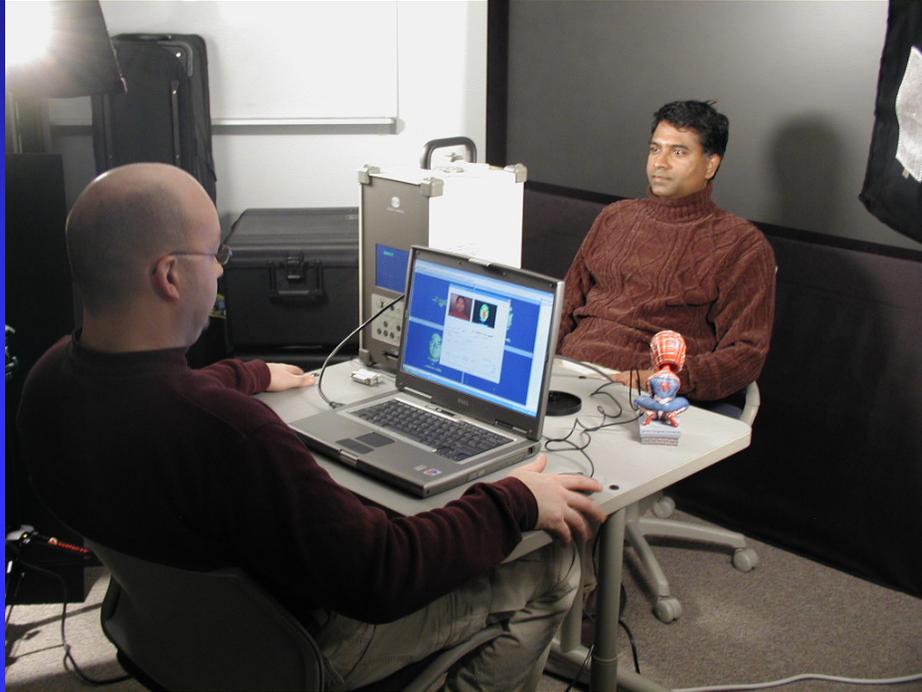
11. Gestational weeks at exam _____
(g. weeks)

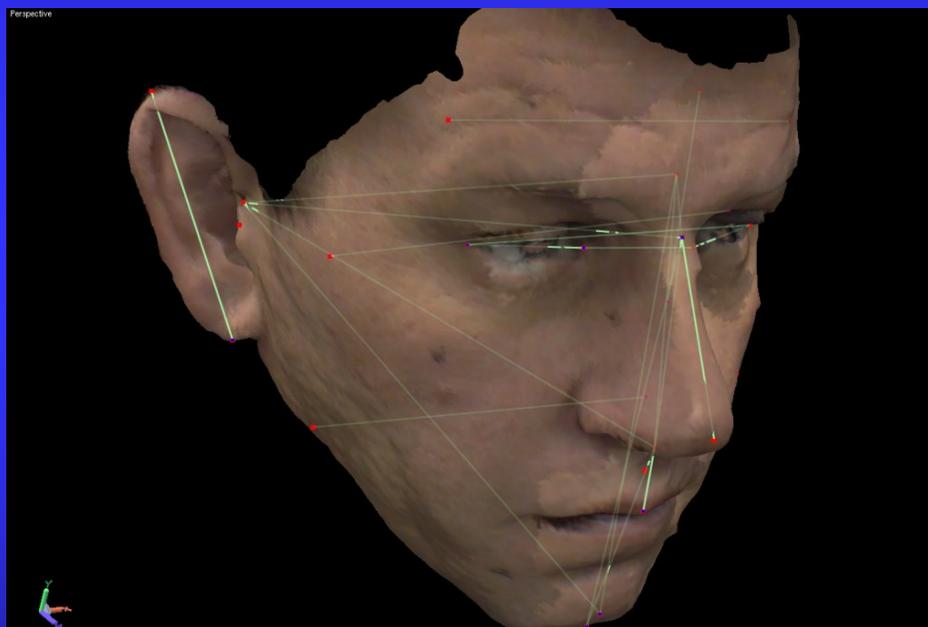
12. Adjusted Age _____
(months) (weeks)

- 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**