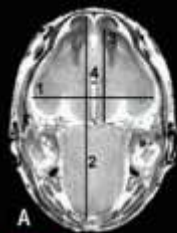


EFFECTS OF PRENATAL ALCOHOL EXPOSURE ON FACE, BRAIN, AND BEHAVIOR

Edward P. Riley, Ph.D.

**SDSU/UCSD Joint Doctoral Program in Clinical Psychology
Center for Behavioral Teratology
San Diego State University**

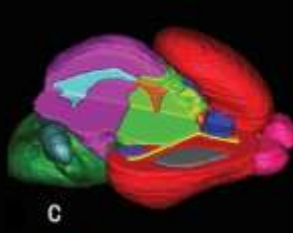
**The First Baltic Conference
“Prevention of Fetal Alcohol Spectrum Disorders”
September 26, 2014
Vilnius, Lithuania**



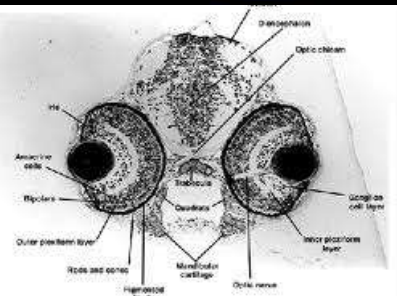
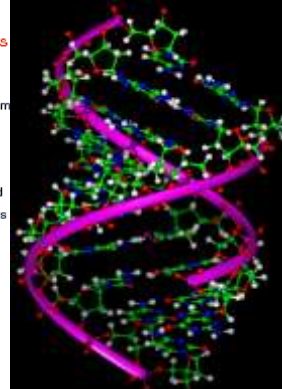
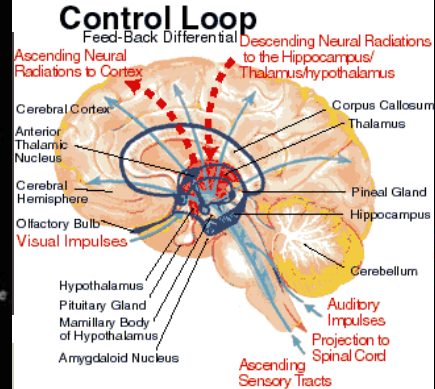
■ Cerebral Cortex
■ Lateral Ventricles
■ Striatum
■ Olfactory Bulbs



■ Hippocampus
■ Septal Region
■ Diencephalon
■ 3rd Ventricle



■ Mesencephalon
■ Mesencephalic & 4th Ventricle
■ Pons and Medulla
■ Cerebellum



CIFASD

- **CIFASD is the Collaborative Initiative on Fetal Alcohol Spectrum Disorders.**
- **An international collaboration funded by the National Institute on Alcohol Abuse and Alcoholism for the last 13 years.**

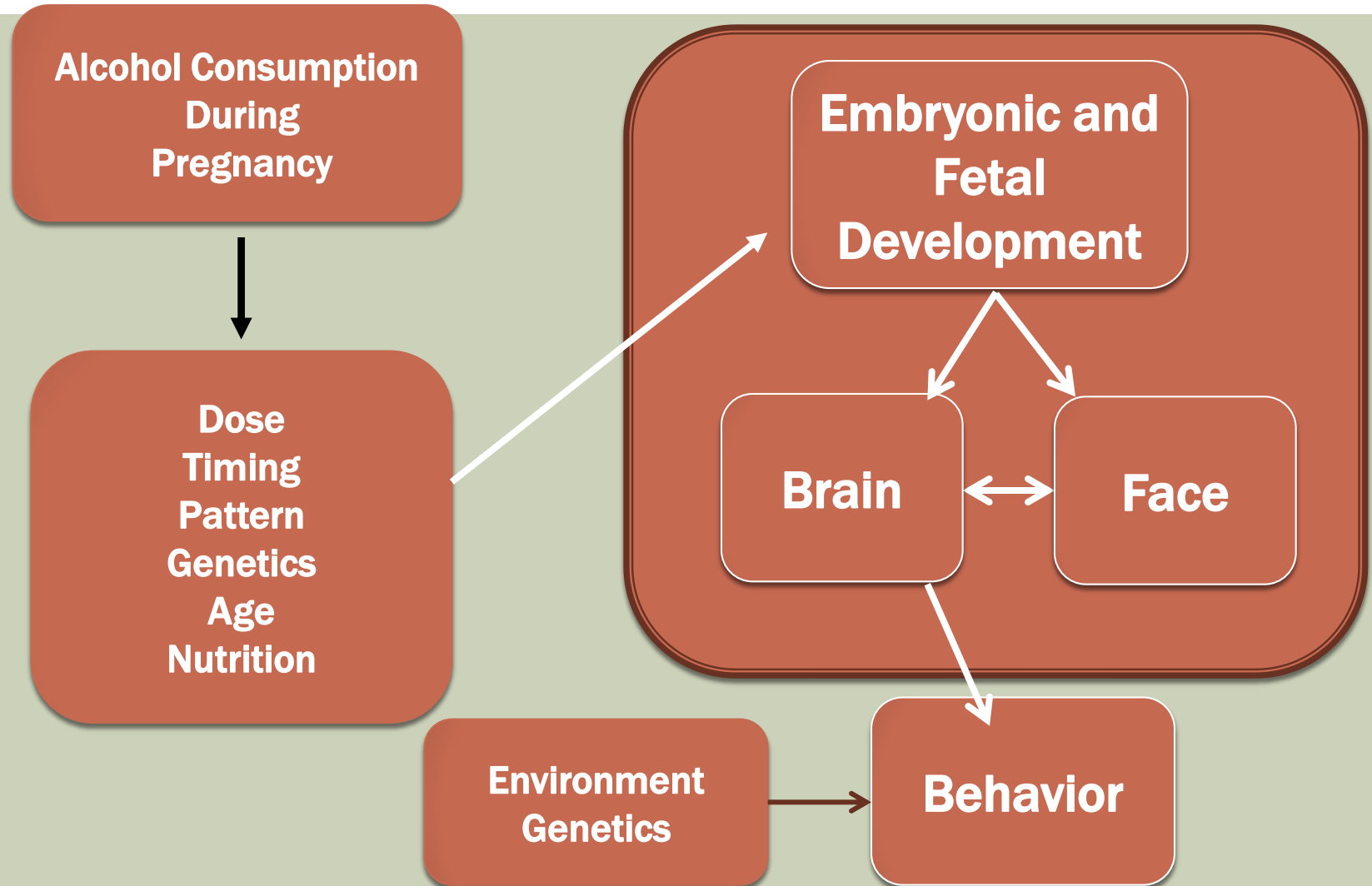


CIFASD – INTERNATIONAL CONSORTIUM ON FASD



- San Diego State University
- University of California, San Diego
- Harvard University
- Indiana University School of Medicine
- Indiana University-Purdue University School of Science
- Texas A&M
- Children's Hospital Los Angeles
- Emory University
- University of California, Davis
- University of California, Los Angeles
- University of New Mexico
- University of North Carolina at Chapel Hill
- University of Southern California
- Wayne State University
- University of North Carolina – Chapel Hill
- Ukrainian-American Birth Defects Program
- University of Cape Town
- Folkhälsan Research Center-Helsinki
- Moscow Institute of Obstetrics and Gynecology
- Queens University of Belfast
- Catholic University of Korea
- Queensland Institute of Medical Research
- University La Sapienza, Rome
- Stellenbosch University

CIFASD CONCEPTUAL FRAMEWORK

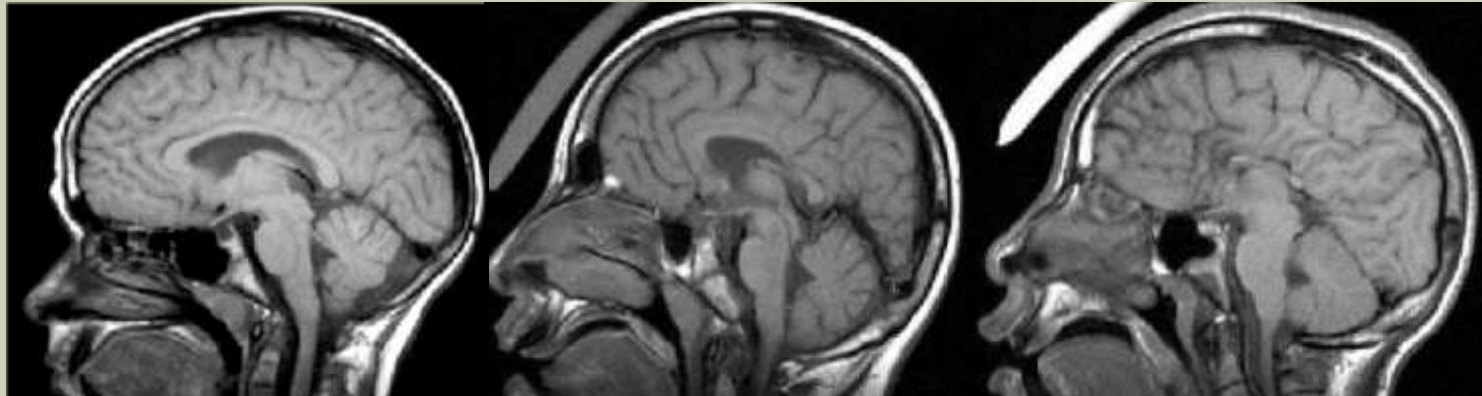


RESEARCH CHALLENGES

- Refine our understanding of the alterations in brain that underlie the neurobehavioral problems that occur in these individuals
 - Total change in attitude when one understands that this is a brain based problem
 - May inform interventions

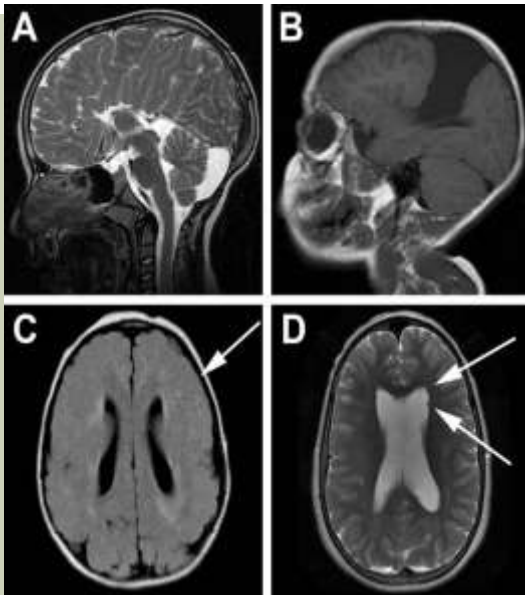
MOST SERIOUS IMPACT IS ON THE BRAIN

- **Structure and functioning of brain is effected**
 - Some brain areas appear to more affected than others.



WHAT DO FAS BRAINS LOOK LIKE

SOME ANOMALIES ARE FAIRLY OBVIOUS - BUT RARE
USUALLY QUITE UNREMARKABLE BY VISUAL INSPECTION



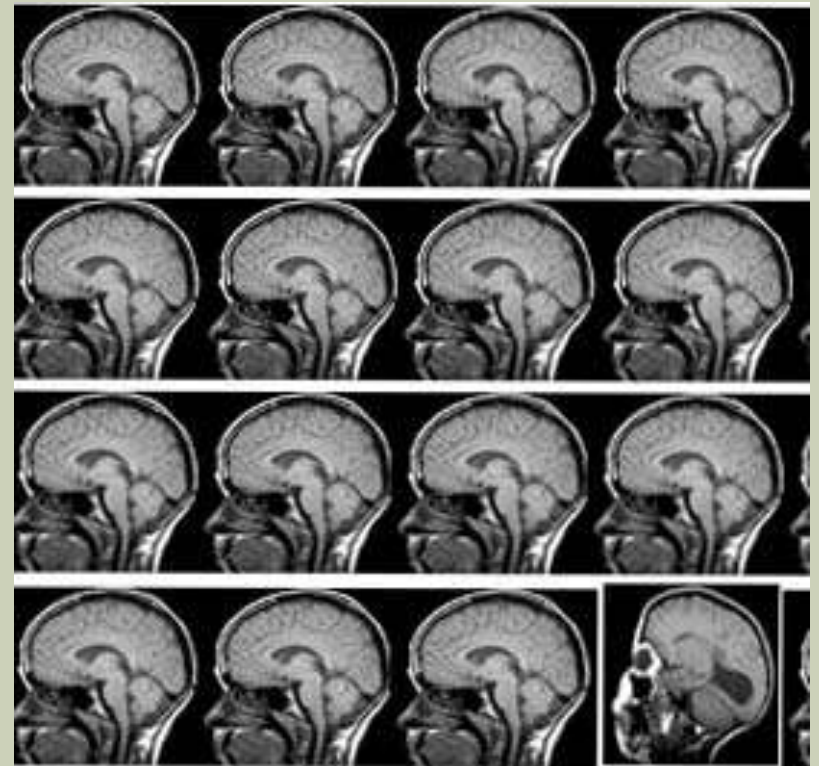
A. Agenesis of the corpus callosum.

B. Schizencephaly.

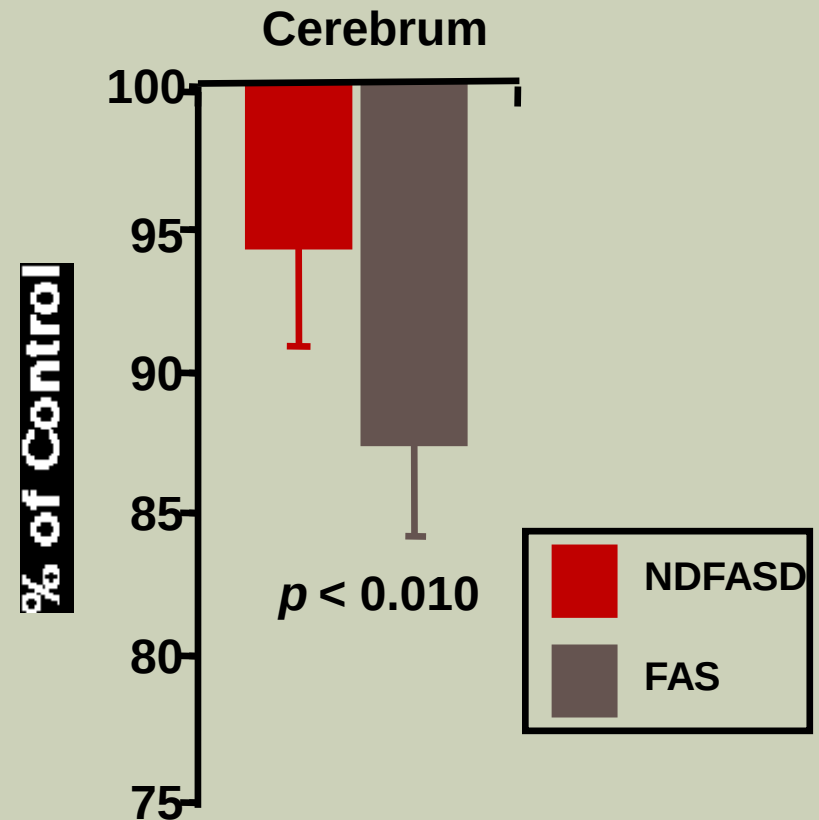
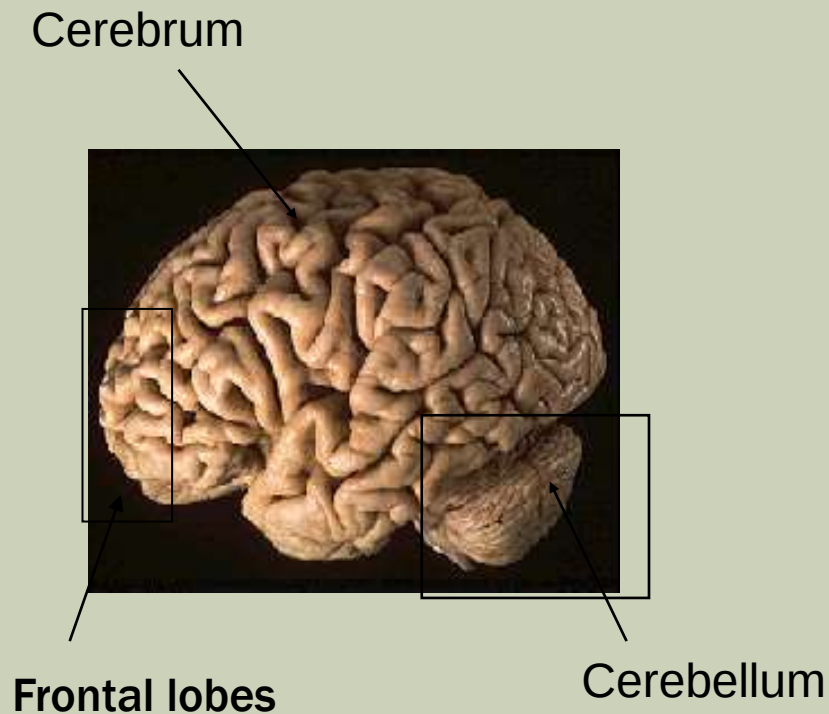
C. Lissencephaly.

D. Heterotopias.

Image courtesy of D. Atkinson, MD.

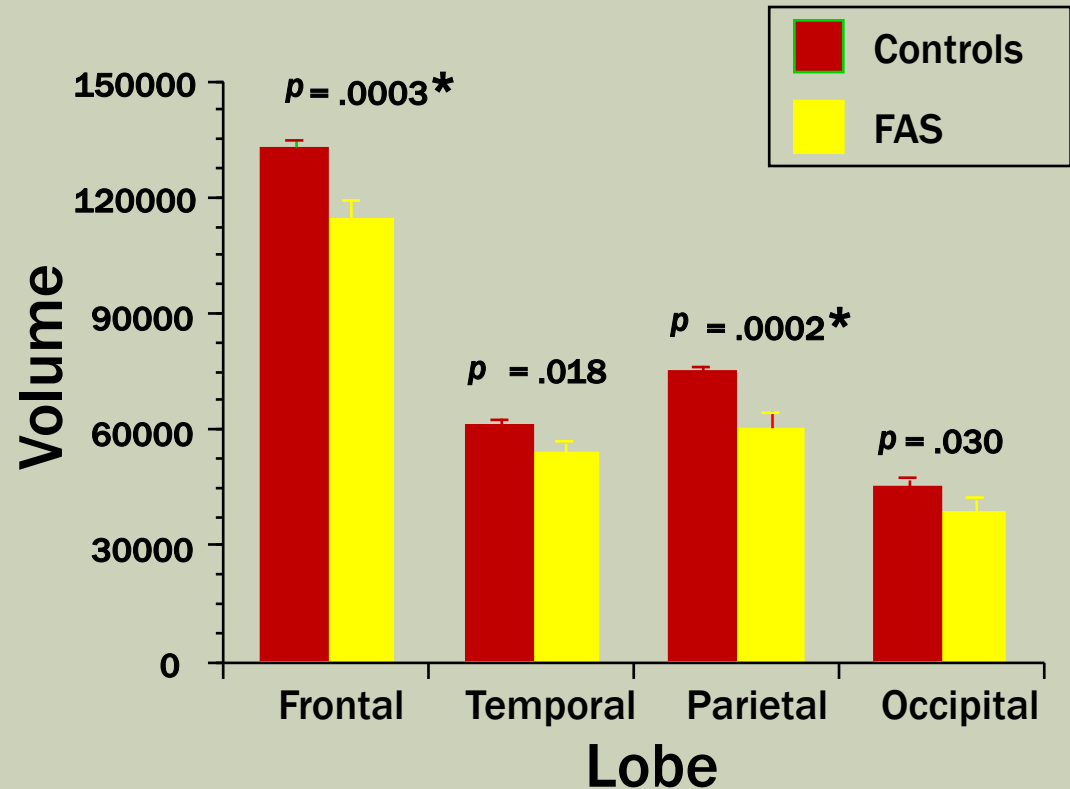
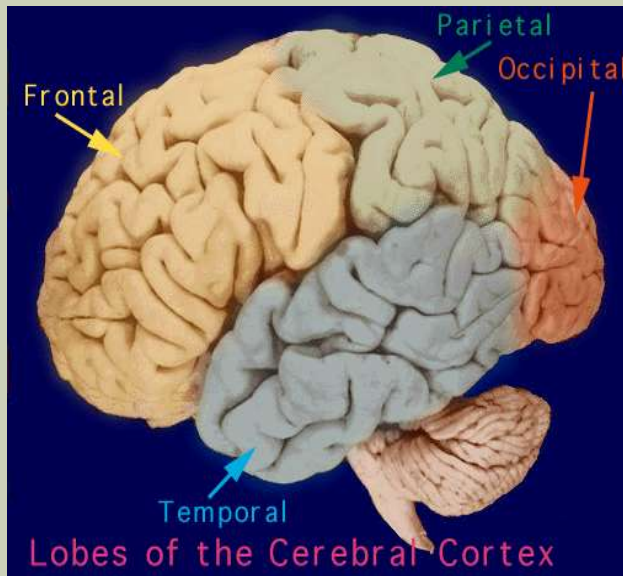


CHANGE IN CEREBRAL SIZE



Mattson et al., 1994

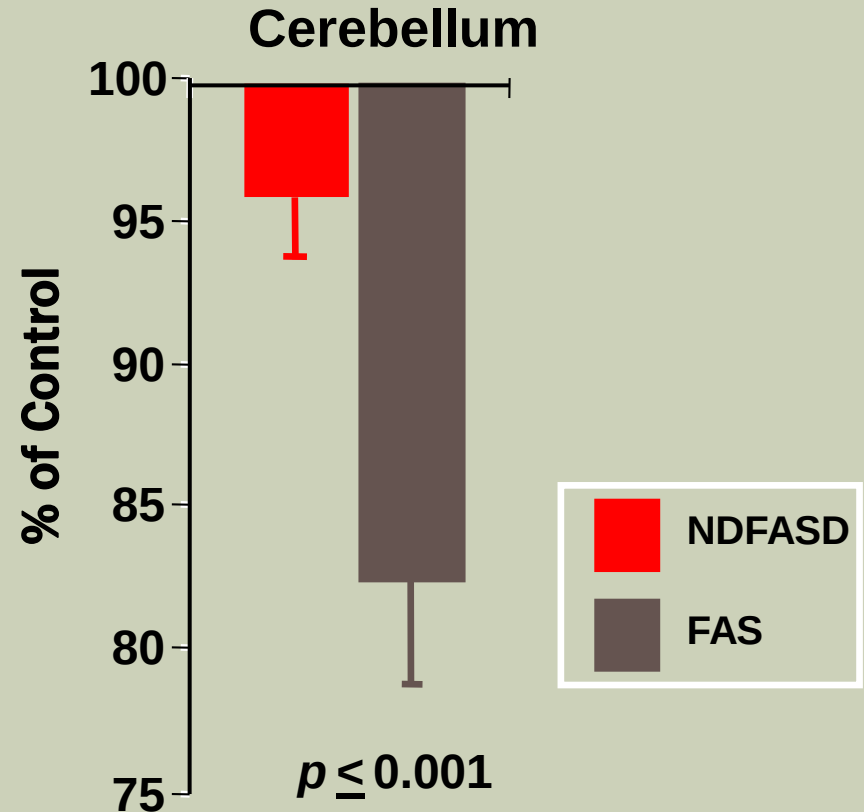
LOBE ANALYSIS



*

* Significant after controlling for overall brain size

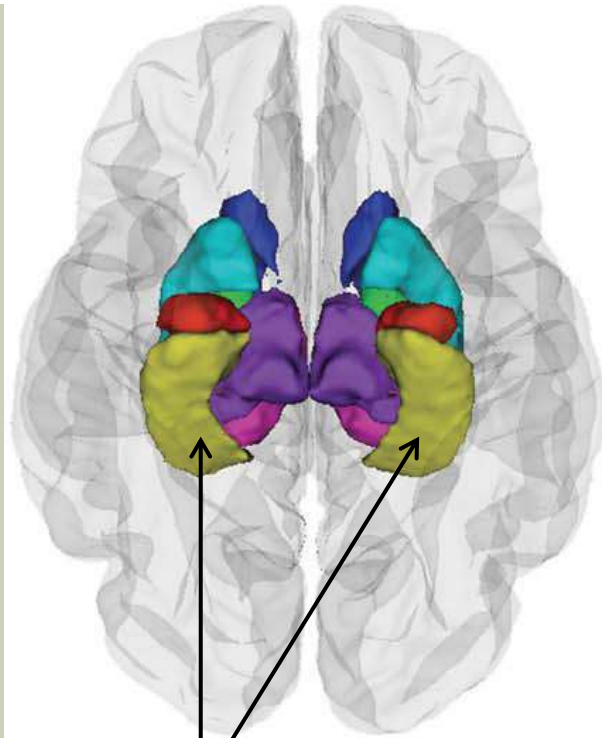
OVERALL BRAIN SIZE - CEREBELLUM



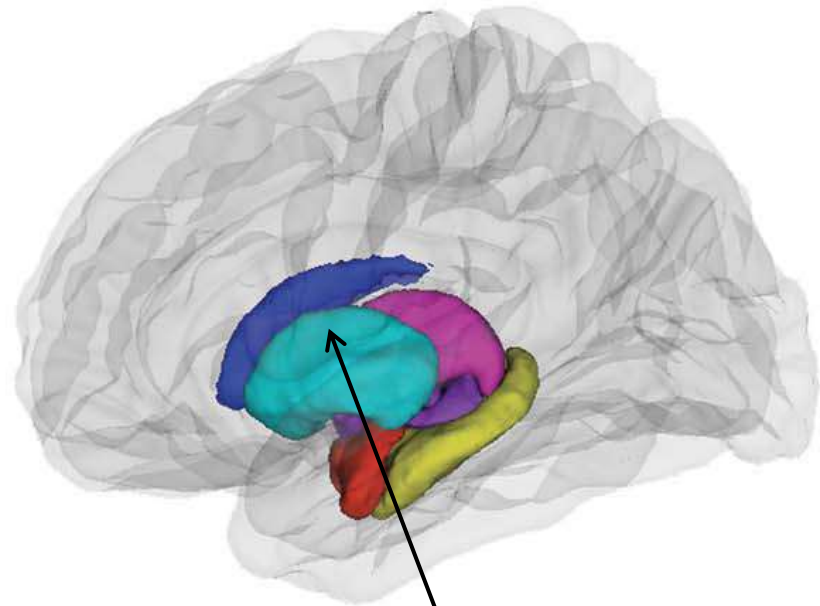
*

Mattson et al., 1994, *Alcohol Health & Research World*, 18(1), 49-52; Mattson et al., 1992; Archibald et al., 2001; Autti-Ramo et al., 2002; O'Hare et al., 2005

REDUCED VOLUME AND INTEGRITY IN VARIOUS SUBCORTICAL AREAS



hippocampus: formation of new memories

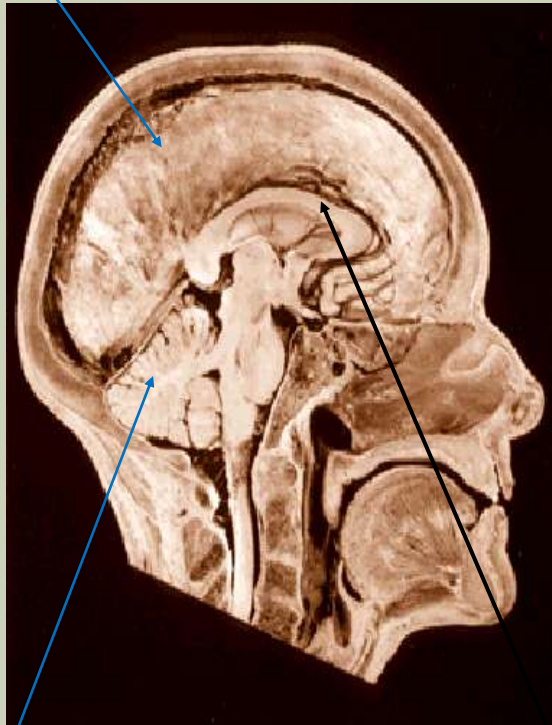


basal ganglia: motor control, cognitive and emotional functions

Slide courtesy of E. Sowell. Mattson et al, 1996; Archibald et al, 2001; Mattson et al, 2002; Riikonen et al, 2005; Astley et al, 2009; Roussotte et al, 2011

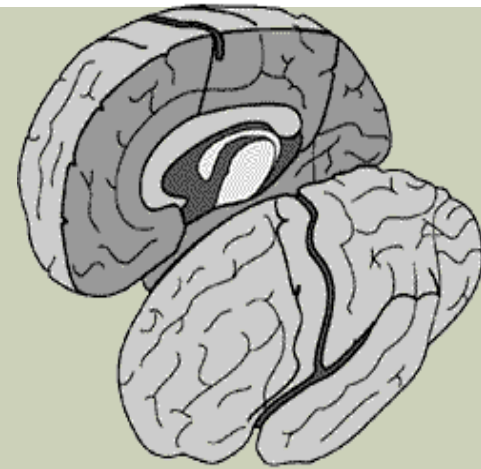
THE CORPUS CALLOSUM

Cerebrum



Cerebellum

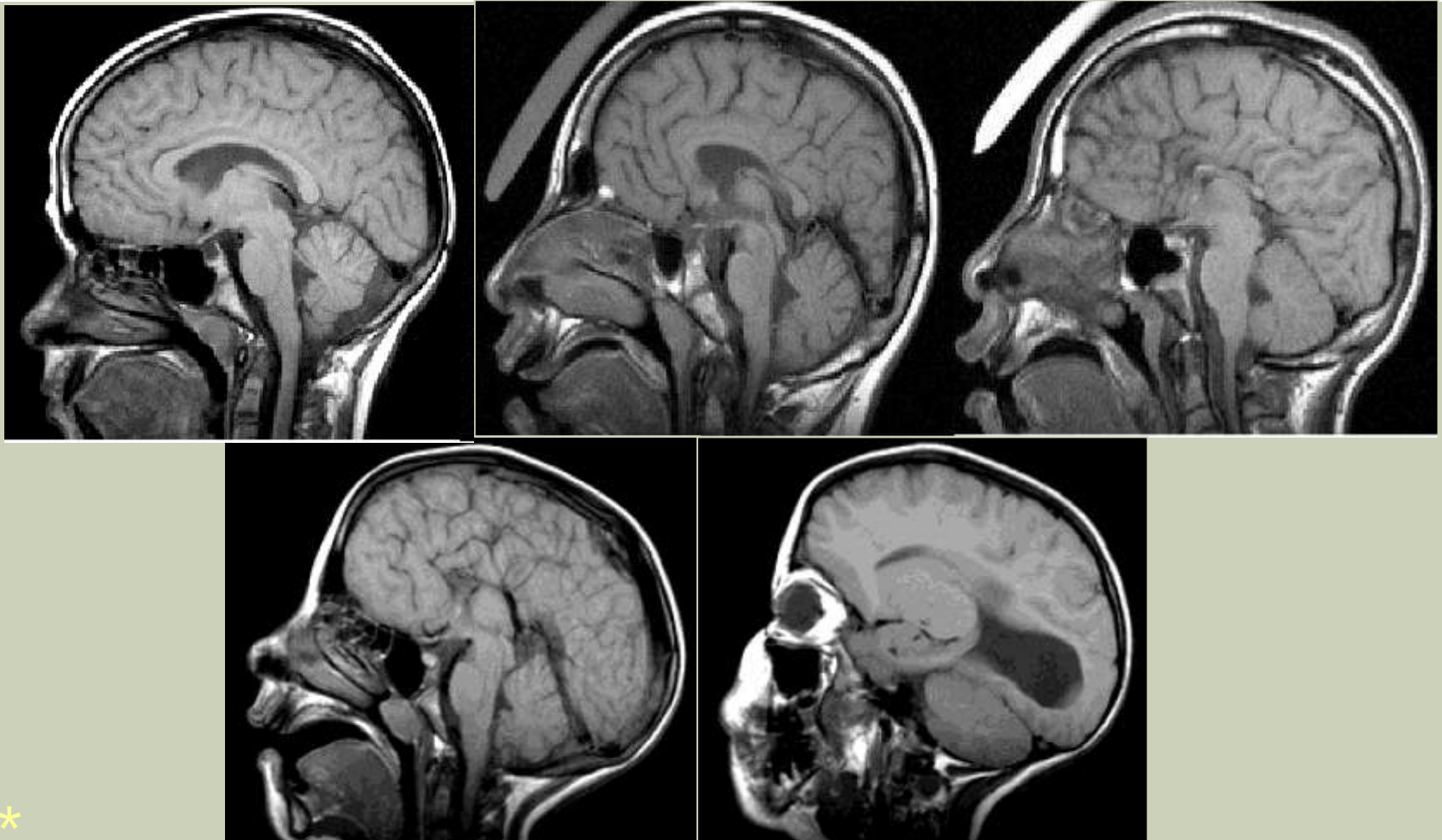
Corpus Callosum



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



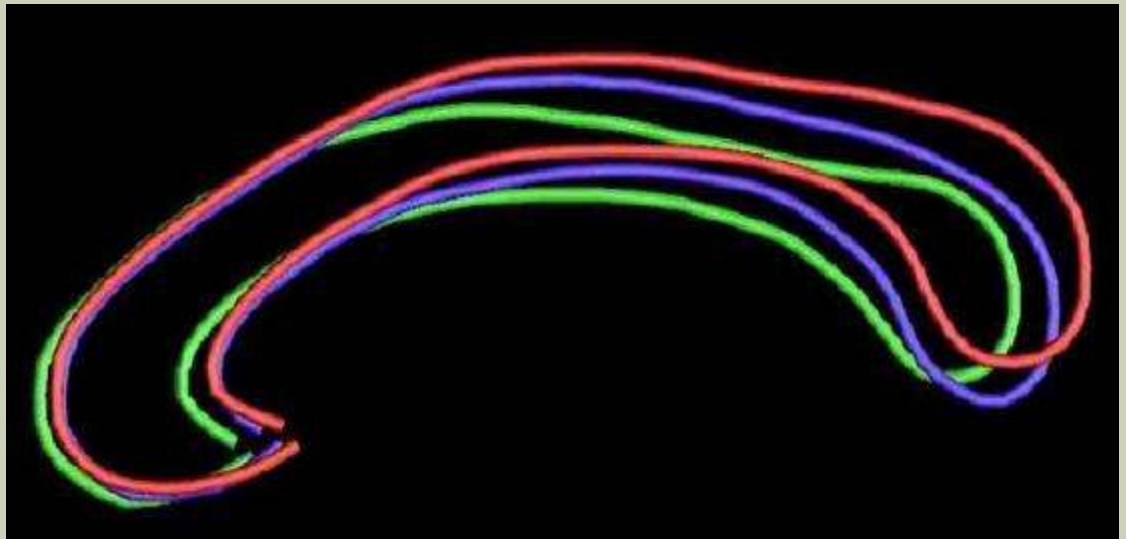
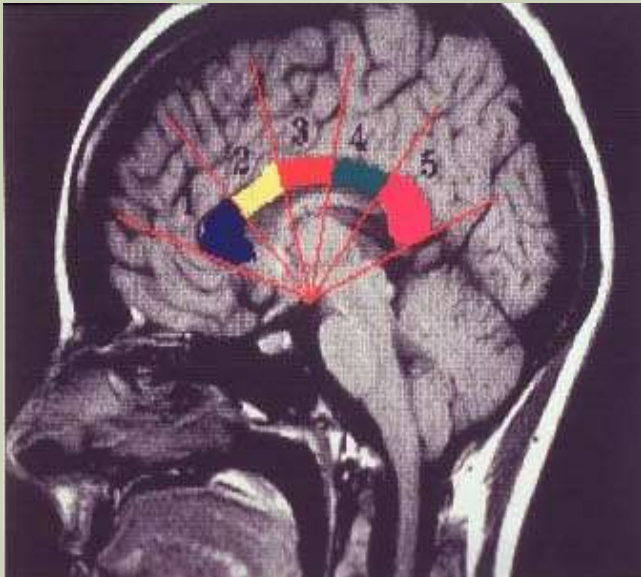
CORPUS CALLOSUM ANOMALIES



*

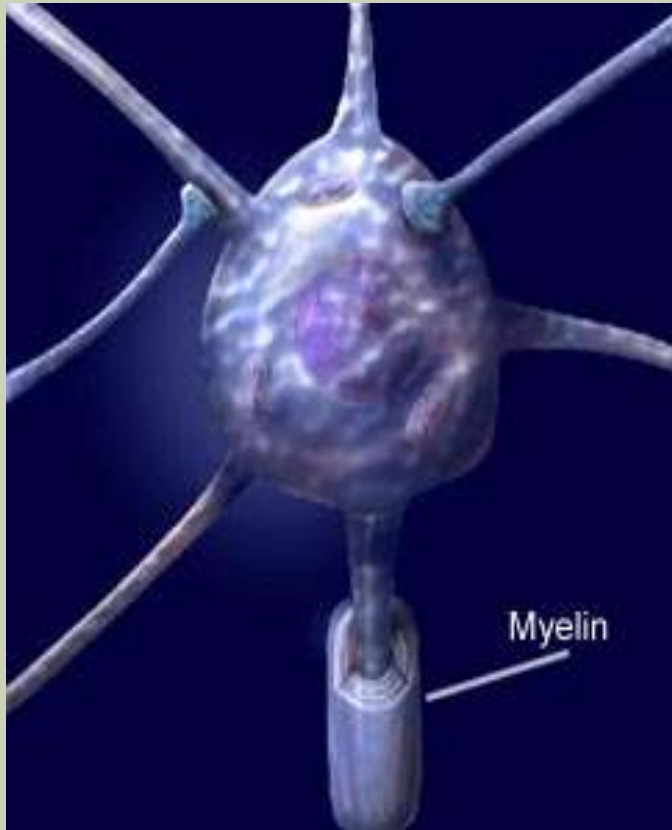
Mattson, et al., 1994, Mattson & Riley, 1995; Riley et al., 1995, Alcohol Health and Research World, 18, 19,

REDUCTIONS IN CORPUS CALLOSUM AREA



■ CON ■ NDFASD ■ FAS

WHITE VERSUS GRAY MATTER



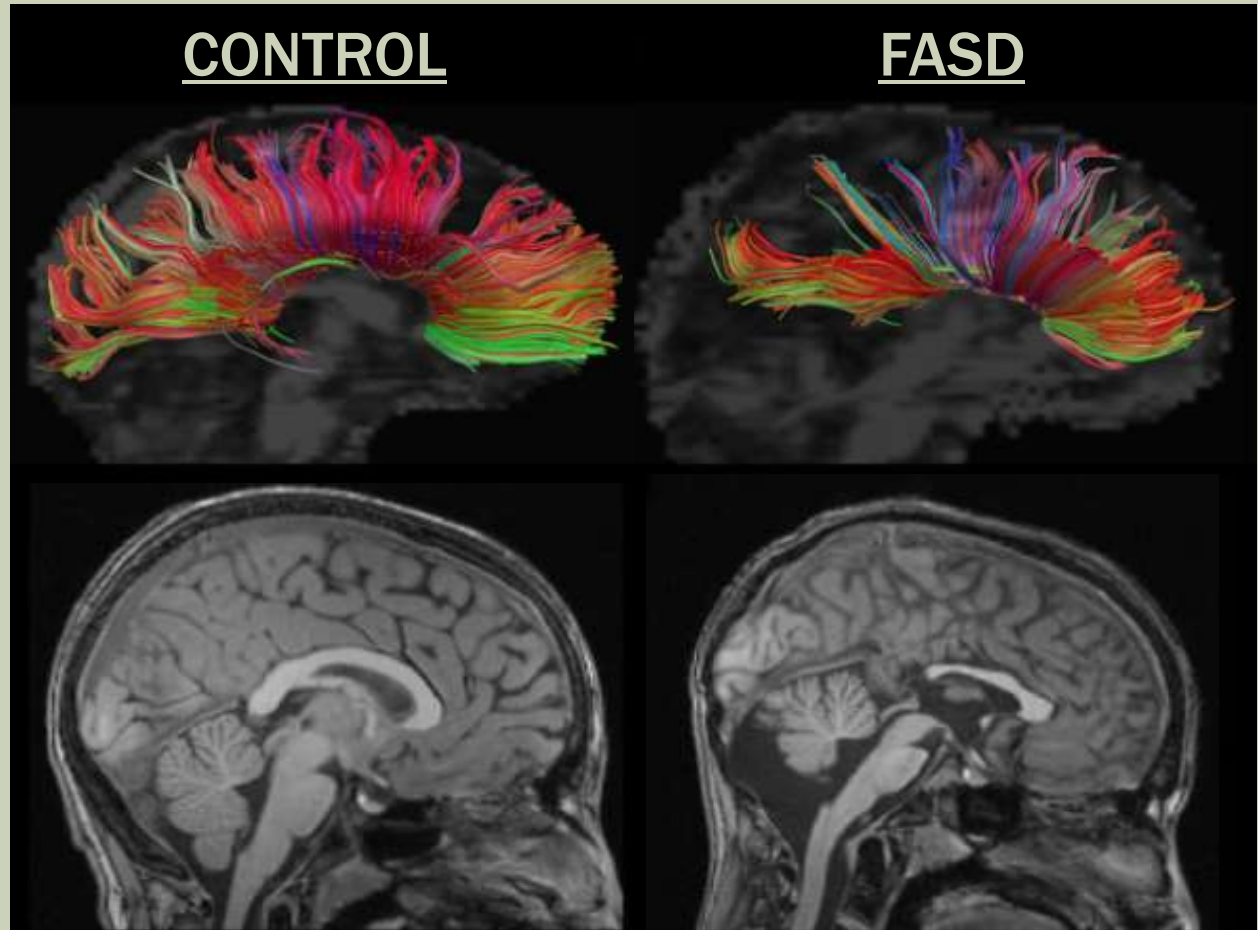
- The white matter coating our nerves. Composed of a layer of proteins packed between two layers of lipids.
 - Produced by specialized cells: oligodendrocytes in the CNS. Myelin sheaths wrap themselves around axons, the threadlike extensions of neurons that make up nerve fibers.
 - Make nerve conduction faster.

DIFFUSION TENSOR IMAGING IN FASD

- Diffusion Tensor Imaging (DTI)

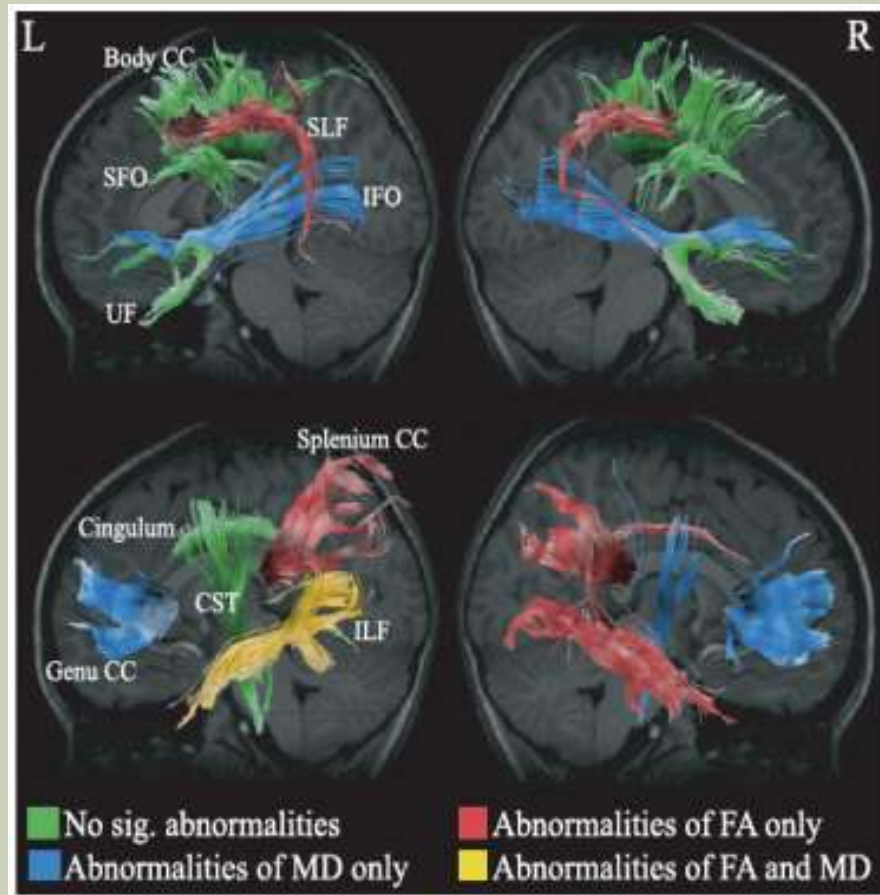
Corpus Callosum

- Decreased integrity of white matter
- Malformed, underdeveloped



(Wozniak & Meutzel, 2011)

WHITE MATTER DEFICITS IN FASD

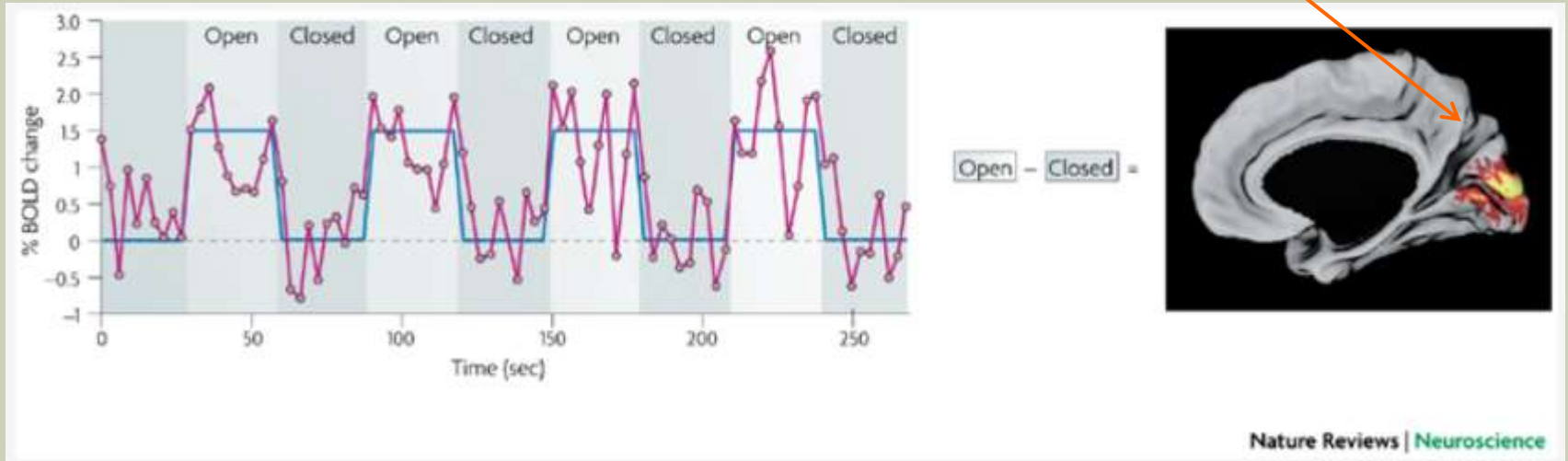


- Found alterations in FA, MD or both in 7 of the 10 tracts assessed.

FUNCTIONAL MAGNETIC RESONANCE IMAGING



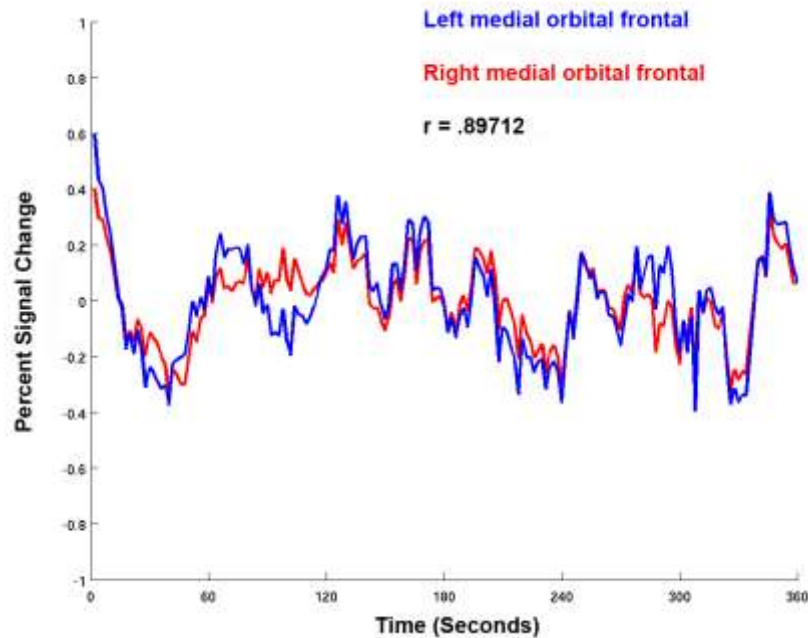
Primary visual cortex



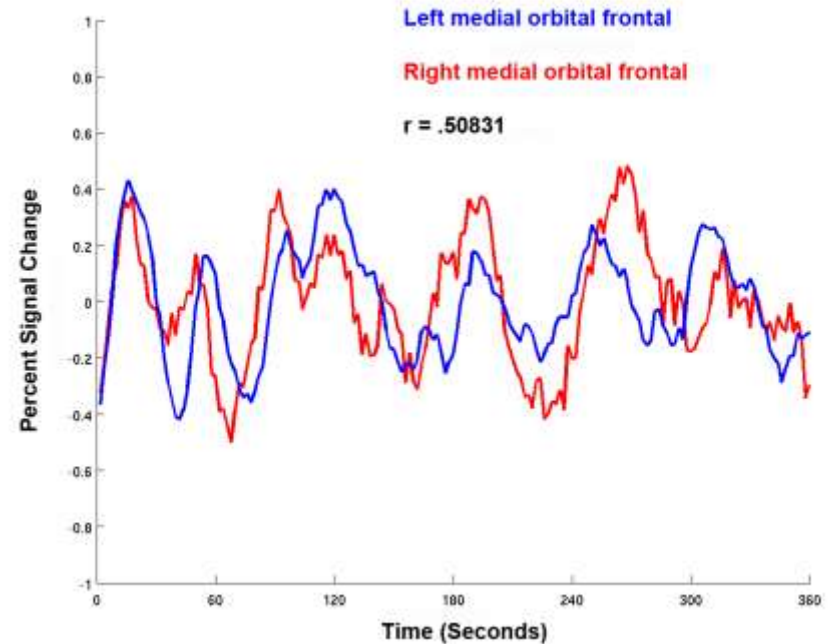
Not what your brain looks like (size, cortical thickness etc.), but, what it is doing, and where.

From Fox and Raichle, 2007

FUNCTIONAL CONNECTIVITY IS IMPACTED IN FASD

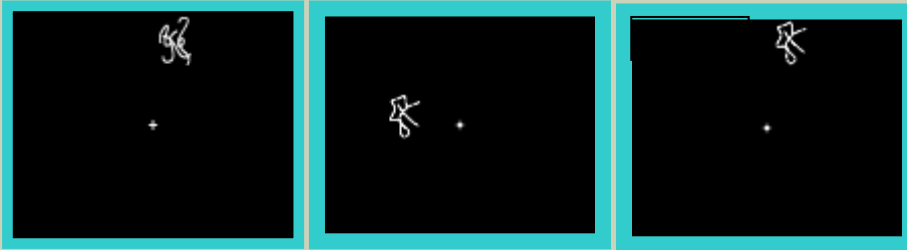


fMRI time-series from one control subject illustrating **high correlation** between brain activity in right and left medial orbital frontal cortex.



fMRI time-series from one FASD subject illustrating **low correlation** between brain activity in right and left medial orbital frontal cortex.

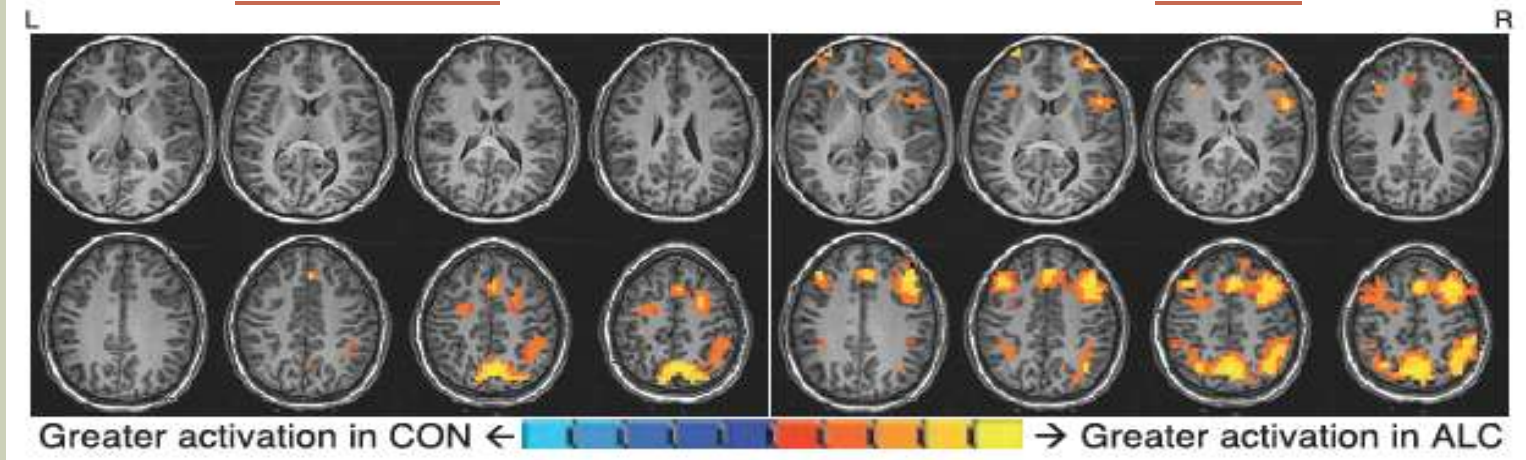
fMRI - SPATIAL WORKING MEMORY TASK



Spatial working memory condition:
“Press the button when a figure appears in the same location that another figure has appeared in.”

CONTROL

FASD

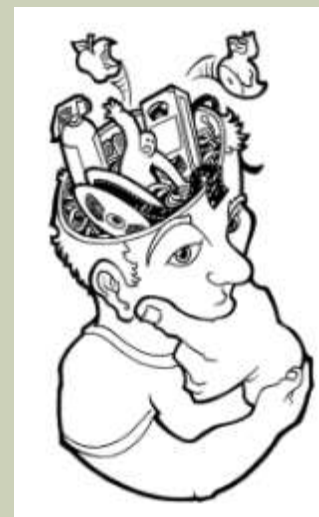


Children with FASD show greater brain activation in the frontal cortex when performing the same level of task demands, compared to normal controls.

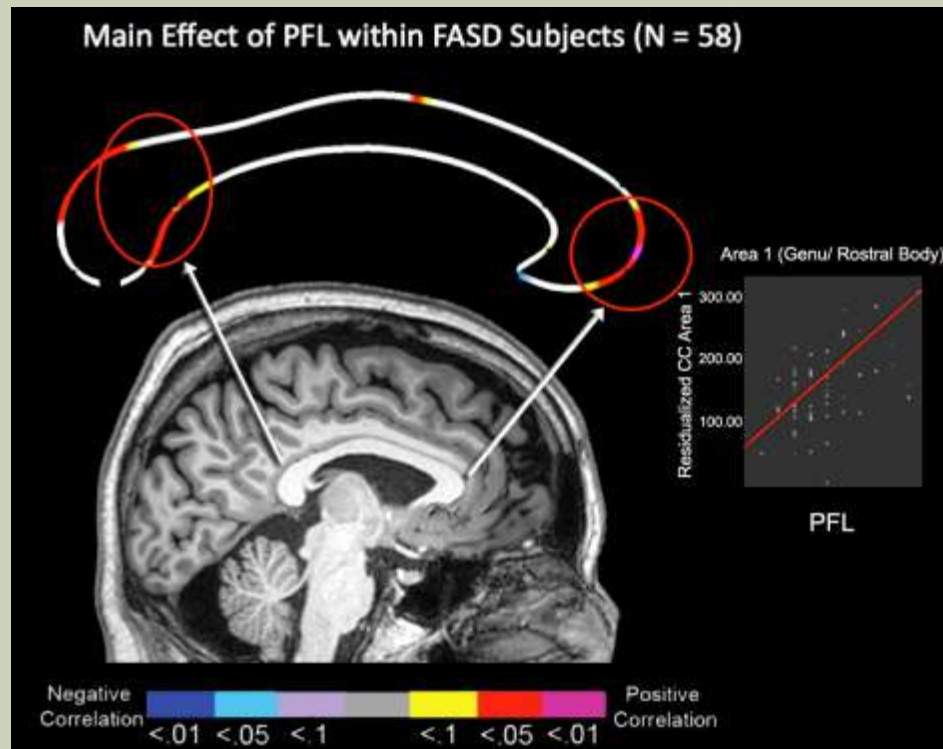
SUMMARY - FMRI IN FASD

■ Abnormal neural functioning in the following domains:

- Memory
- Working memory
- Resting state
- Response inhibition
- Motor functioning



THE FACE IS A WINDOW INTO THE BRAIN



Palpebral Fissure Length (PFL) is the length of the eye opening

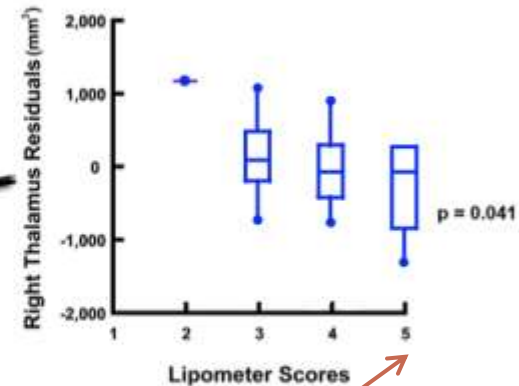
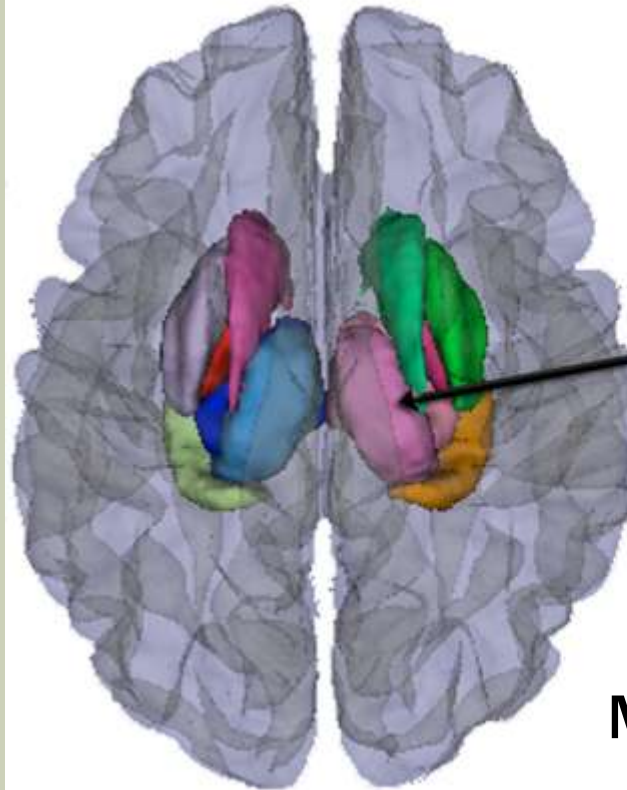


Smaller PFL is related to smaller size of the corpus callosum.

THE FACE IS A WINDOW INTO THE BRAIN:



← **Most severe face**



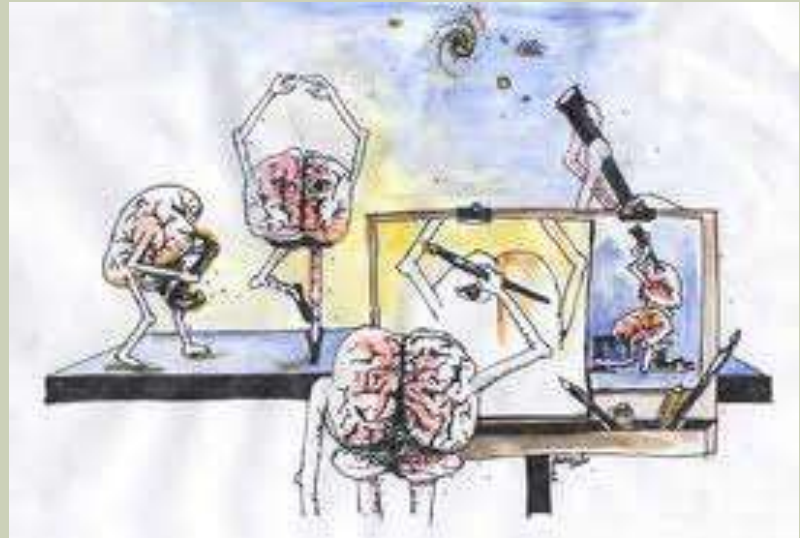
↗ **Most reduced volume**

Adapted from Roussotte et al., 2011, CIFASD

RESEARCH CHALLENGES

- Refine our understanding of the complexities in the neurobehavioral phenotype associated with FASD
 - To achieve more facility in the recognition of these disorders, as many of these individuals go unrecognized as being affected by prenatal alcohol exposure
 - To use this knowledge in the pursuit of appropriate interventions to help those with prenatal alcohol deficits

SO HOW DO THESE ALTERATIONS IN BRAIN IMPACT BEHAVIOR



BEHAVIORAL DYSFUNCTION

Brain changes

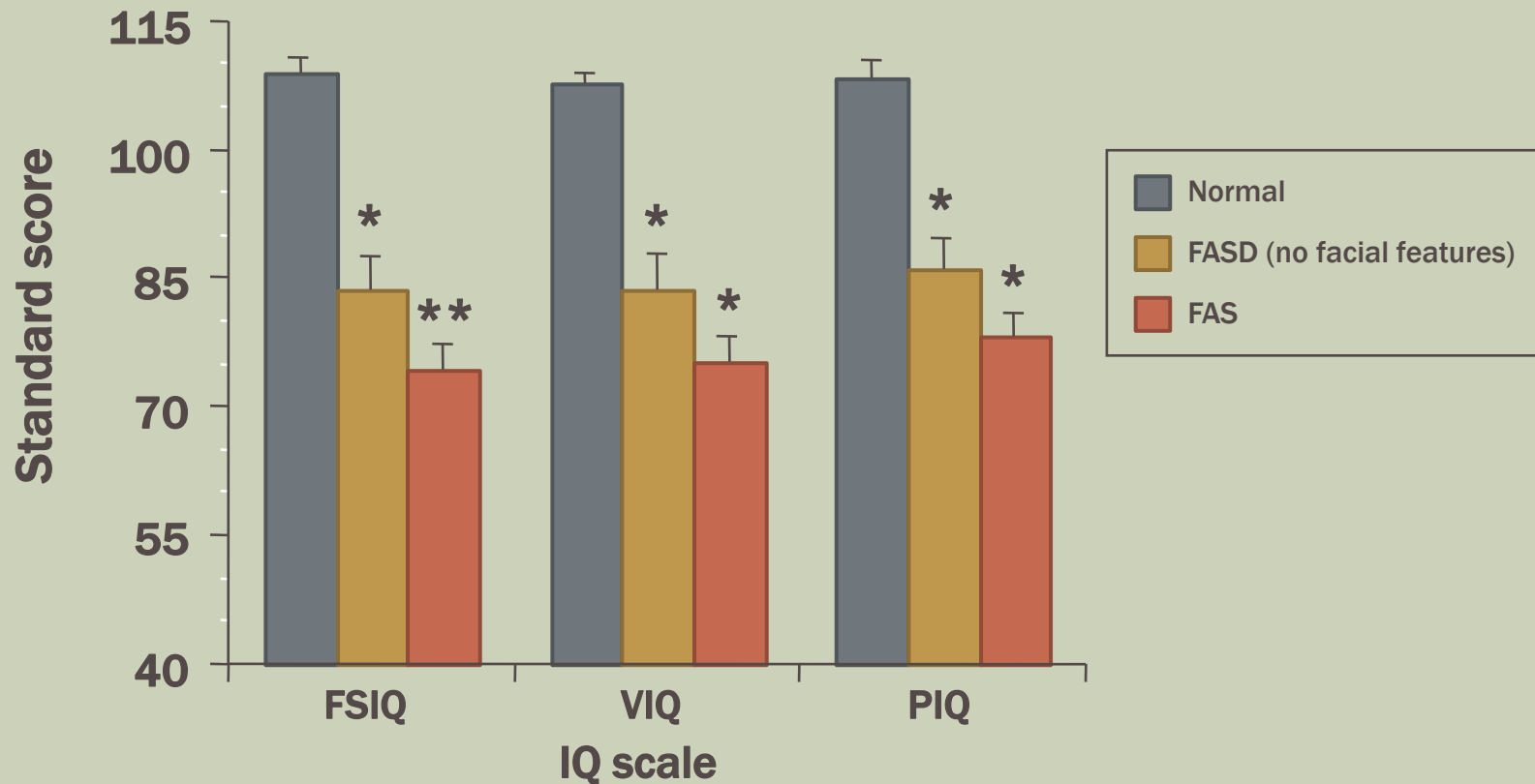
- Global brain
- Cerebral cortex
- Corpus callosum
- Cerebellum
- Hippocampus
- Basal ganglia
- White & gray matter development

Cognition & behavior

- Intellectual development
- Executive function
- Learning & memory
- Visuospatial processing
- Language
- Motor function
- Attention & hyperactivity
- Emotional regulation
- Social cognition

GENERAL INTELLIGENCE

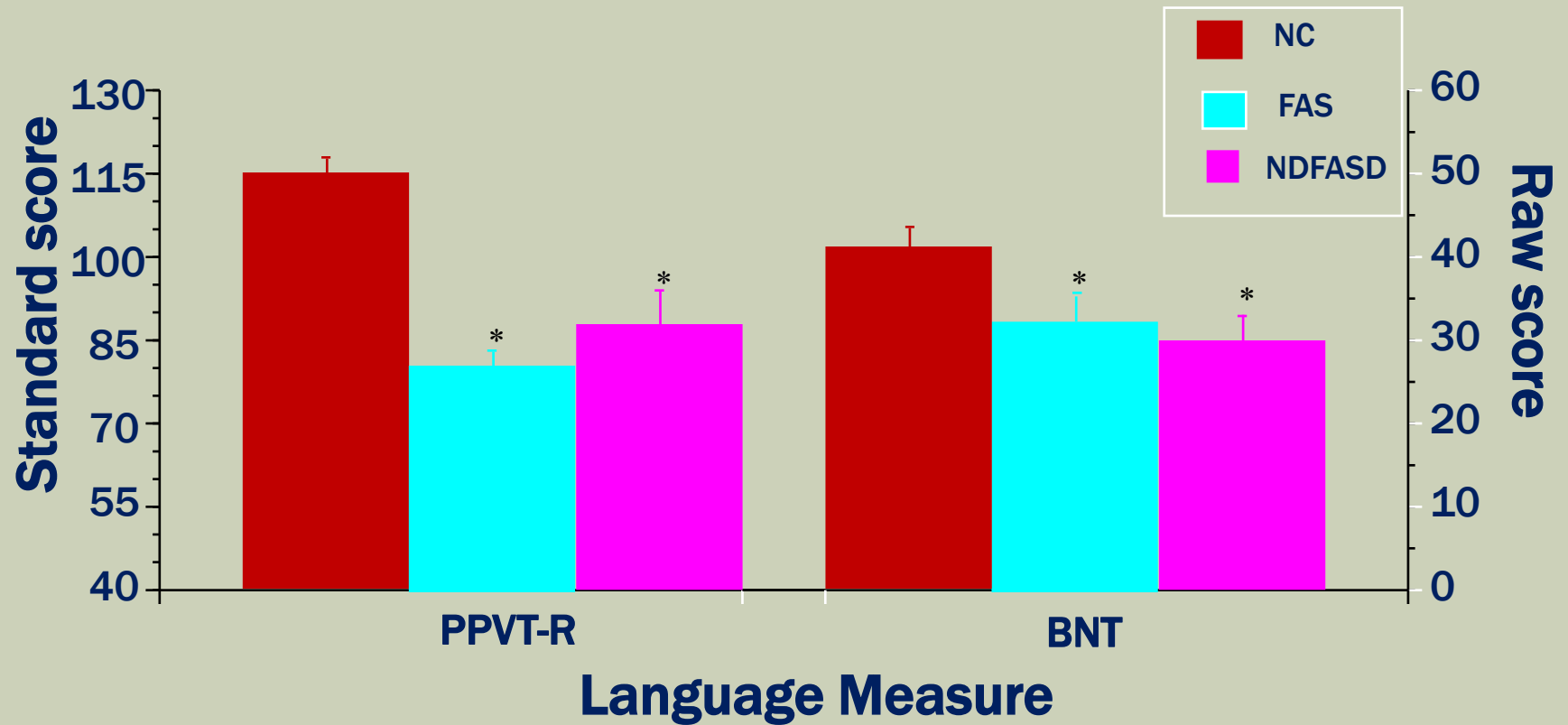
- The average IQ in FAS – low 70's, with facial features – low 80's



BOSTON NAMING TEST AND PPVC



LANGUAGE TEST PERFORMANCE

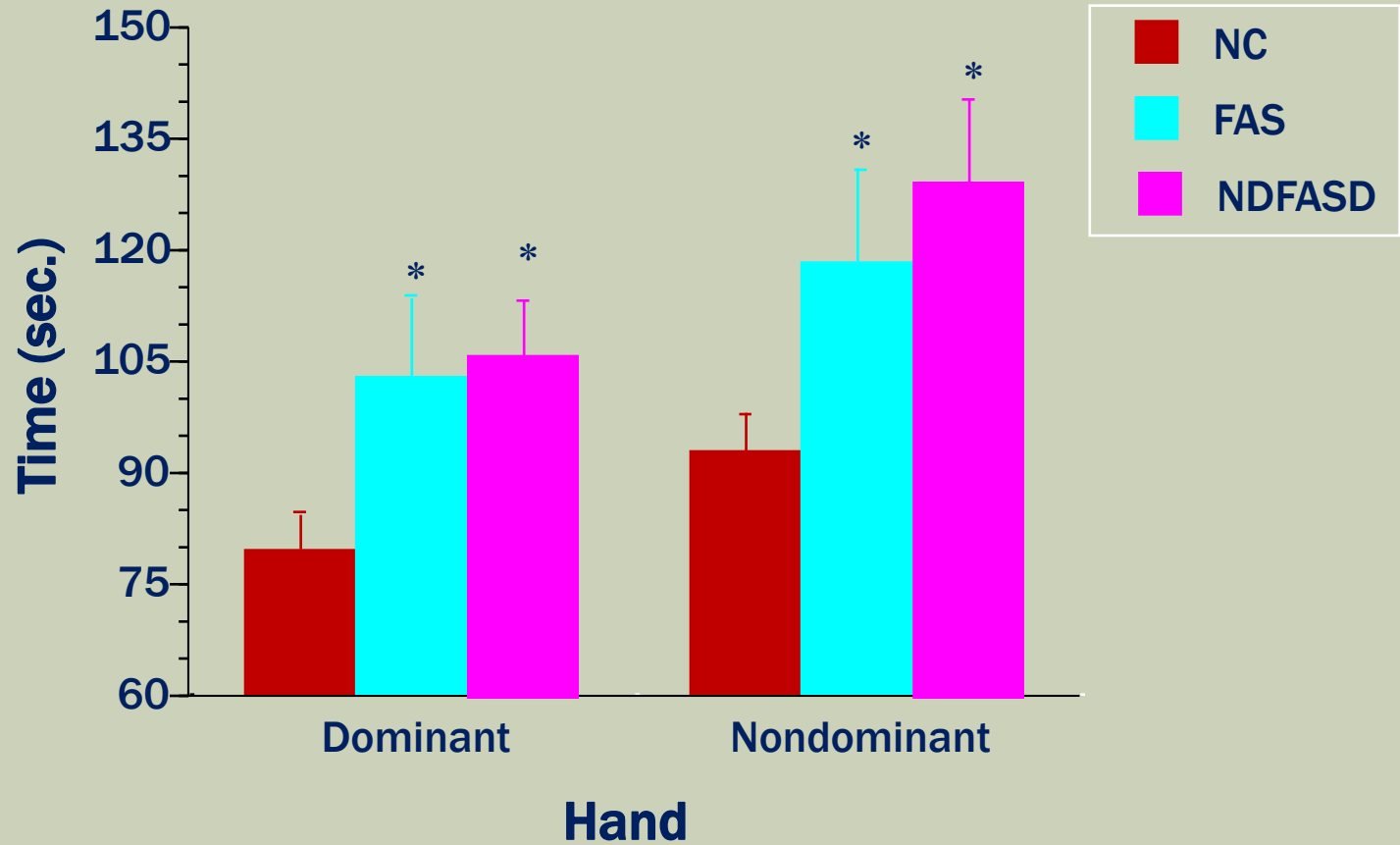


MOTOR FUNCTION

- Children prenatally exposed to alcohol experience a number of motor impairments in both gross and fine motor skills:
 - Poor hand-eye coordination
 - Unstable balance
 - Delayed reaction time
 - Gait difficulties
 - Slowed motor speed
 - Poor force control



FINE-MOTOR SKILL: GROOVED PEGBOARD TEST



ASSESSMENT OF ISOTONIC FORCE

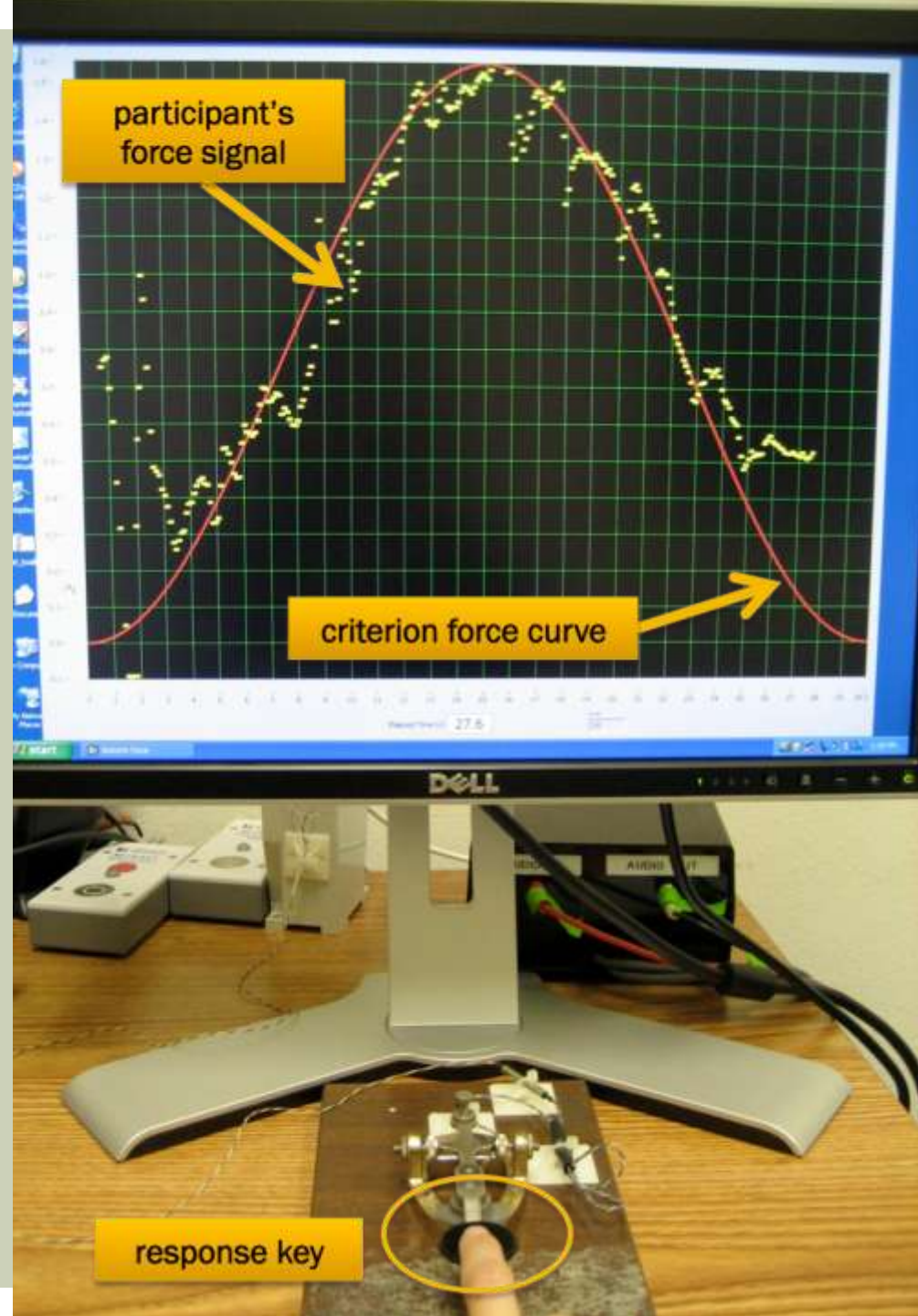
Isotonic force



Isotonic Force

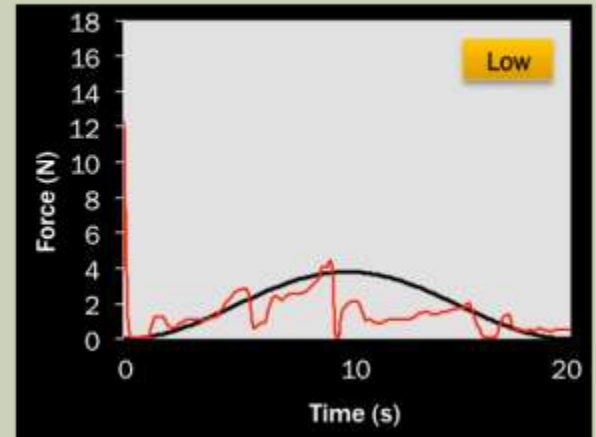
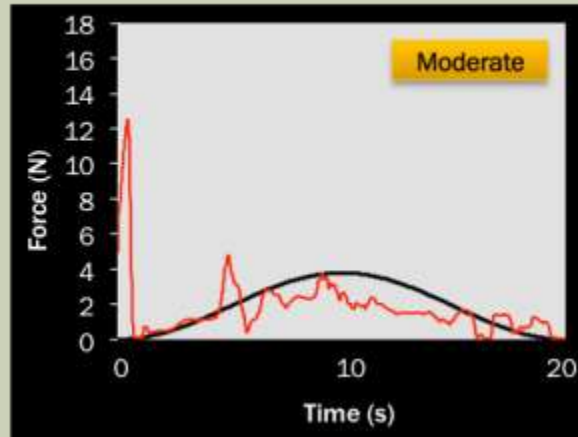
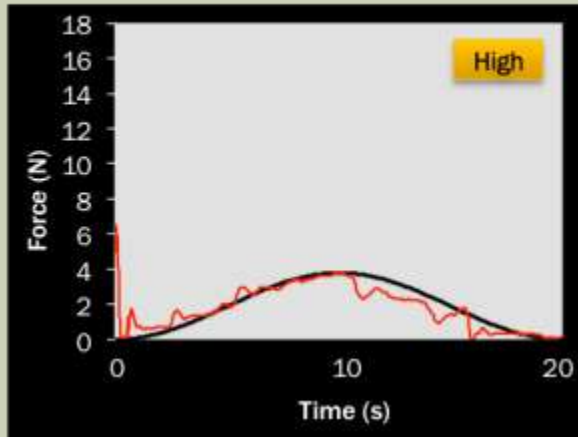
- Participant tried to superimpose their force signal over the target force by increasing or decreasing force to match the bell-shaped curve.
- Visual feedback was provided as a series of yellow dots, which were manipulated to appear at high, moderate, and low frequencies.

Isotonic force contractions based on Deutsch & Newell, 2001

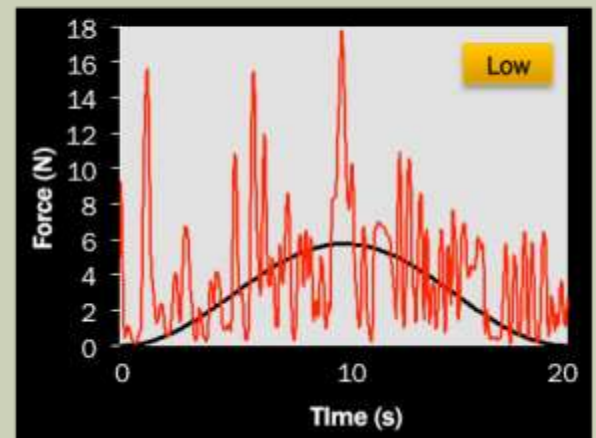
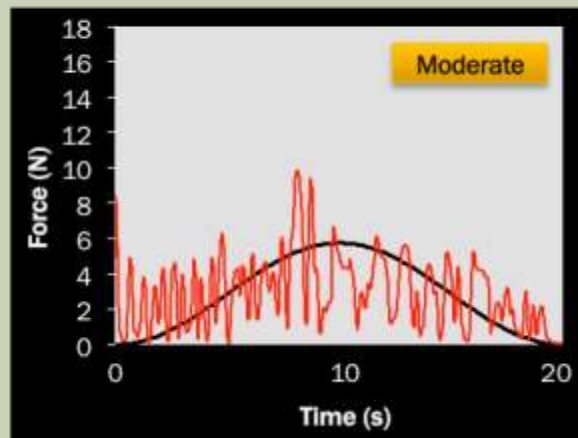
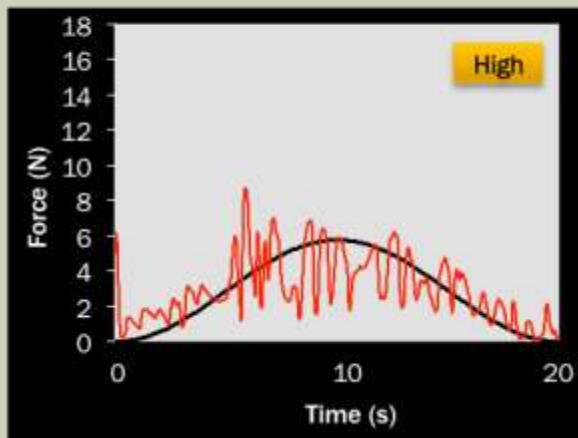


REPRESENTATIVE ISOTONIC RESPONSES

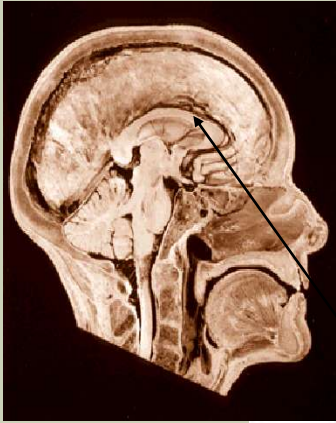
CON Group



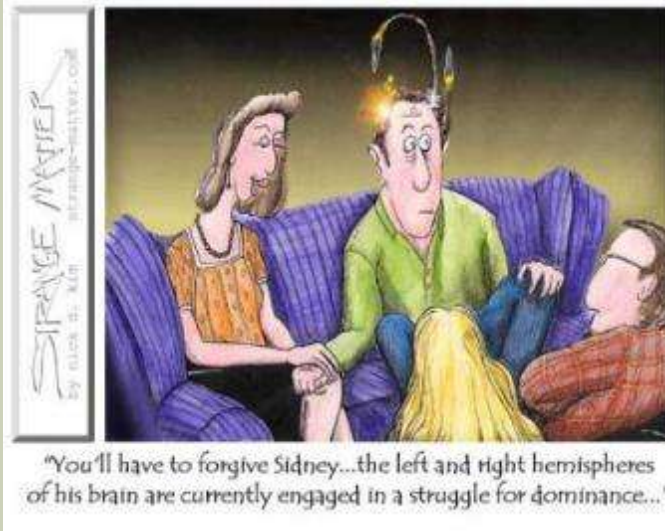
ALC Group



INTERHEMISPHERIC DEFICITS



Corpus Callosum



Cooperation Between the Hemispheres and “Innocent Delinquency”

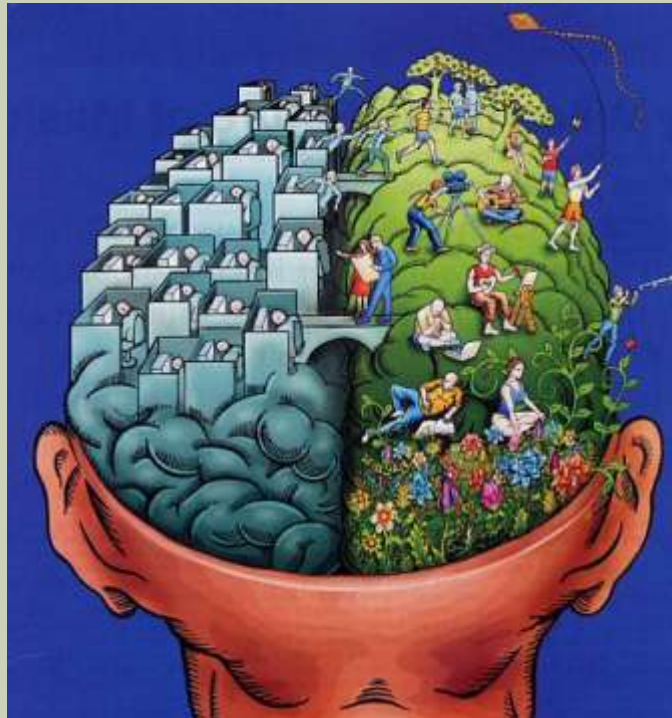
We expect changes in behavior where information has to cross the corpus callosum

LEFT BRAIN/RIGHT BRAIN

THE CORPUS CALLOSUM

Left Brain

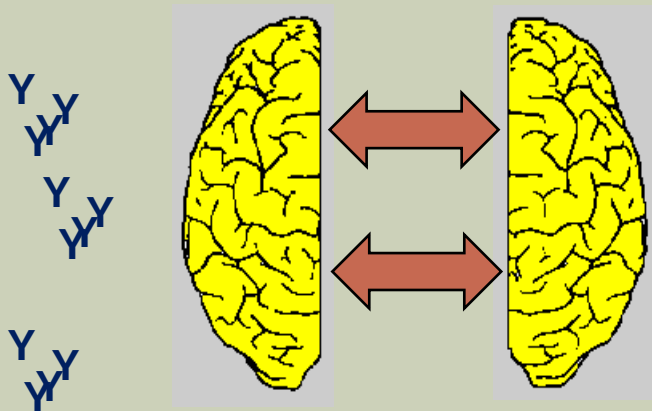
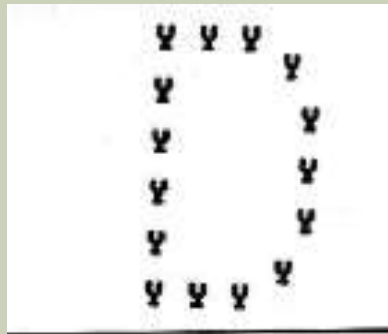
- Language
- Math
- Logic



Right Brain

- Spatial abilities
- Face recognition
- Visual imagery
- Music

WHAT EACH HALF OF THE BRAIN SEES



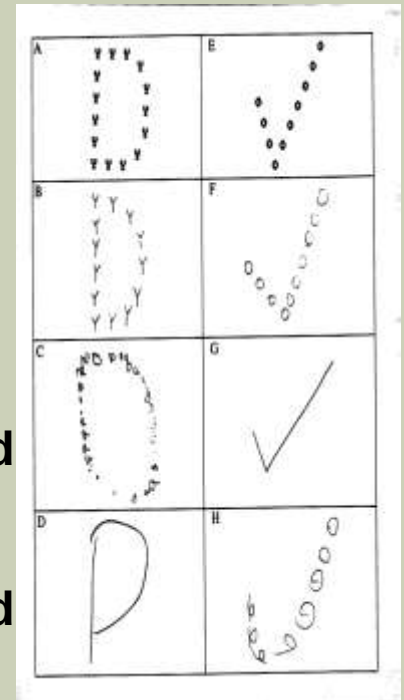
D

Stimuli

Controls

Alcohol-exposed

Alcohol-exposed



EXECUTIVE FUNCTIONS

“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)

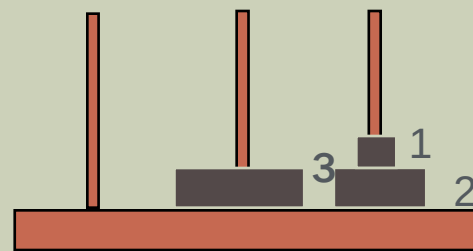
EXECUTIVE FUNCTIONING

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

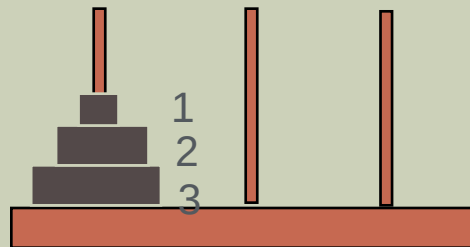
- **The ability to organize and plan**
- **Focus and maintain attention**
- **Be able to store memories and retrieve them**
- **Issues related to affect and inhibition, e.g. preventing anger from getting out of control**
- **Relies heavily on frontal lobes and subcortical structures connecting to frontal areas**



EXECUTIVE FUNCTIONING TOWER OF CALIFORNIA TEST

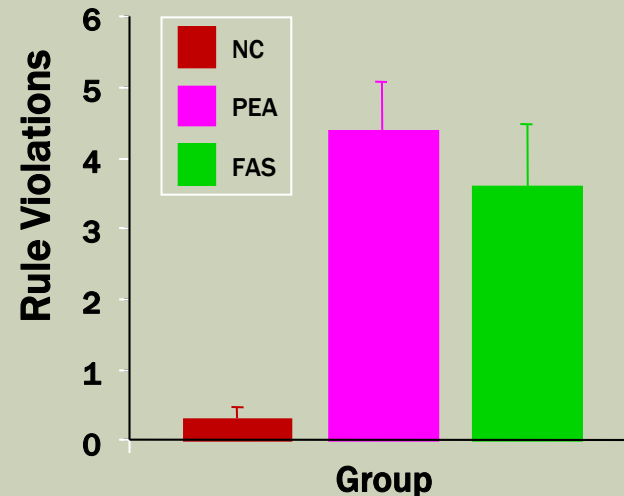
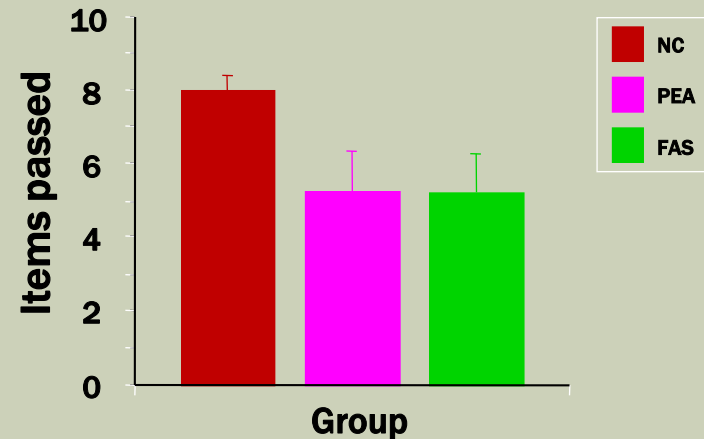


Starting position



Ending position

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



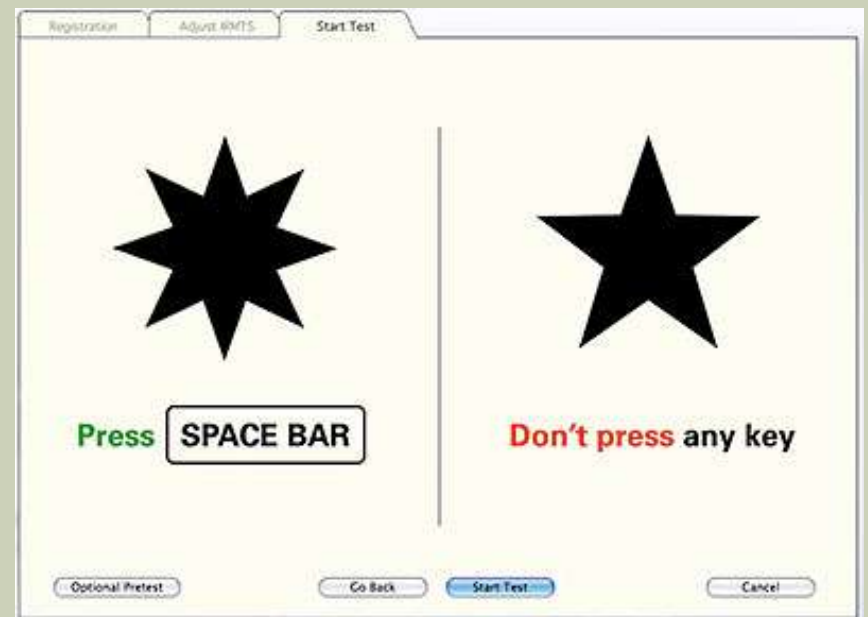
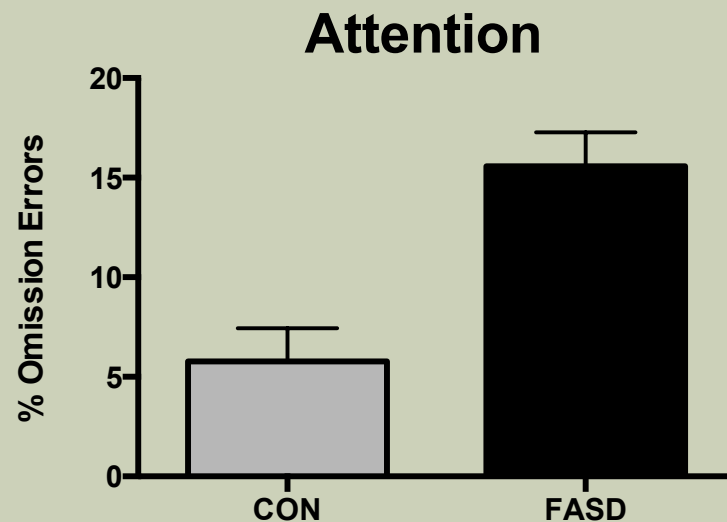
CONCEPT FORMATION TWENTY QUESTIONS



ATTENTION

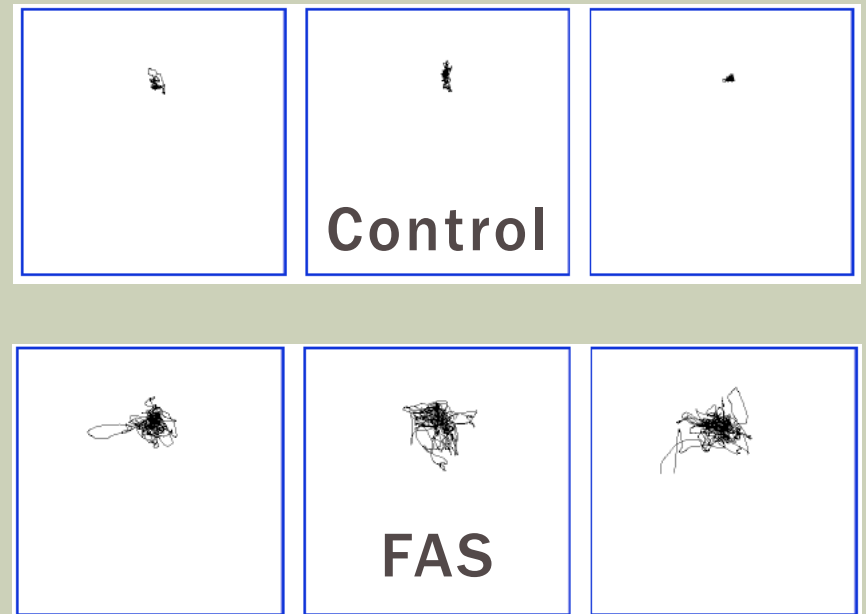
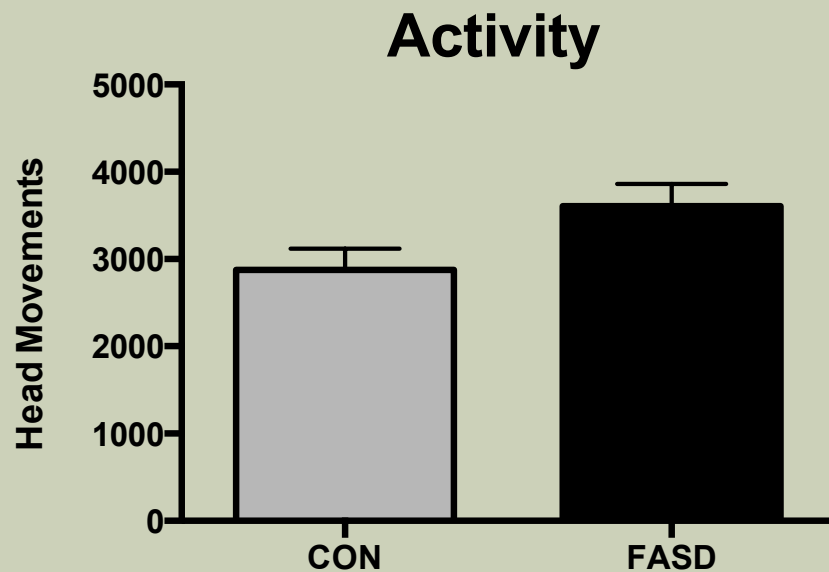


ATTENTION TASK



Infante et al., submitted

HEAD MOTION



RESEARCH CHALLENGES

- **Improve Diagnostic Capabilities to:**
 - Determine the full prevalence of all of the disorders that lie within the spectrum of FASD
 - Develop simple, reliable methods to make these diagnosis
 - Identify women at risk for giving birth to a child with an FASD
 - Identify individuals in need of care and services along the full range of the FASD Spectrum

Adapted from talk by K. Warren

FACIAL FEATURES OF FETAL ALCOHOL SYNDROME

Discriminating Features

Short palpebral fissure

Indistinct philtrum

Thin upper lip

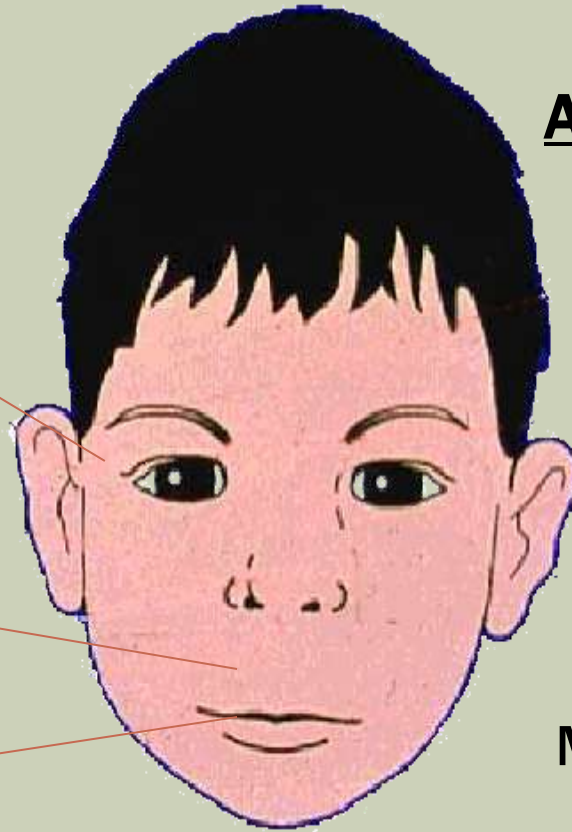
Associated Features

Epicanthal folds

Low nasal bridge

Minor ear anomalies

Micrognathia



In the child

Streissguth, 1994

Ways to Improve Diagnosis

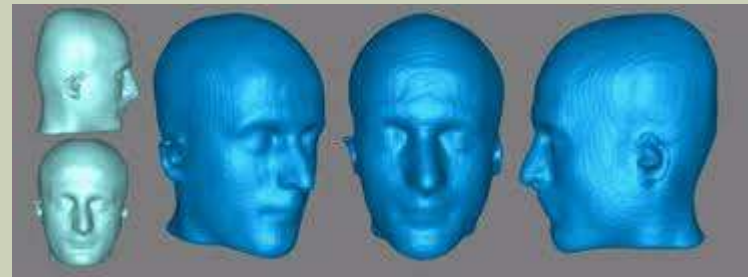
3 D Facial Imaging and Analysis



FAS



FASD



Peter Hammond and Tatiana Foroud

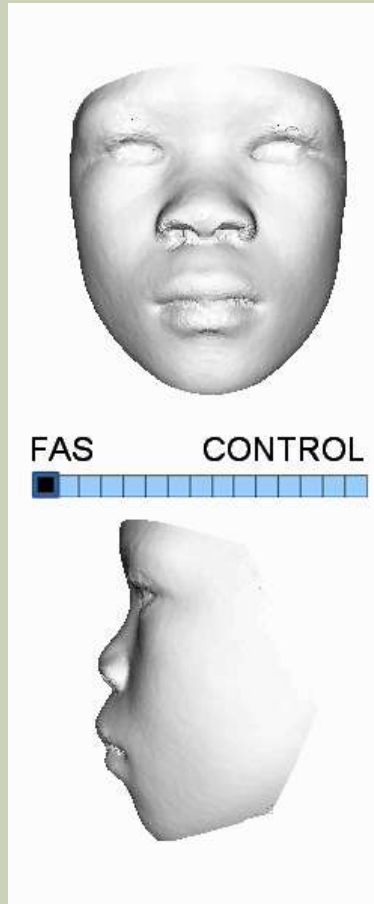
COMPARISON OF FACE OF CHILD WITH FAS TO AVERAGE OF MATCHED CONTROLS

Front view

smooth upper lip
inner eye folds

Profile view

short nose
flat nasal bridge
mid-facial flatness
backward rotation of jaw

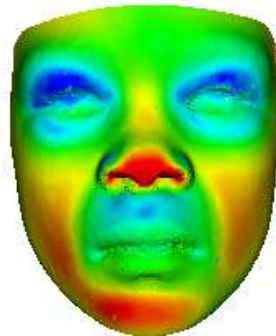


FAS - MALE

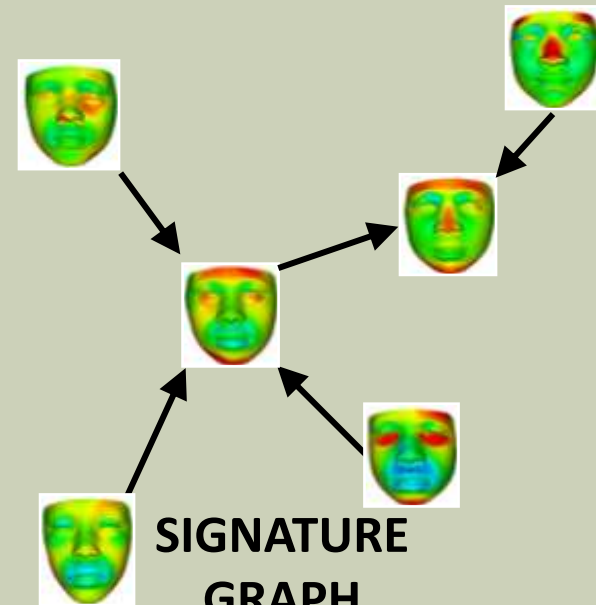


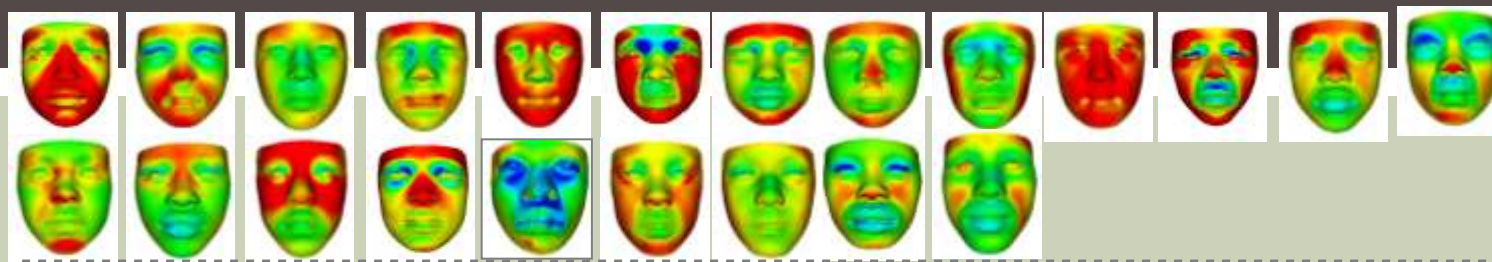
3D FACE ANALYSIS AND RELATION TO BEHAVIOR

FAS - MALE

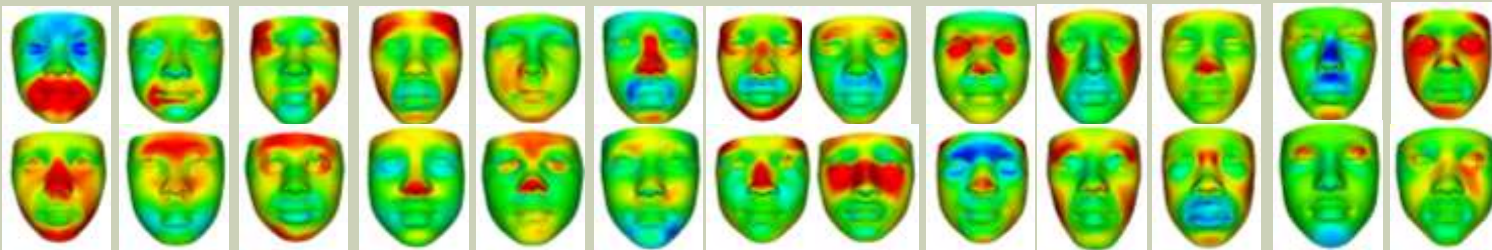


FACE
SIGNATURE
red-contracted
blue-expanded

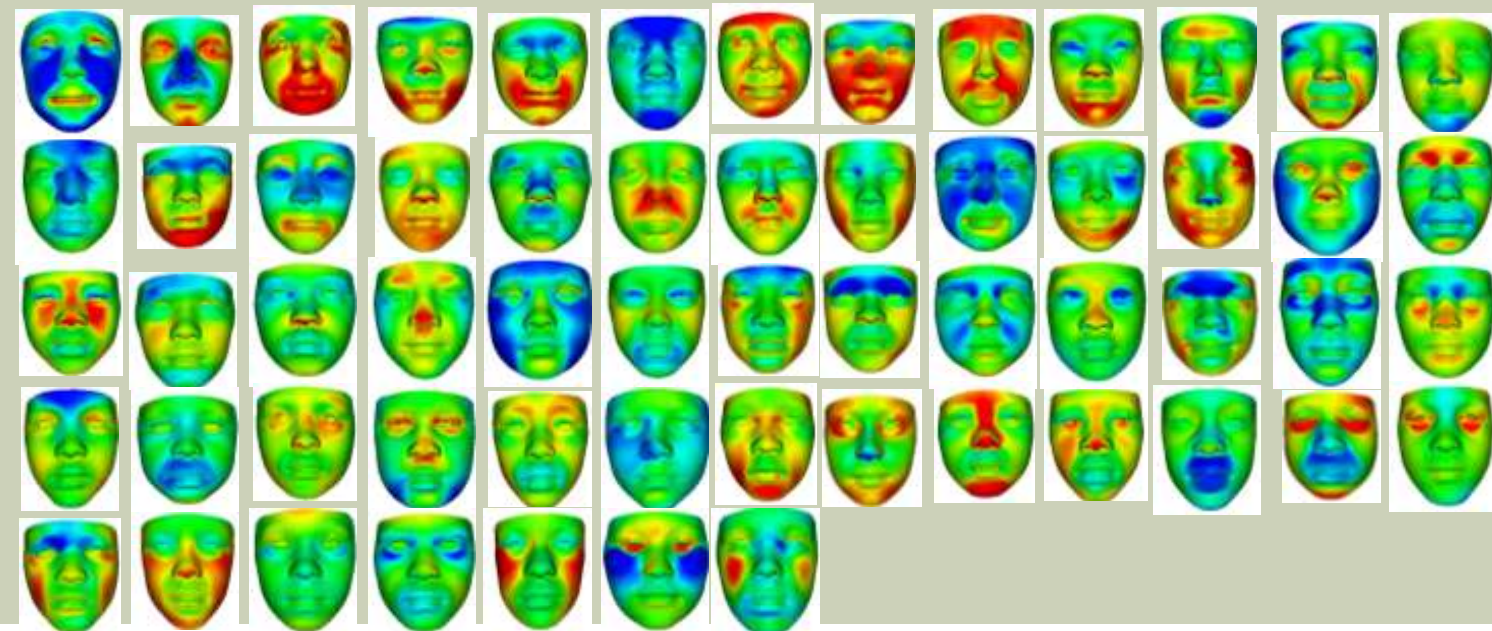




FAS



PFAS



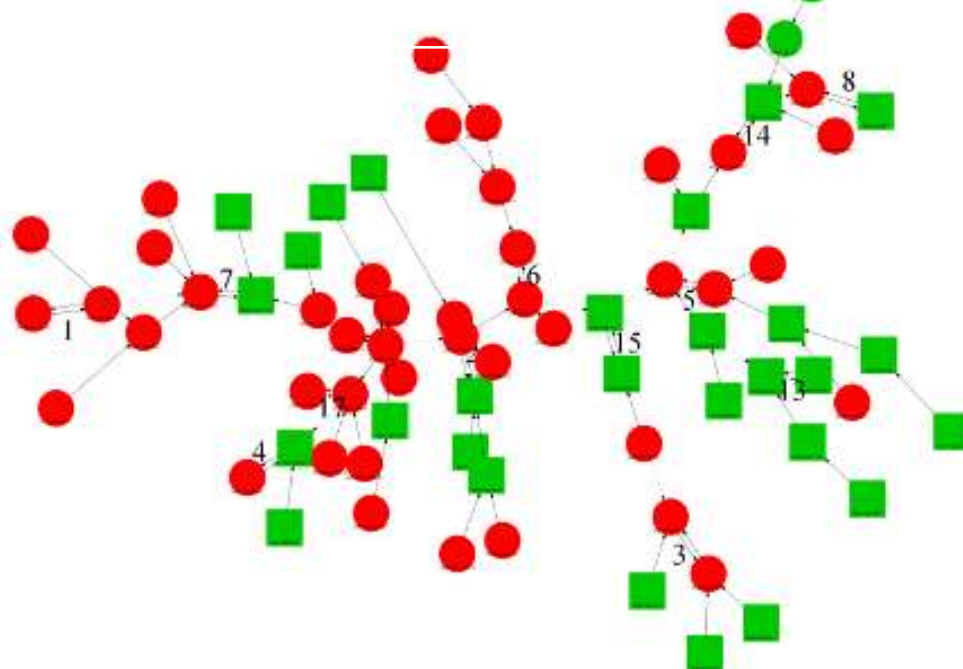
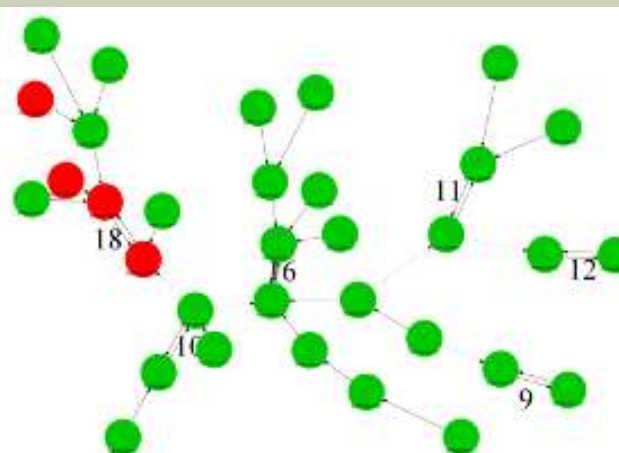
HE

FACE CLUSTERS: FAS, PFAS & HE

	HE2	HC
WISC IQ	73.3	73.3
CVLT-C 1	47.3	45.8
CVLT-C 2	93.7	93.2

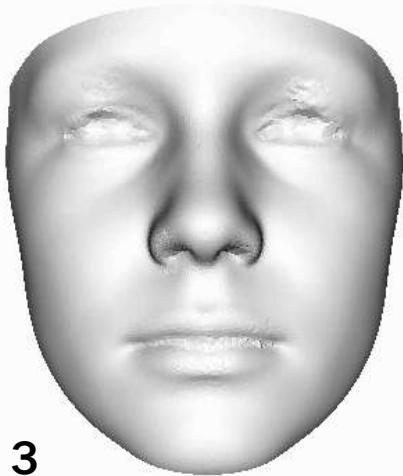
es more

7

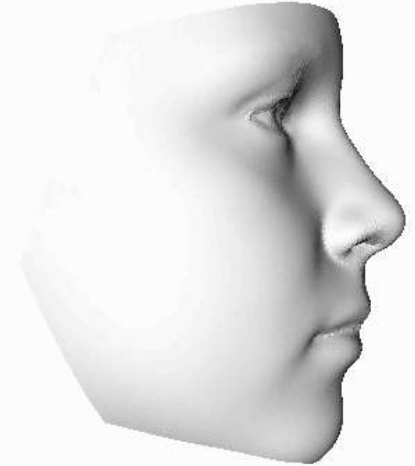
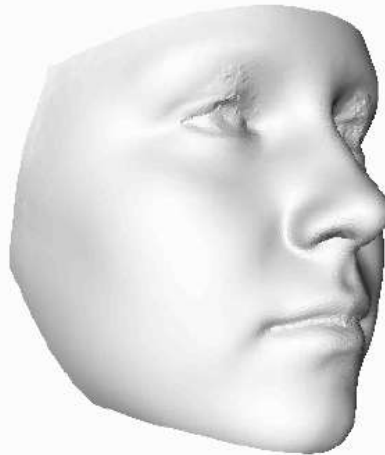


HF1	HE1	FAS	PFAS
WISC IQ	65.5	65.4	63.0
CVLT-C 1	40.0	42.7	41.5
CVLT-C 2	84.3	88.5	88.3

TELEMEDICINE



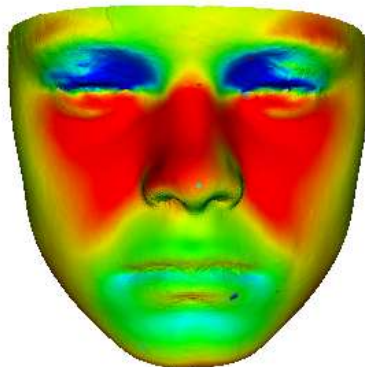
ID: 3
Male age 12



Age Matched
Control



Individual



- ☐ Unaffected control
- ☐ FAS
- ☐ Deferred
- ☐ Unknown/other

Additional Comments:





HENRI CARTIER-BRESSON

Rue Mouffetard Paris 1954

Incidence of
FAS in
subsequent
births per
1,000 live
births

771

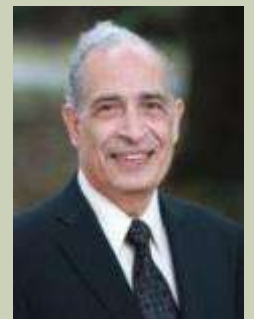
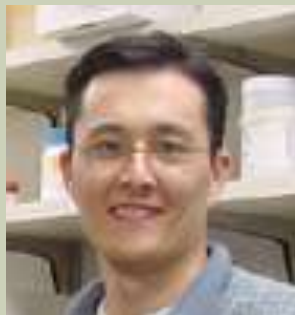
THANKS TO MY COLLEAGUES, STUDENTS, POSTDOCS, AND THE FAMILIES



**Eileen Moore
Alejandre Infante
Robyn Migliorini**



MANY THANK TO THE NIAAA AND THE FOLKS THERE



THANK YOU

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