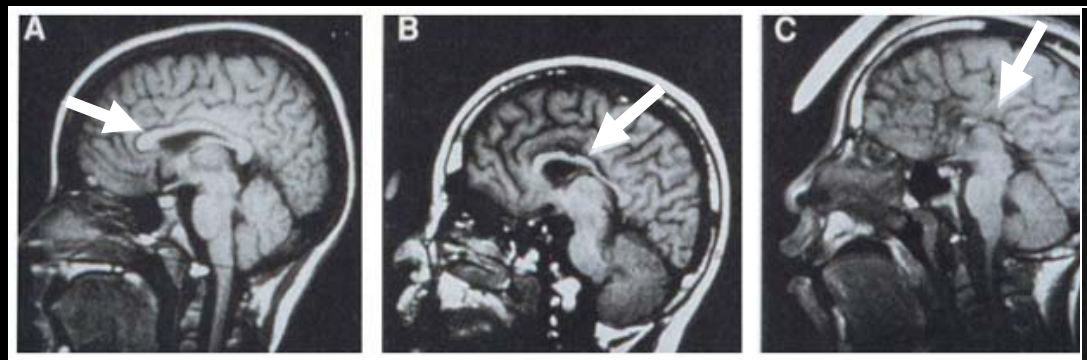
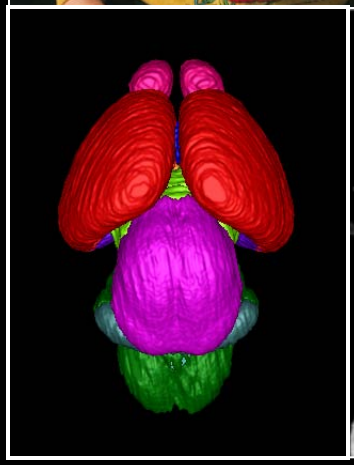
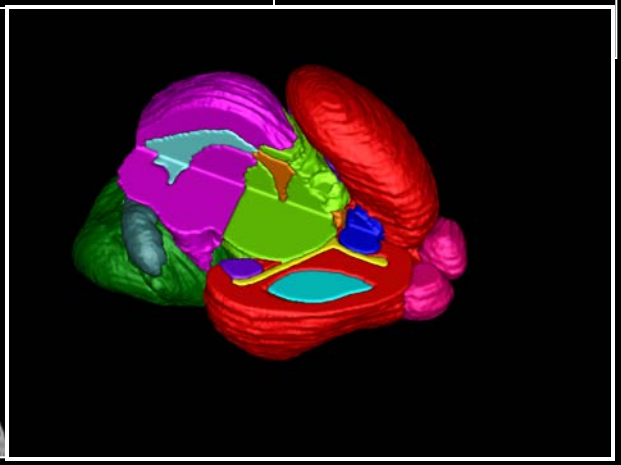


THE IMPACT OF MATERNAL ALCOHOL USE ON PRE- AND POSTNATAL DEVELOPMENT

Kathleen K. Sulik, Ph.D.
Department of Cell and Developmental Biology &
Bowles Center for Alcohol Studies, UNC-CH

with Research Support from NIH/NIAAA





- Full blown Fetal Alcohol Syndrome (FAS) occurs in approximately 1 in 750 live births, and Fetal Alcohol Spectrum Disorder (FASD; an umbrella term that includes all prenatal alcohol exposure-affected individuals) is estimated to occur in as many as 1% of live births in the US.

- Prenatal alcohol exposure is the leading known cause of congenital mental disability in this country.

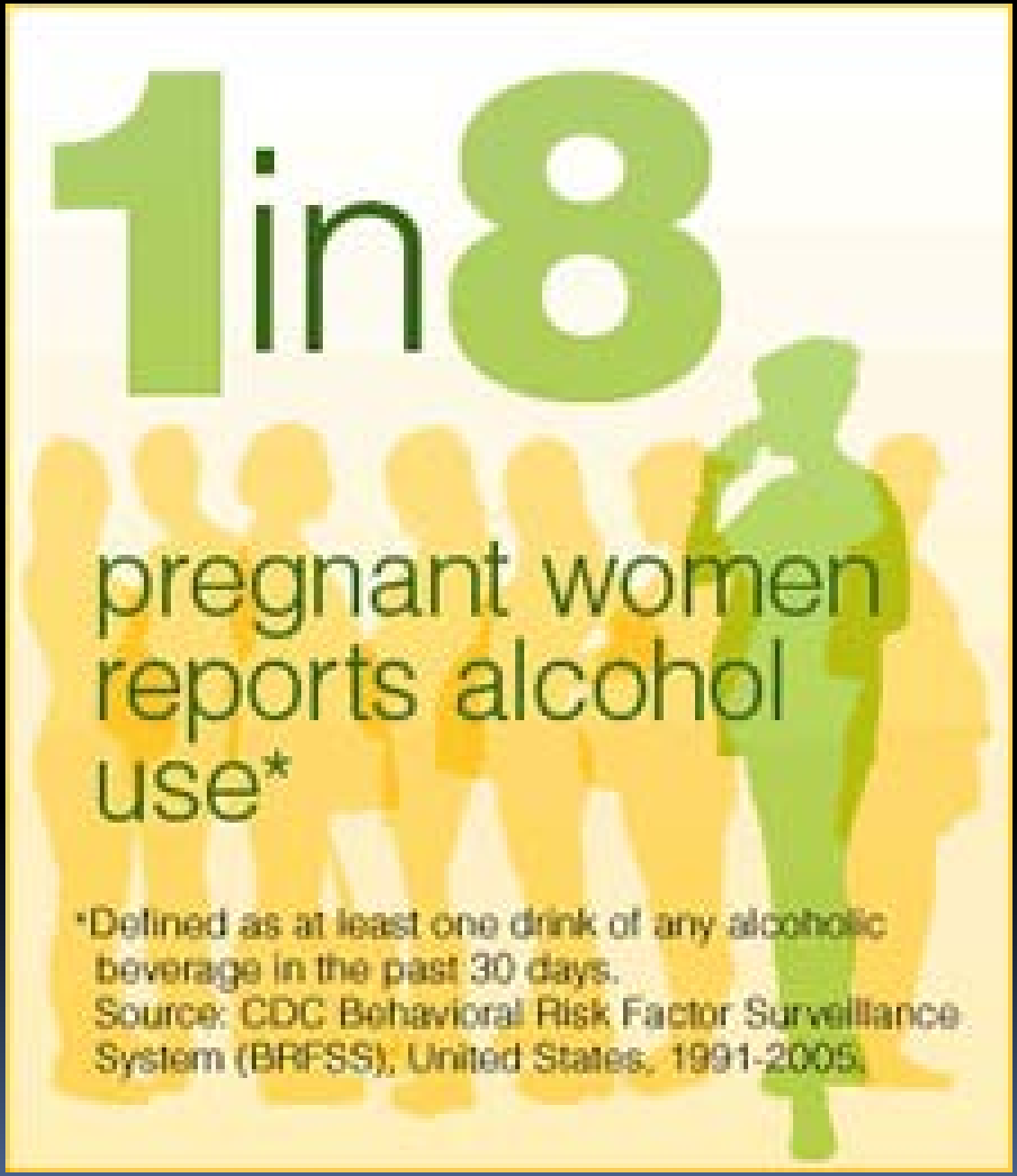
- FASD occurs in all races and socioeconomic groups and is a worldwide problem. Other countries in which FASD has been studied include Canada, Finland, Italy, the United Kingdom, South Africa, Australia, Ukraine, and Russia.

New General Population Prevalence Estimates of FASD: In-School Studies

Estimates per 1,000:

	Current	In-school
FAS	0.5 – 3.0	**2.0 – 7.0**
FASD	9.1 **(1%)**	**20 – 50 (2-5%)**

Source: May et al., DDRR, 2009.



from the Centers for Disease Control website

The lifetime cost for one individual with FAS in 2002 was estimated to be $2 million. This is an average for people with FAS and does not include data on people with other FASDs.

People with severe problems, such as profound intellectual disability, have much higher costs.

It is estimated that the cost to the United States for FAS alone is over $4 billion annually.

U.S. Surgeon General's Advisory on Alcohol Use In Pregnancy

February 21, 2005

A pregnant woman should not drink alcohol during pregnancy.

A pregnant woman who has already consumed alcohol during her pregnancy should stop in order to minimize further risk.

A woman who is **considering** becoming pregnant should abstain from alcohol.

Recognizing that nearly half of all births in the United States are unplanned, women of child-bearing age should consult their physician and take steps to reduce the possibility of prenatal alcohol exposure.

Health professionals should inquire routinely about alcohol consumption by women of childbearing age, inform them of the risks of alcohol consumption during pregnancy, and advise them not to drink alcoholic beverages during pregnancy.

United States Department of Health & Human Services

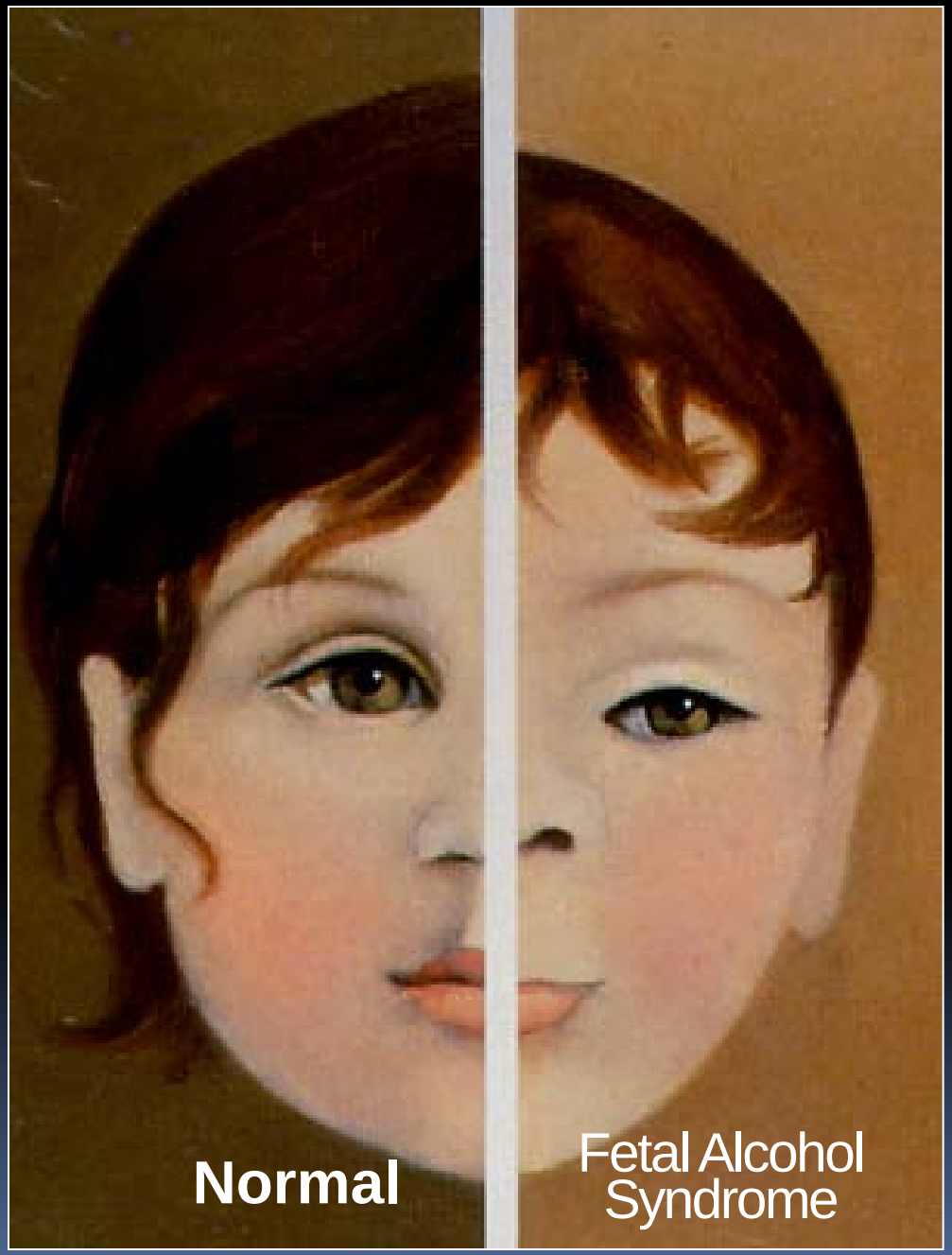
Full blown Fetal Alcohol Syndrome is characterized by

- distinctive facial features
- CNS dysfunction
- growth deficiency

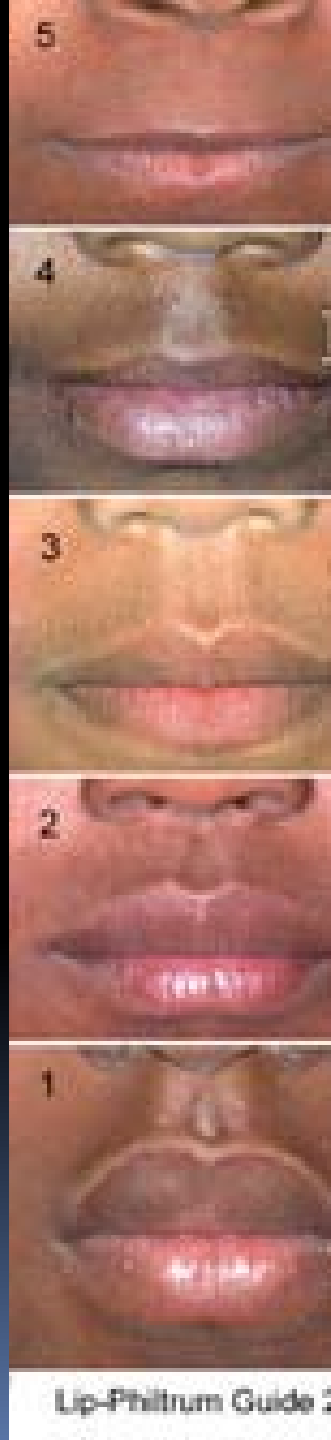
FAS was first described in France in 1968 and in the US in 1973.

Compared to a
normal individual,
a person with FAS has a
small head
(microcephaly),
indicating that
the brain is small.

Additionally,
the palpebral fissures,
the nose, philtrum,
and the vermillion border
of the upper lip
are reduced in size.



A smooth philtrum and an upper lip having a thin vermillion border ("lip score" of 4 or 5) are characteristic of FAS.



Can you tell she has

BRAIN DAMAGE?

Alcohol can harm your baby's brain at any time during pregnancy, and that means lifelong problems for you and your child.

Play it Smart. Alcohol and Pregnancy Don't Mix.

NIAAA
National Institute on Alcohol Abuse and Alcoholism

TO LEARN MORE, PLEASE CALL
202-785-4585

N.O. FAS
National Organization on Fetal Alcohol Syndrome

The vast majority of persons with FASD do not have outward or obvious physical findings that would lead one to think “birth defect”; the primary locus of their birth defects is in the brain.

As the child with FASD grows into adulthood, these “primary disabilities” do not disappear, or even diminish, with age. Their disabilities become ever more obvious, difficult to manage and appear to be exacerbated with the expectations for autonomous, acceptable function within mainstream society that partner with increasing age.

The average IQ in FASD is between 75 and 85, with the full range in FASD being between 20 and 140+ (IQ <70 is considered intellectual mental handicap) but almost all individuals with FASD have an adaptive quotient (AQ) <70 (AQ <70 is considered adaptive mental handicap).

AQ measure one's ability to function day to day without support in the areas of communication, socialization, daily living skills (personal and community), time management, employment, critical thinking, judgment, etc. Adaptive functioning can be measured and scored, using test instruments in the same way as IQ.

For those adults with FASD over the age of 21, fully 80% are unable to live independently.

This finding is independent of IQ scores (Streissguth et al., 1996).

Alcohol's Effect on the Developing Human Brain

Cognitive and behavioral characteristics:

Average IQ of 75-85

Deficits in executive functioning

Deficits in information processing and memory

Fine motor performance deficits

Frequently considered hyperactive, disruptive, impulsive or delinquent

Structural Abnormalities Involve:

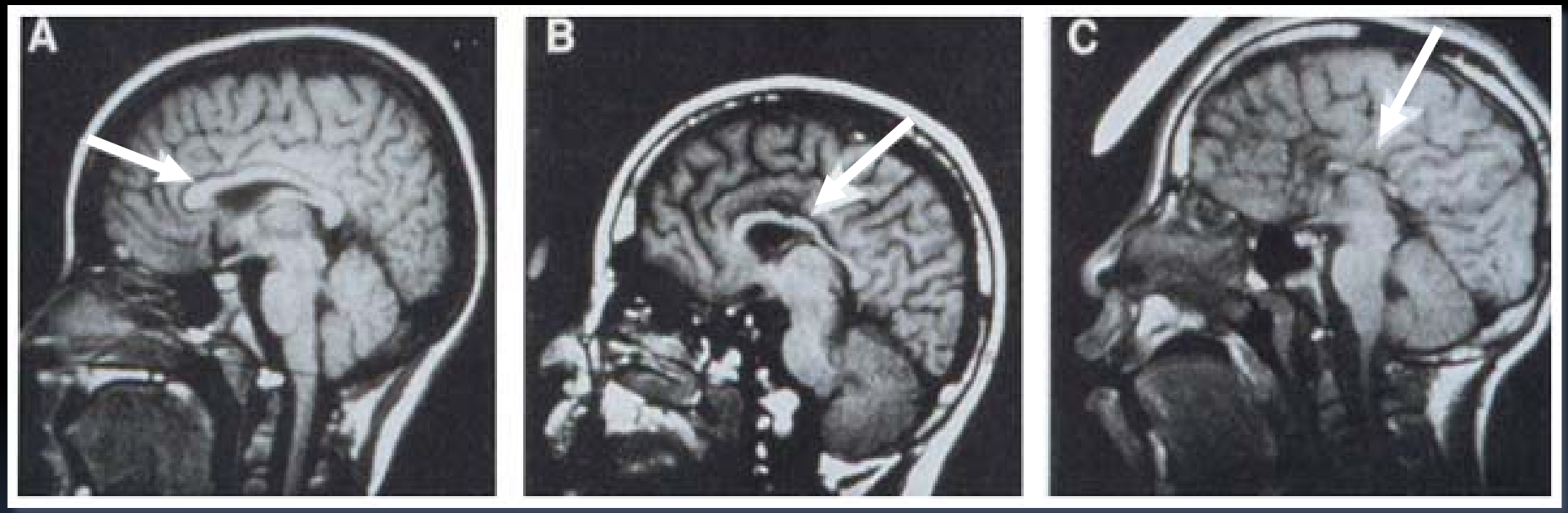
Corpus callosum
- The rate of agenesis may be higher in FAS than in any other developmental disorder

Basal ganglia
- Involved in motor abilities and cognitive functions

Hippocampus
- Involved in memory

Cerebellum
- Vermis is most affected

Magnetic Resonance Imaging (MRI) illustrates loss of portions of the corpus callosum in the brains of individuals with FAS

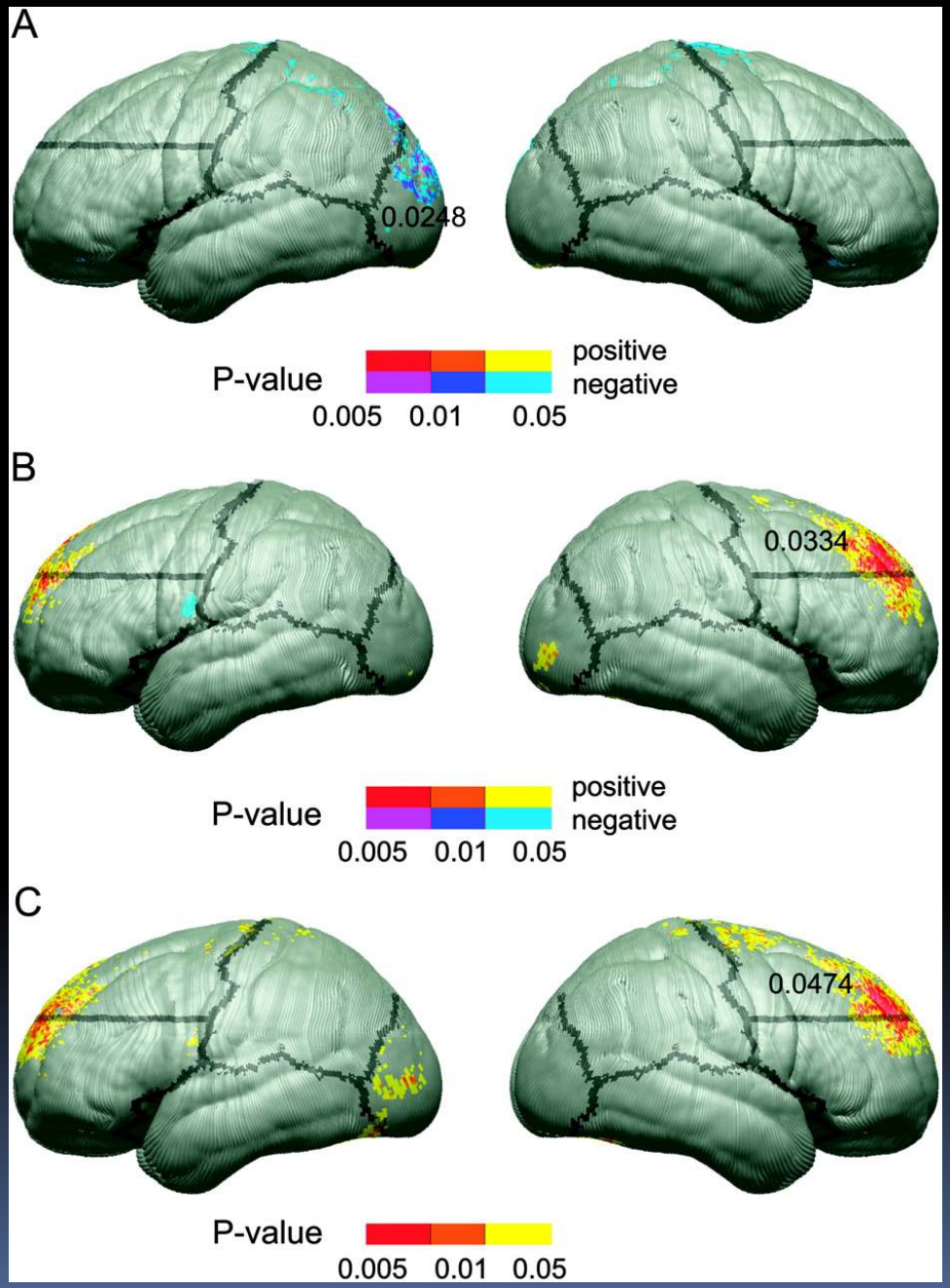


NORMAL FAS FAS

Images courtesy of Dr. S. Mattson

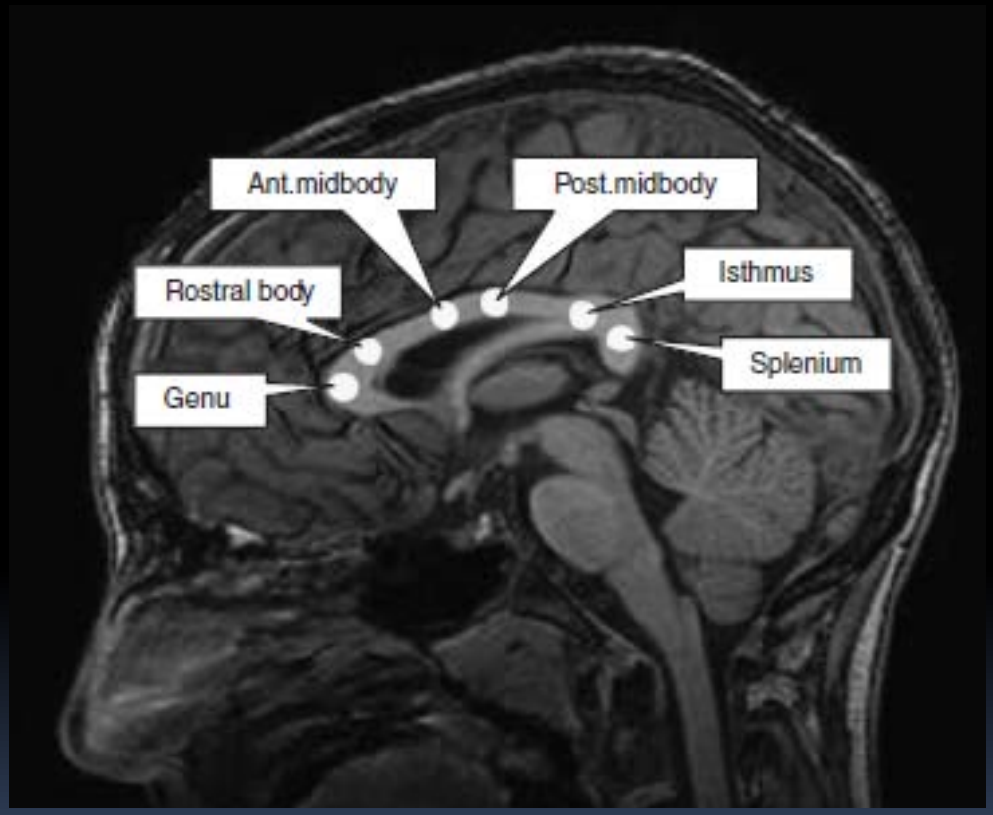
In 3D brain reconstructions made from MRI scans, color coding identifies brain areas that differ in individuals with FASD as compared to normal.

[See A.L. Norman et al, 2009 (review); Astley et al, 2009; and others for additional human FASD MRI data]



from Sowell et al., 2008

Diffusion Tensor Imaging (DTI) studies of individuals with FASD have shown alterations in the corpus callosum



from Wozniak et al, 2006

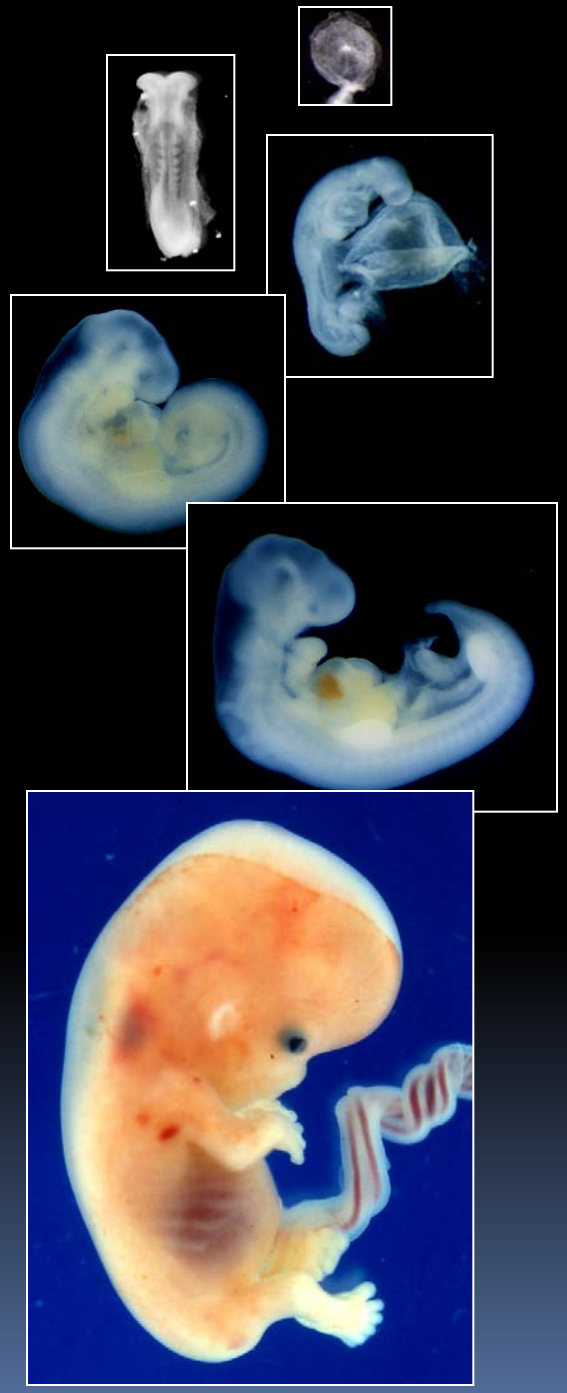
from Wozniak et al, 2009

BEEFEAT

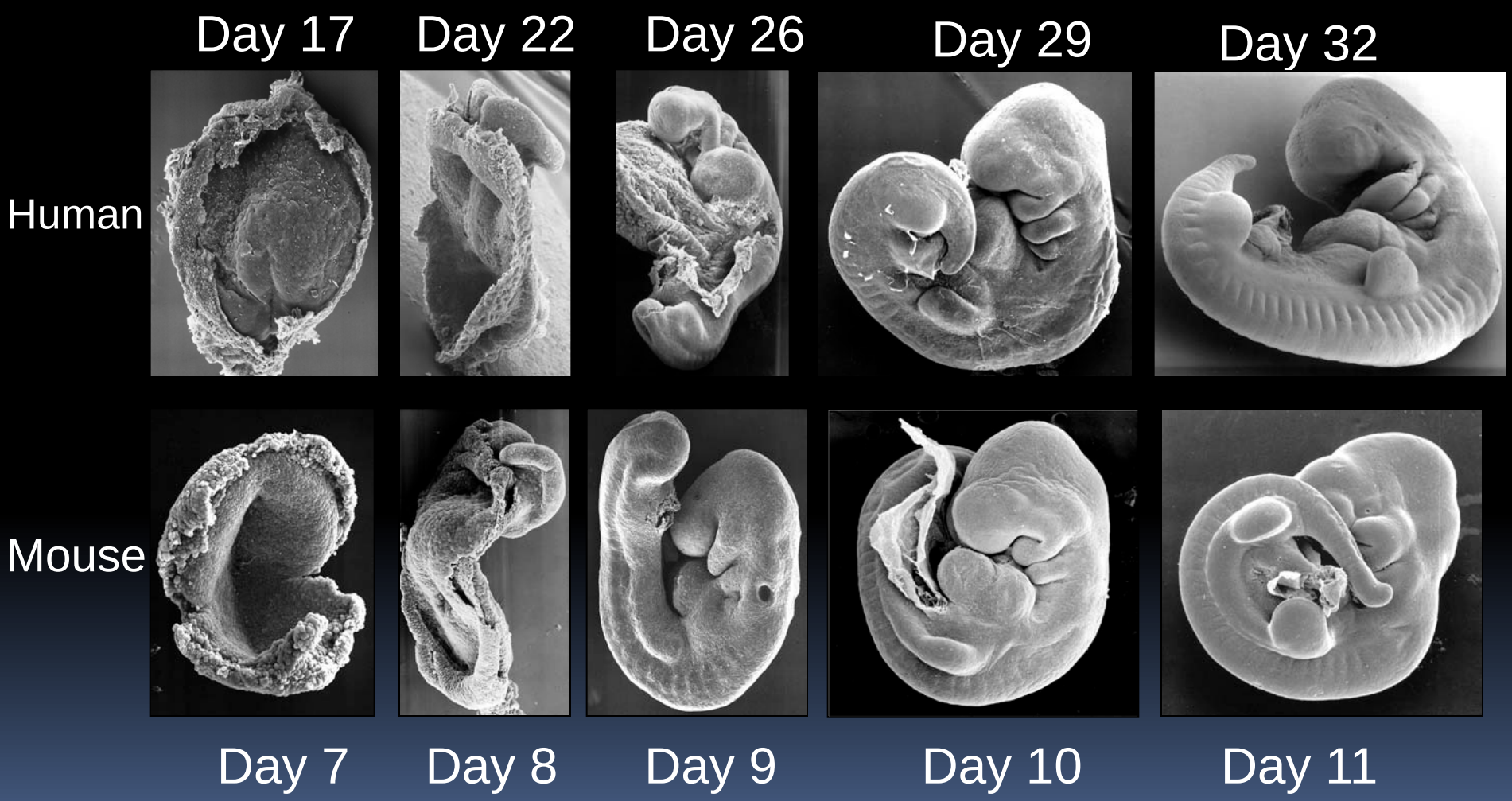
Studies of FASD animal models allow:

- ✓ Identification of critical exposure periods and dose-response relationships
- ✓ Detailed analyses of affected brain areas of interest
- ✓ Correlation of structural and functional changes
- ✓ Verification and expansion of diagnostic criteria for FASD

The amount and timing of maternal alcohol use determine the type and extent of resulting birth defects



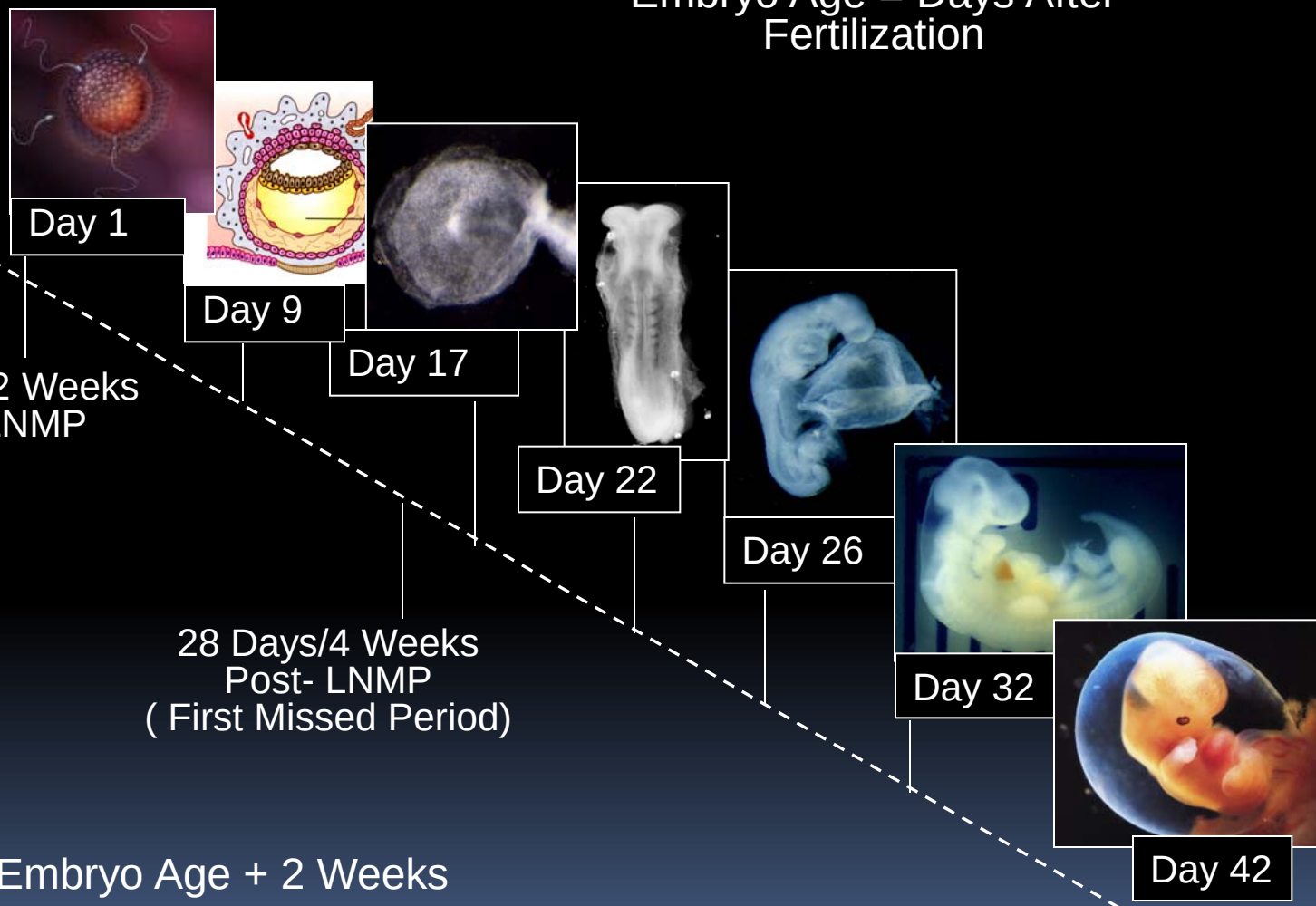
Human development from day 17-32 post-fertilization corresponds to day 7-11 in the mouse



Much Of Embryogenesis Occurs Prior To The Time That Pregnancy Is Typically Recognized

Menses
(Beginning
Of Last Normal
Menstrual
Period; LNMP)

Embryo Age = Days After Fertilization

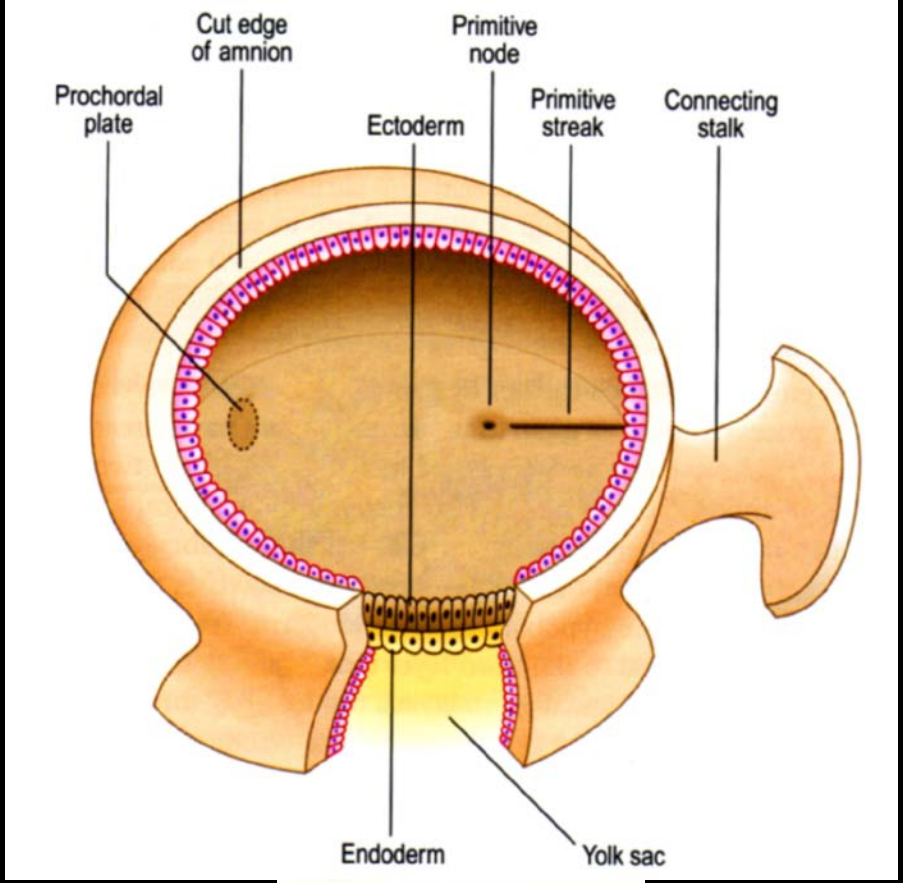


14 Days/2 Weeks
Post-LNMP

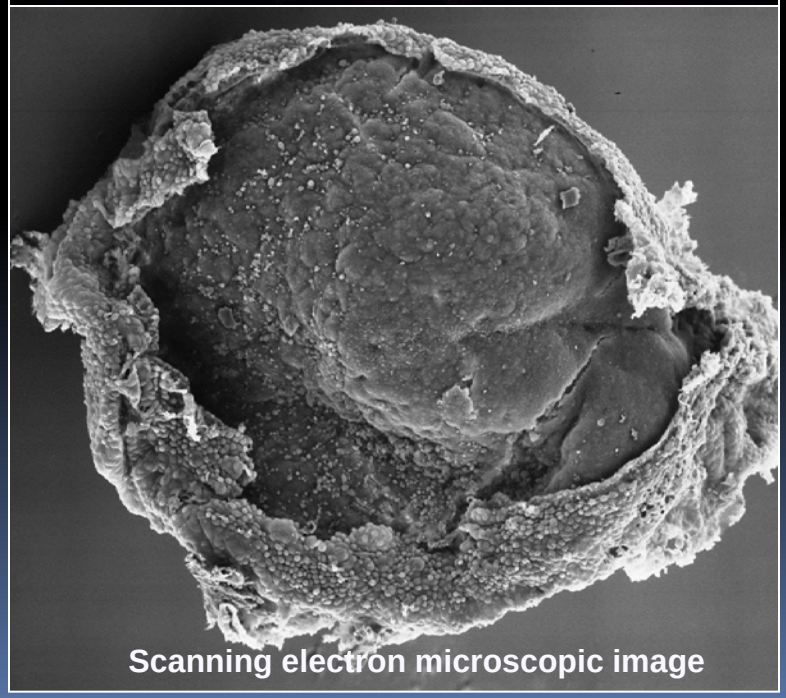
28 Days/4 Weeks
Post- LNMP
(First Missed Period)

8 Weeks
Post-LNMP
(Second Missed Period)

Age Post LNMP = Embryo Age + 2 Weeks

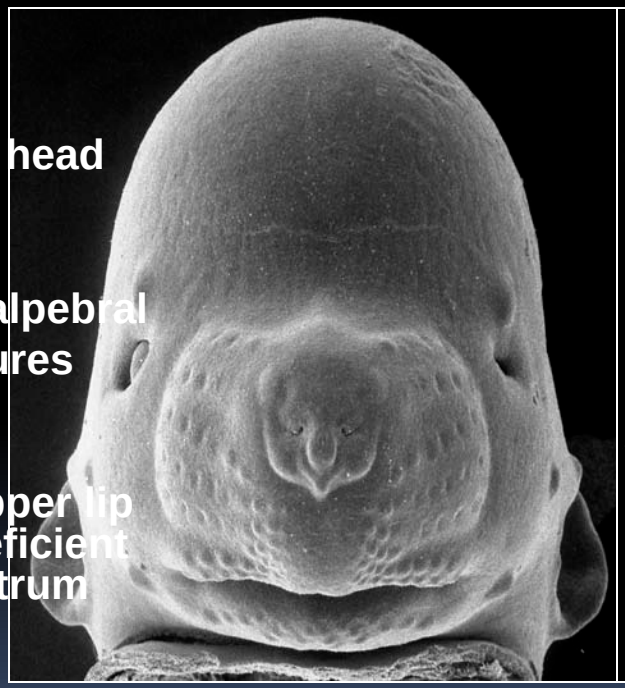


The 17 day human embryo is approximately 0.5 mm in diameter

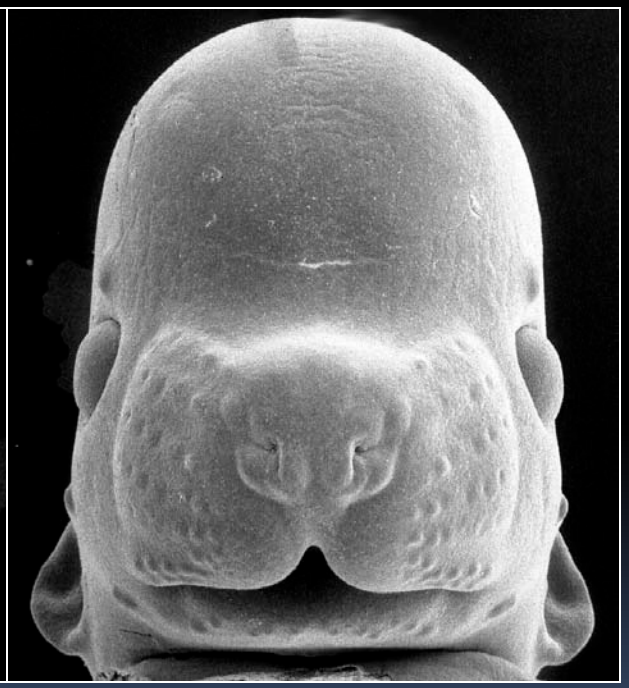


The characteristic facial features of Fetal Alcohol Syndrome can be seen in both a child and a mouse fetus that were exposed to alcohol during development. Alcohol exposure occurred on Gestational Day (GD) 7 in the mouse.

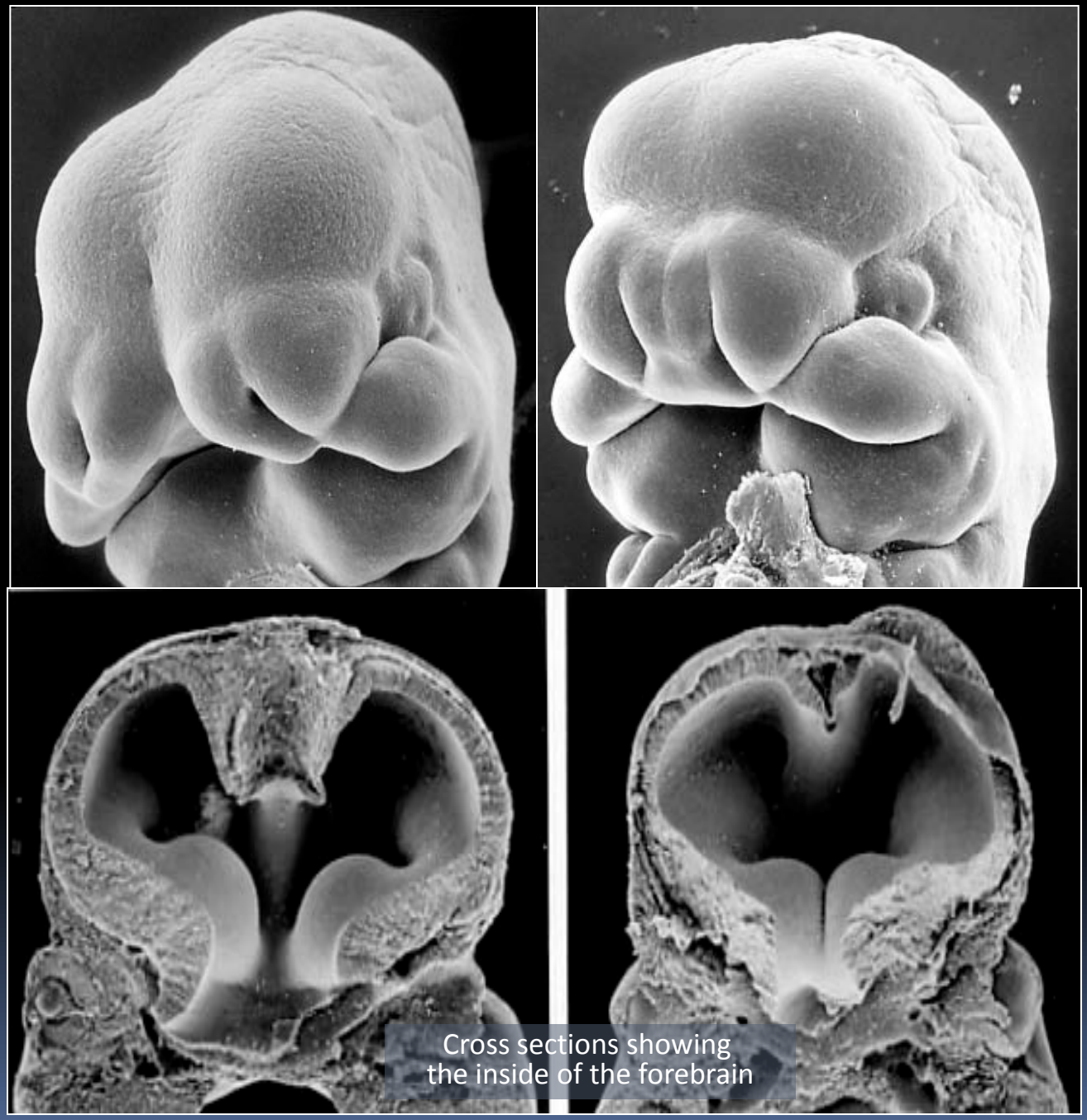
Child with FAS



Alcohol-exposed mouse fetus



Normal mouse fetus



Normal **Alcohol-exposed**

Alcohol-induced deficiencies in the upper midface are accompanied by failure of the central portion of the forebrain to form

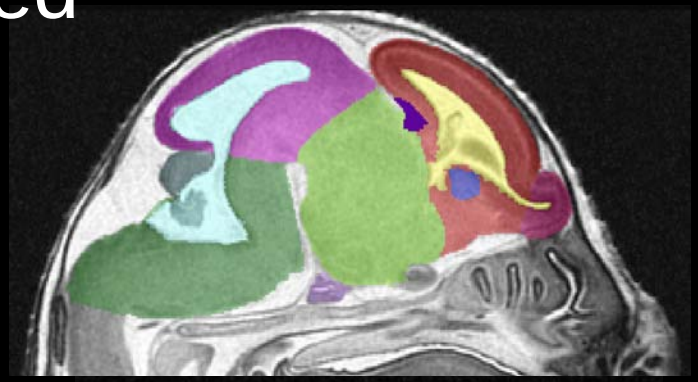
MRI is used to study fetal mouse brains

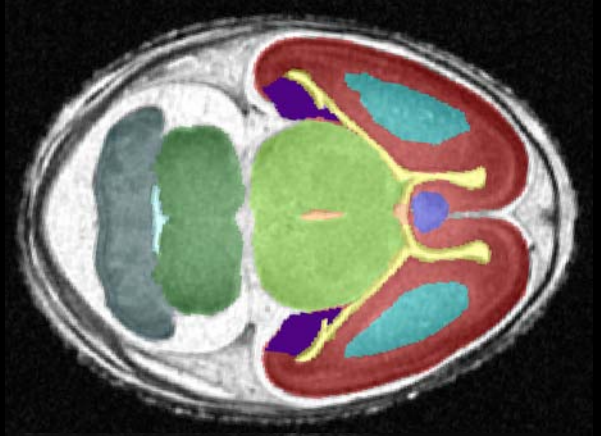
Gestational Day (GD)17
Mouse Fetus
17 mm crown rump length

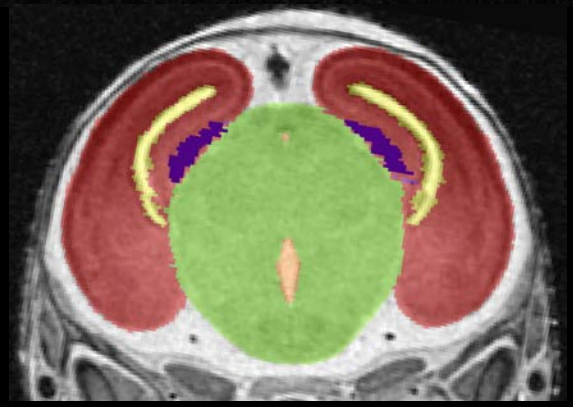
=

Week 13 Human Fetus
92 mm crown rump length

MRI scans of fetal mouse brains are manually segmented

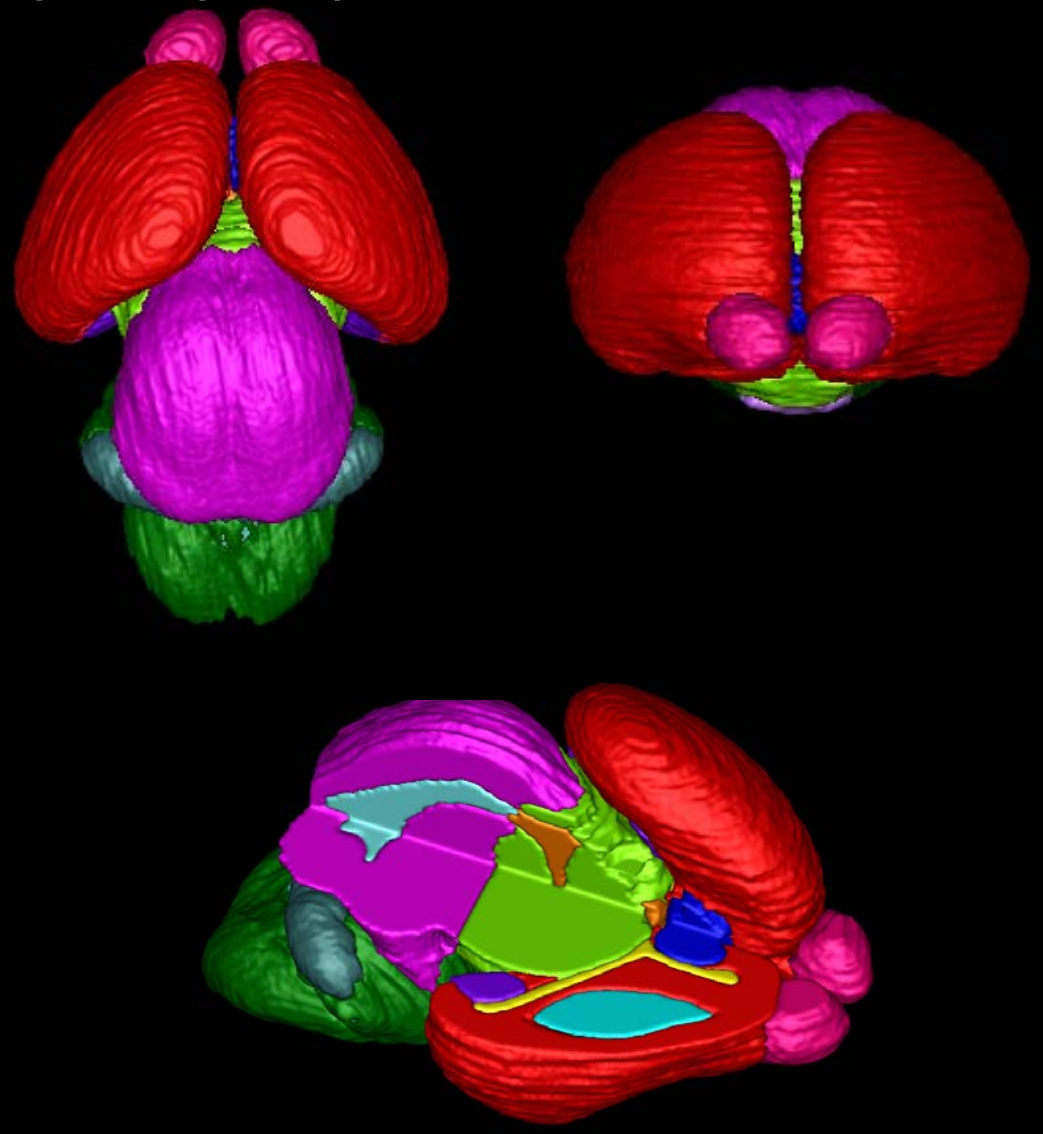






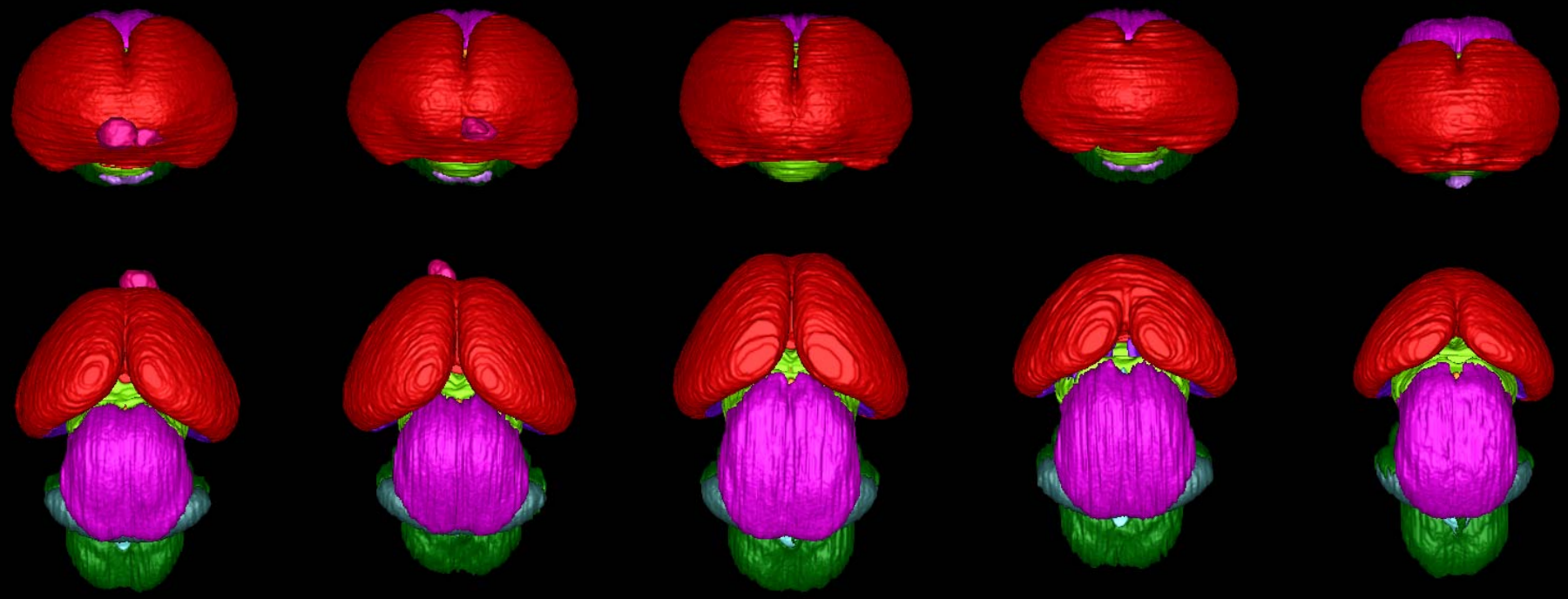
3-D reconstructions made from segmented MRI scans provide information regarding shape and volume.

- CEREBRAL CORTEX
- LATERAL VENTRICLES
- CAUDATE NUCLEUS
- OLFACTORY BULBS
- HIPPOCAMPUS
- SEPTAL NUCLEI
- THALAMUS
- THIRD VENTRICLE
- MIDBRAIN
- 4th VENT AND CA
- PONS AND MEDULLA
- CEREBELLUM
- PITUITARY

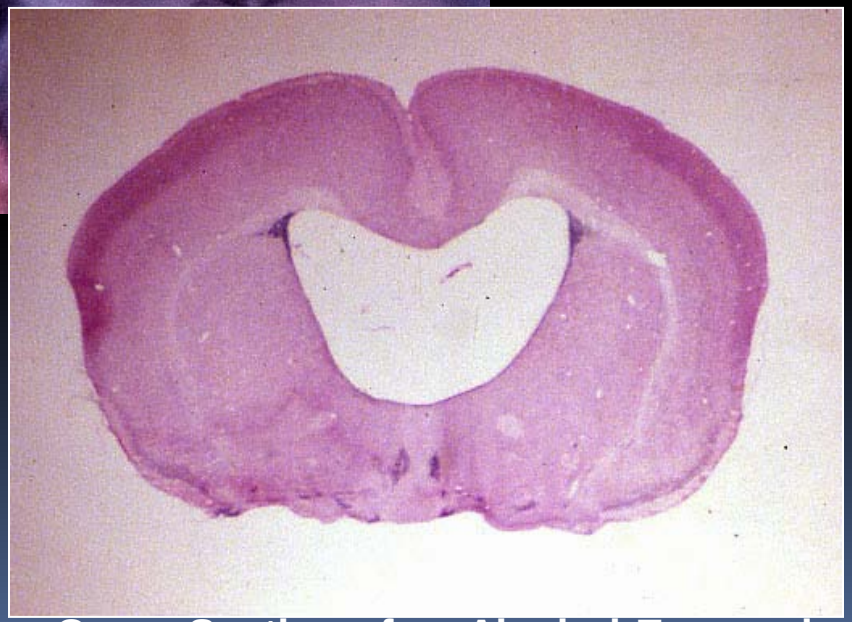


GD 17 Control

GD 17 Alcohol-exposed (GD7 Treatment)

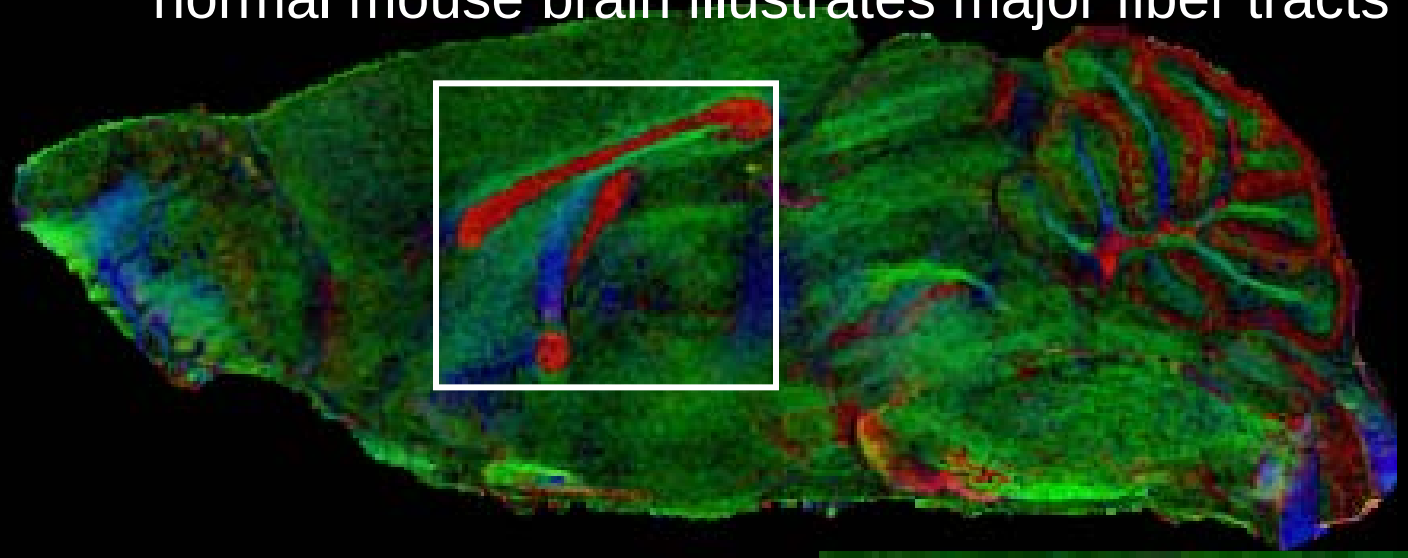


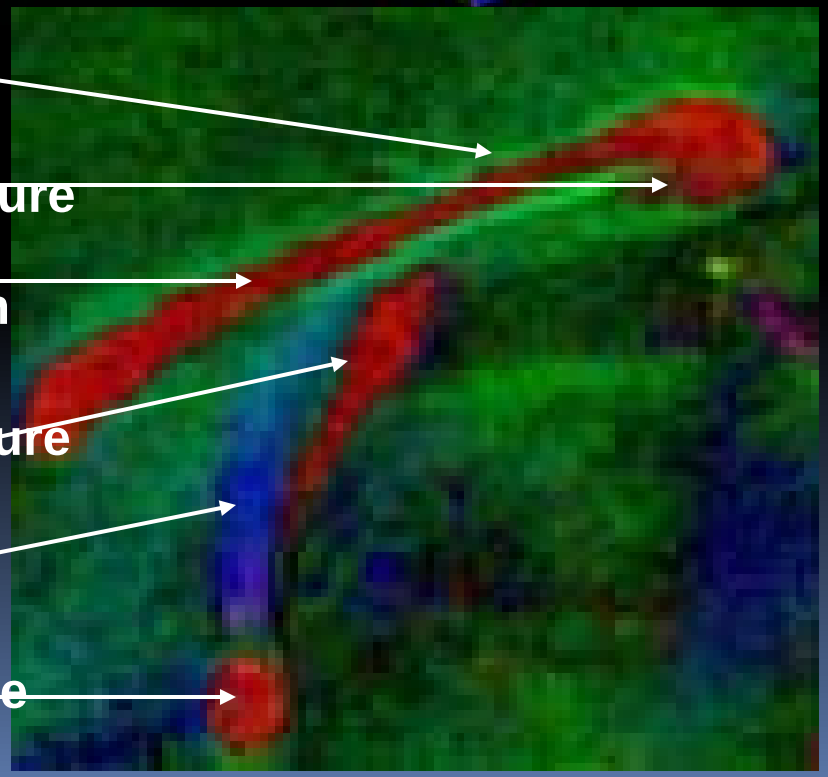
Cross Section of
a Normal Mouse Brain



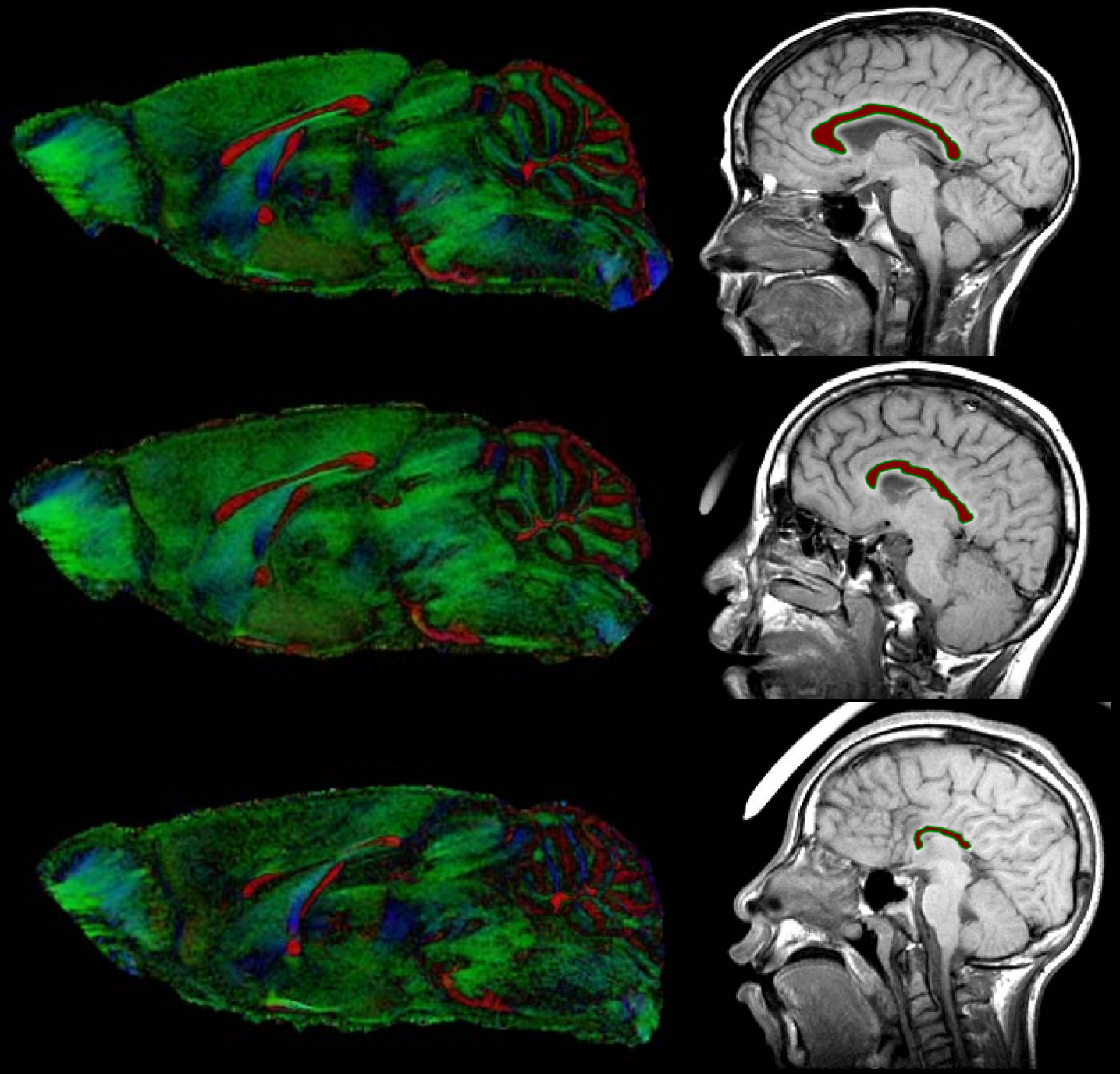
Cross Section of an Alcohol-Exposed
Abnormal Mouse Brain

Diffusion Tensor Imaging (DTI) of a postnatal day 45 normal mouse brain illustrates major fiber tracts

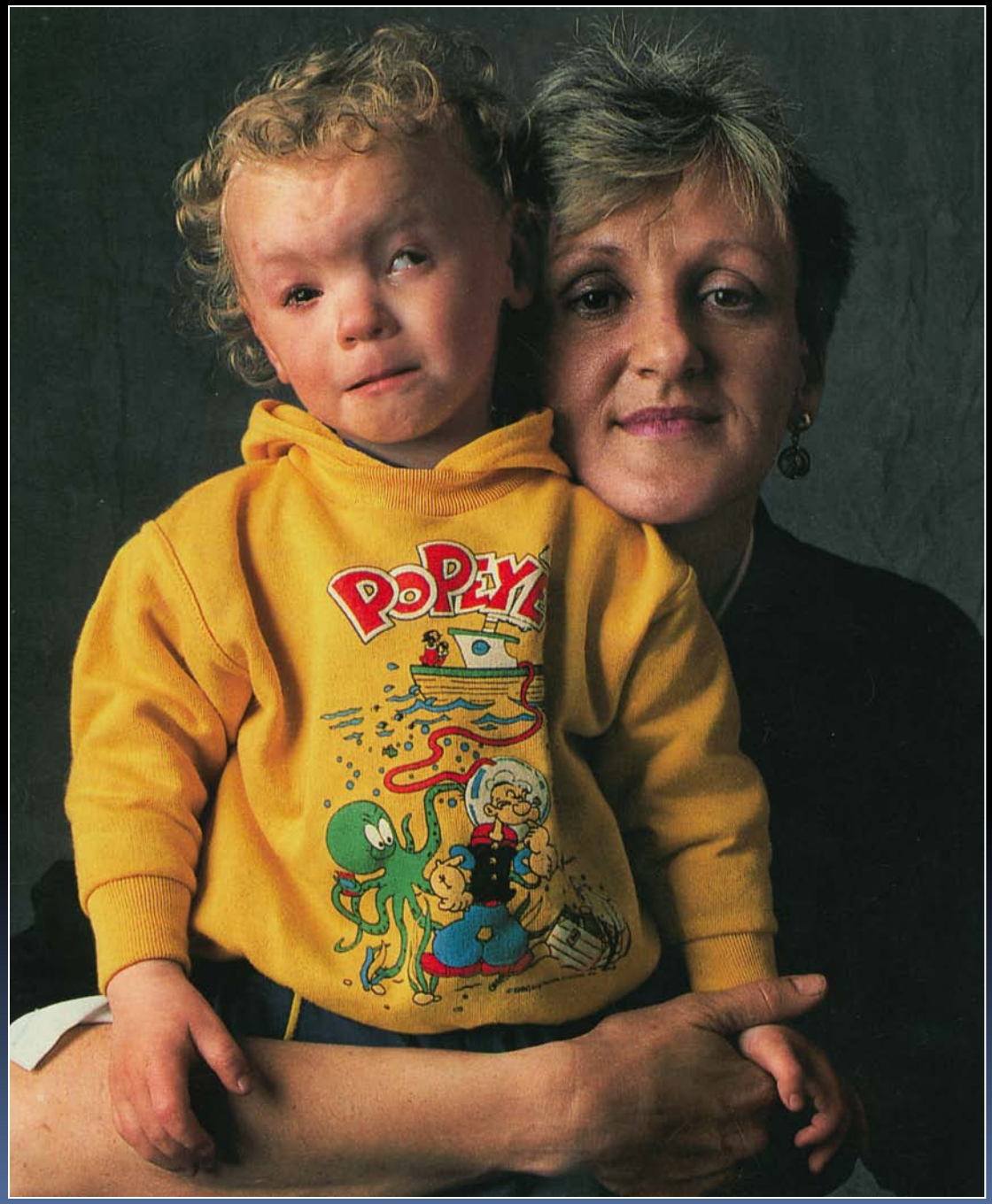




Defects of the corpus callosum are remarkably similar in mice and in human FAS



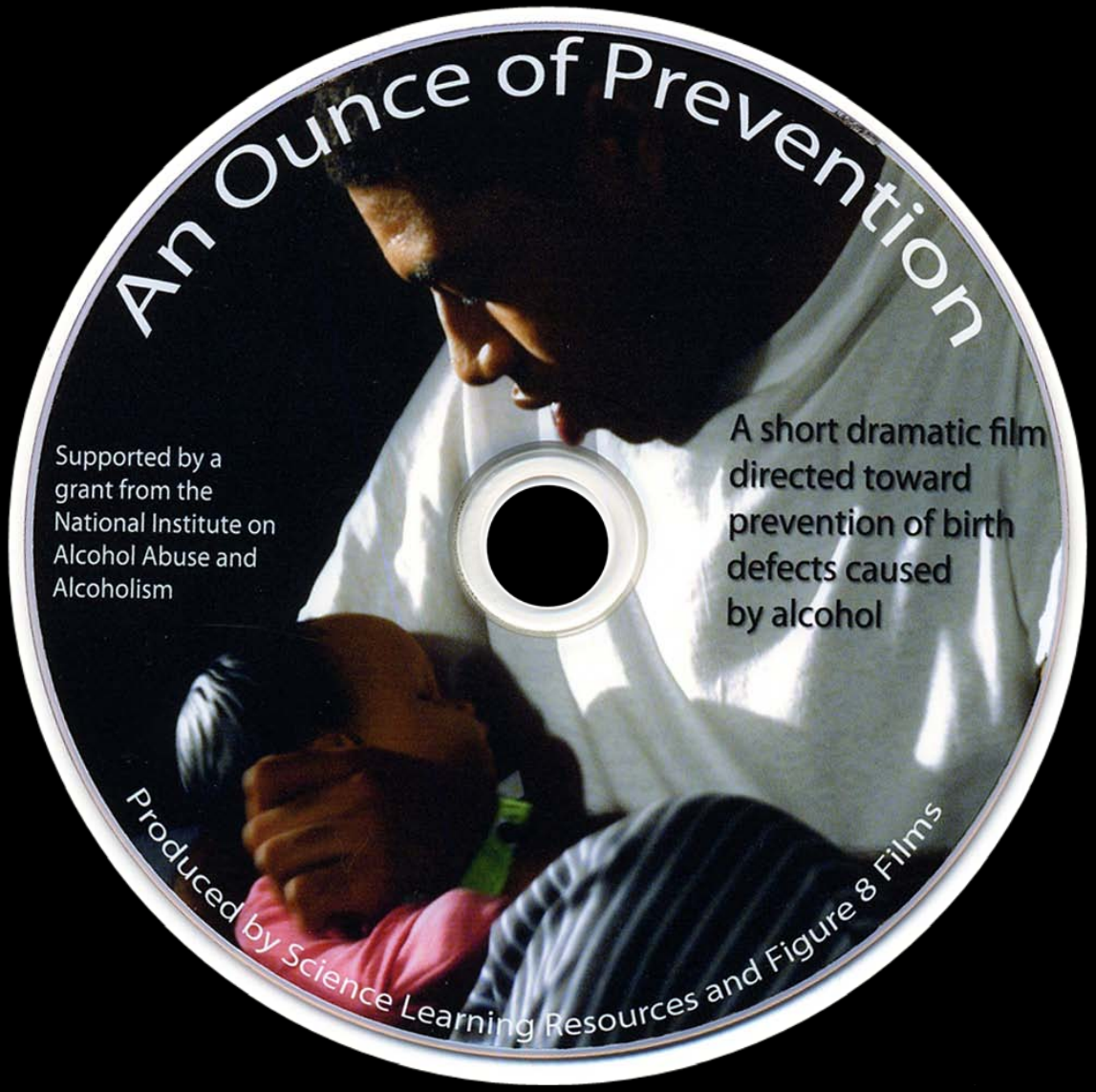
Maternal alcohol abuse can cause permanent CNS damage at virtually any prenatal stage including those stages that occur prior to the time that most pregnancies are recognized



Prevention-directed curricula development

Better Safe Than Sorry: Preventing a Tragedy

http://pubs.niaaa.nih.gov/publications/Science/curriculum.html


An Ounce of Prevention
Supported by a grant from the National Institute on Alcohol Abuse and Alcoholism
A short dramatic film directed toward prevention of birth defects caused by alcohol
Produced by Science Learning Resources and Figure 8 Films

RECOMMENDATIONS

Prevention!!!! – Raise government (including Department of Education and Criminal Justice System), public and medical community awareness and provide education via mass media and school curricula

Provide support and promote early intervention for those affected

Thank You For Your Attention