

# Thank you:

NIMH, NINDS and NICHD

Simons Foundation

Autism Speaks

Cure Autism Now

Organization for Autism Research

NICHD Brain and Tissue Bank

ATP/Harvard Brain and Tissue Bank

*Karen Pierce*

*Taran*

*Sierra*

Tony Wynshaw-Boris & Nik Schork

Steve Glatt & Lisa Eyler & Fred Gage

Laura Schreibman & Aubyn Stahmer

Anders Dale & Clelia Ahrens-Barbeau

Cindy Carter & Melanie Weinfeld

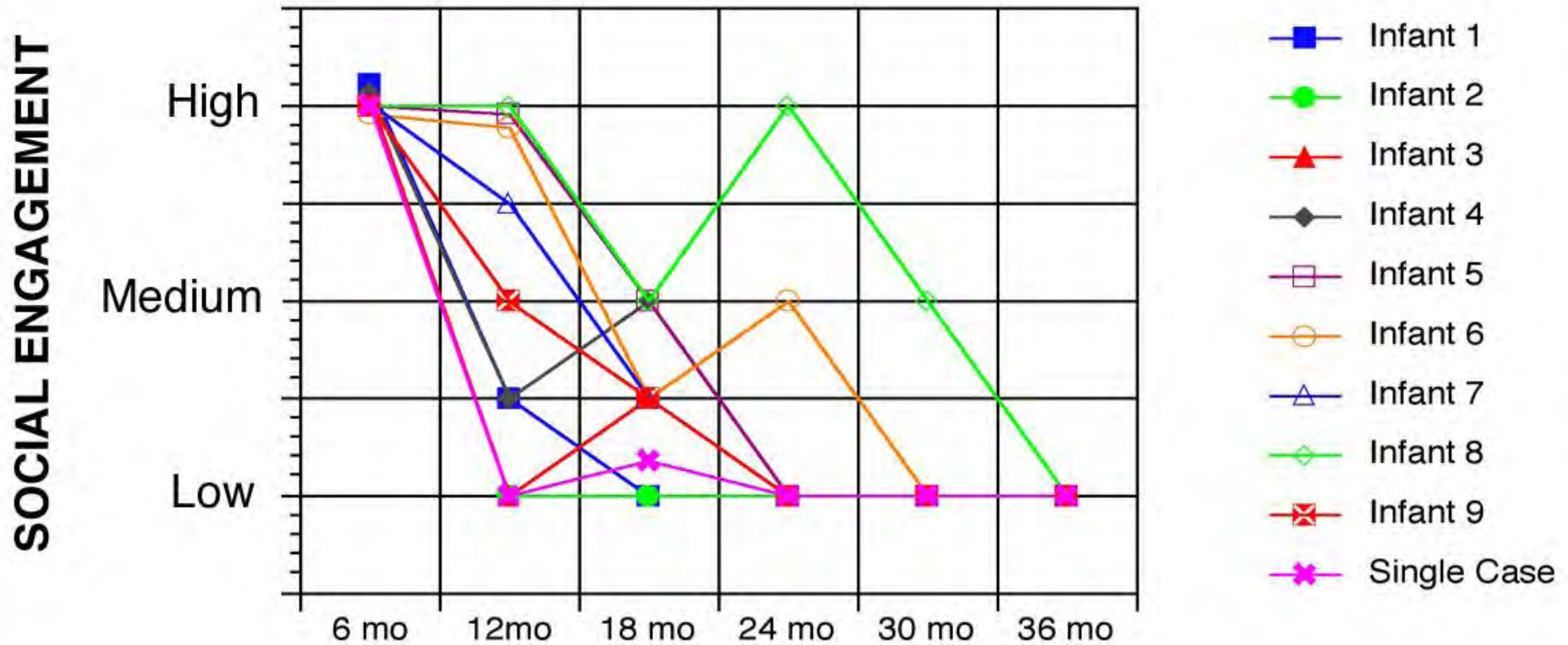
Kathleen Campbell & Stephanie Solso

Rich Stoner & Julia Young

Jamie Desmond & Roxanna Hasin

Julia Young & Stuart Spendlove

# Tracking Infants Eventually Diagnosed as ASD



At 6 mos of age, “infant made a lot of vocalizations during play and responded to social interactions by smiling and cooing”

From Pierce et al., 2008 meta-analysis of Bryson et al., (2007) & Dawson et al., (2000)

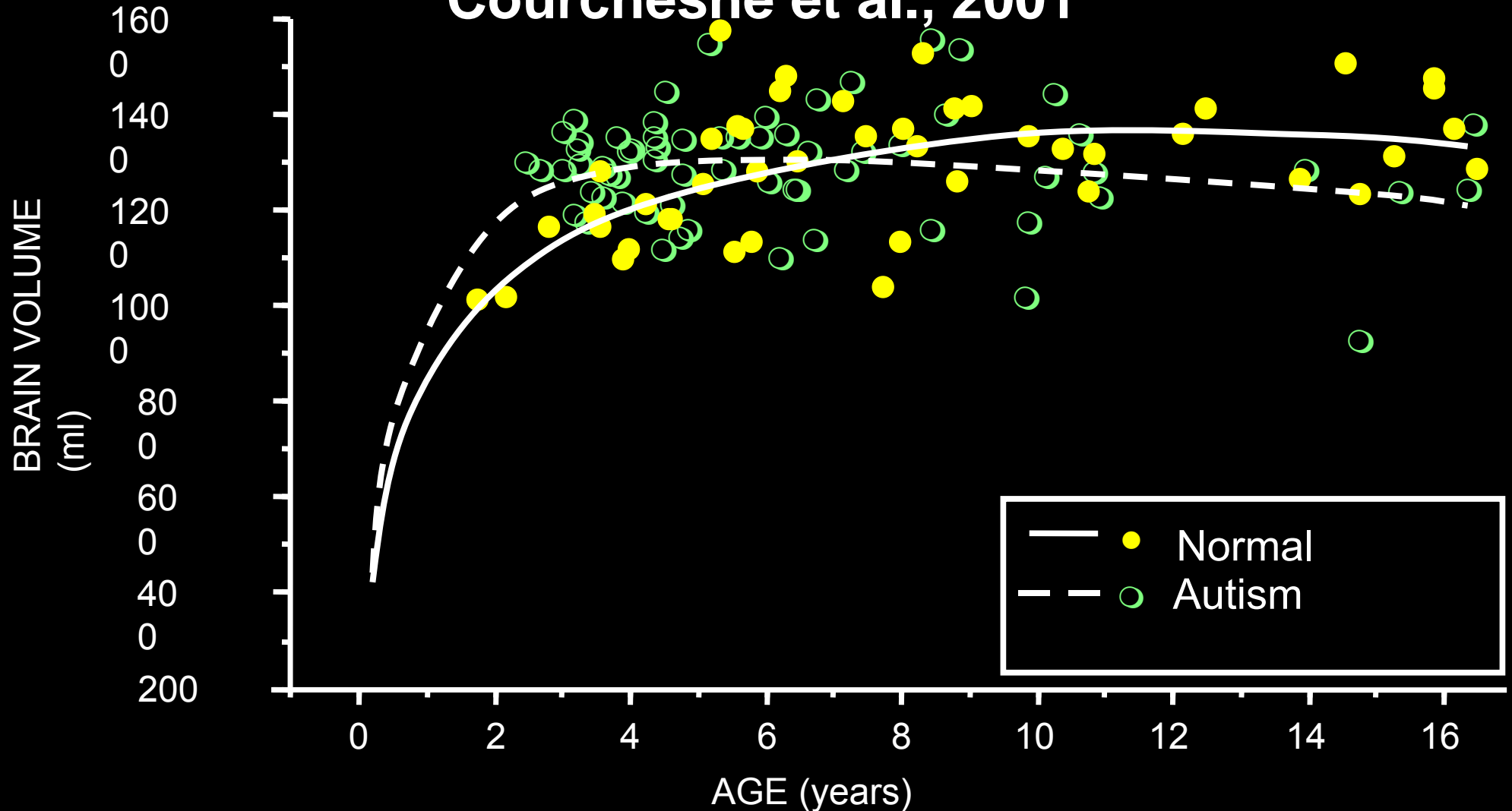
**The great majority of several hundred biological studies of autism have focused on the brain 10, 20 or more years after clinical onset.**

**They have not shown what is abnormal in autism during the first years of life, at the age of clinical onset.**

**Only a dozen MRI studies of early brain development in ASD**

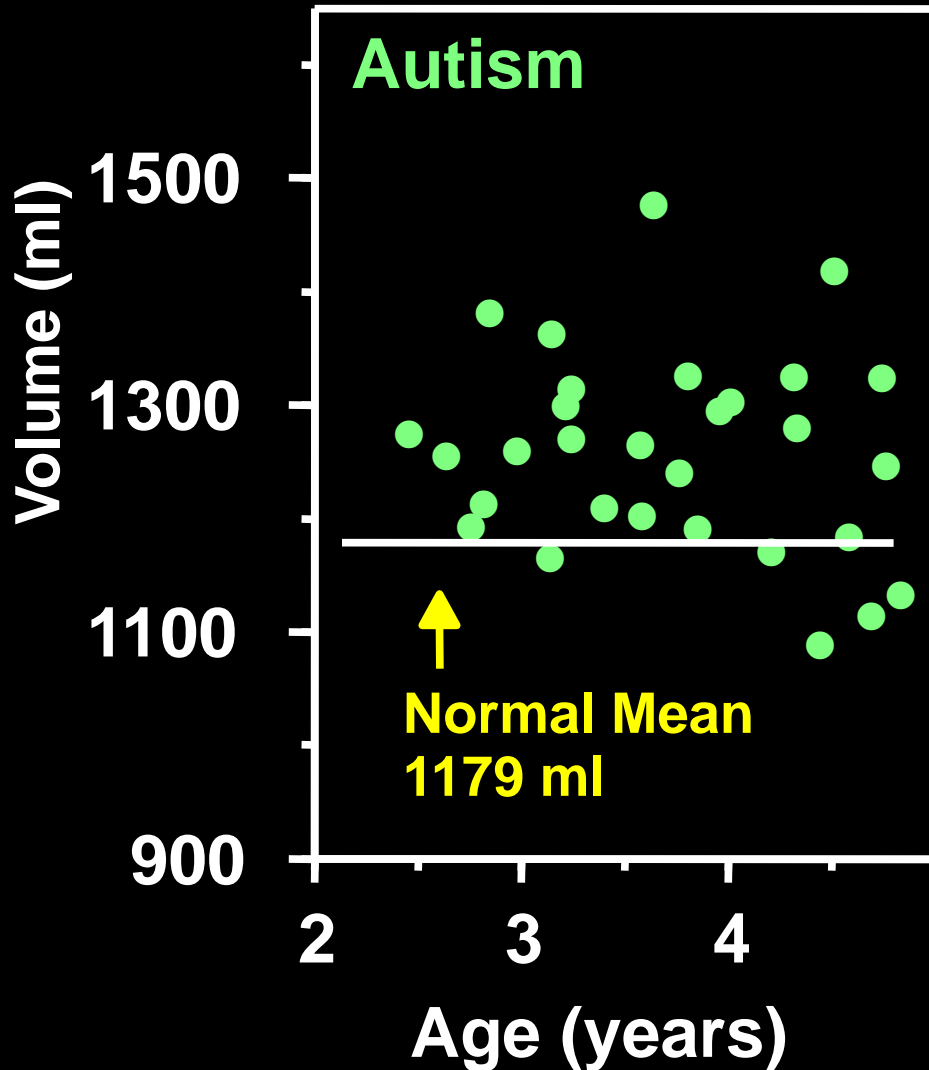
# Unusual Brain Growth Trajectory In Early Life in ASD

Courchesne et al., 2001



# Abnormal Brain Overgrowth in Autism by 2 to 4 Years of Age

**Courchesne et al., 2001**



Recent MRI Studies Also  
Showing Abnormal Brain  
Overgrowth  
in Autism by 2 to 4 Years of Age

**Sparks et al., 2002**  
**Carper et al 2002**  
**Carper & Courchesne 2005**  
**Hazlett et al., 2005**  
**Bloss & Courchese 2007**  
**Schumann, Pierce, Courchesne**  
**Average Normal**  
**2010**

# Abnormal Brain Overgrowth in ASD in First Two Years of Life

Courchesne et al., 2003 JAMA

Dementieva et al., 2005

Dissanayaki et al., 2005

Hazlett et al., 2005

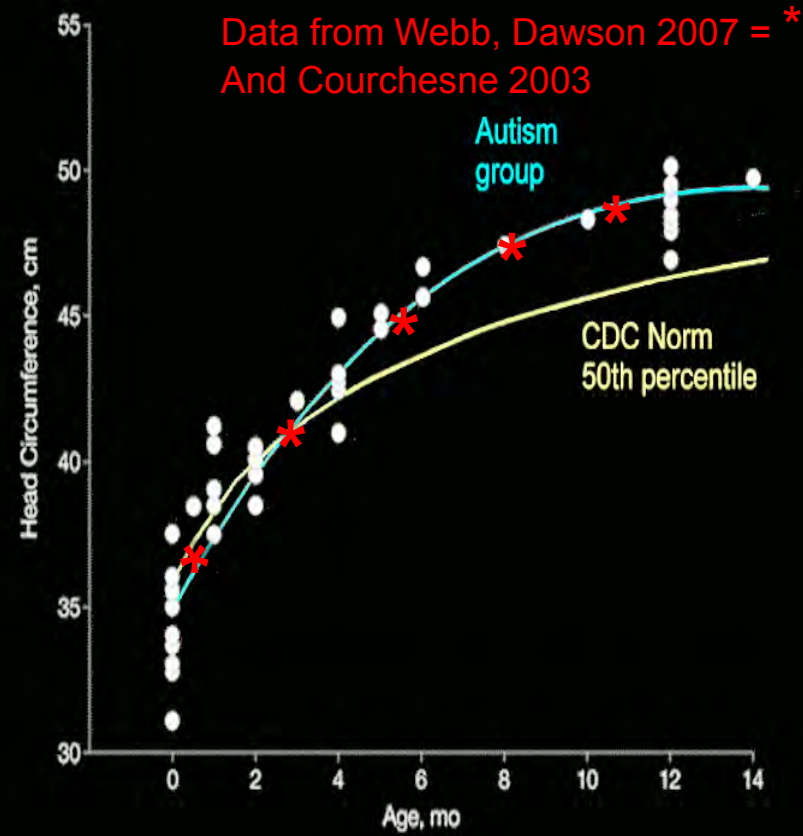
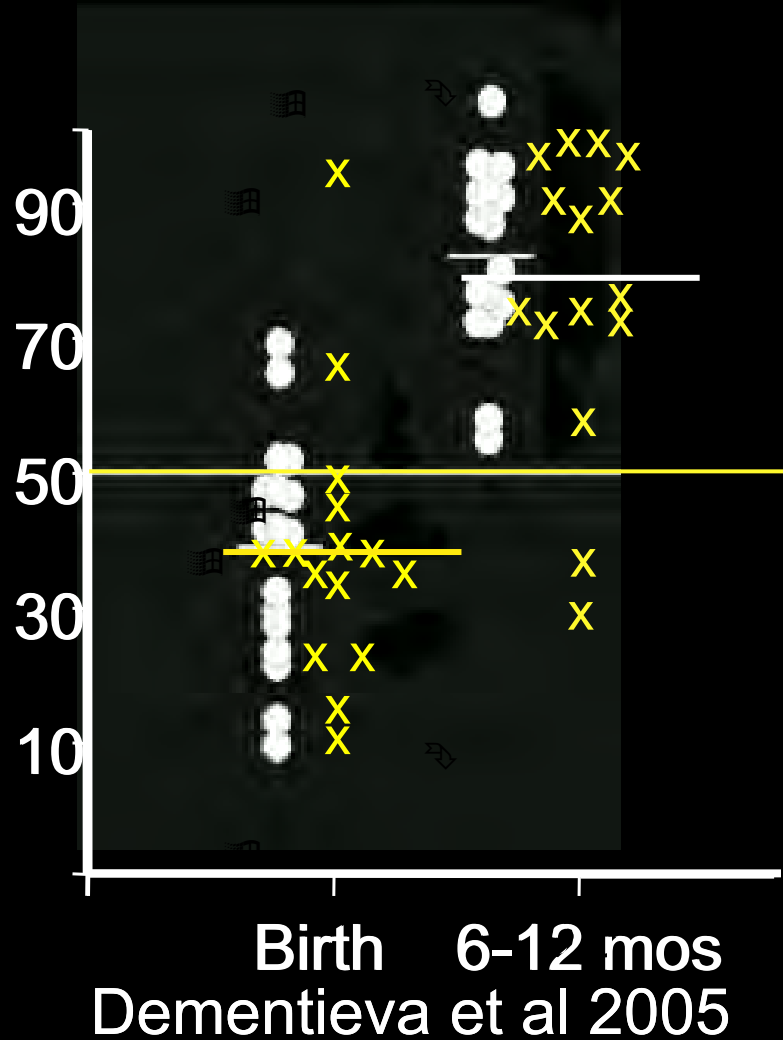
Dawson et al., 2007

Mraz et al., 2007

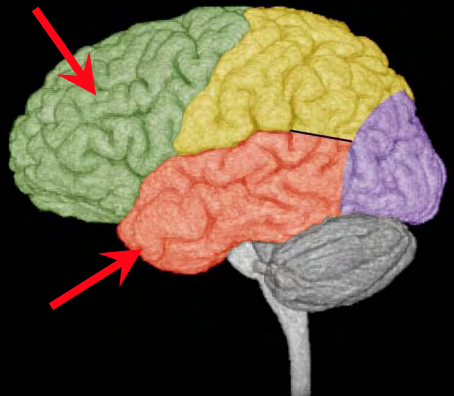
Webb et al., 2007

Elder et al., 2007

Pierce et al in manuscript

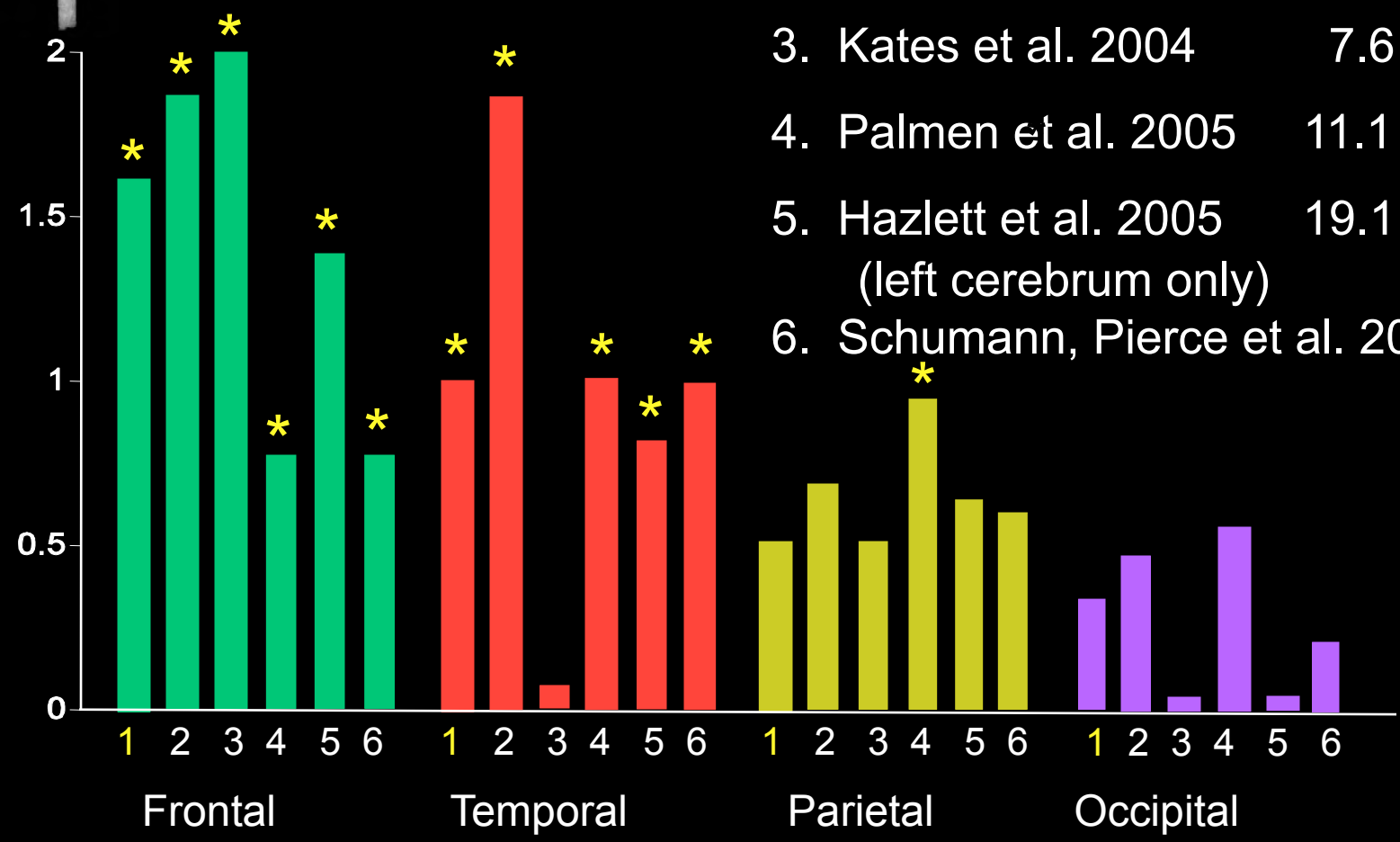


# Gray Matter Overgrowth in ASD

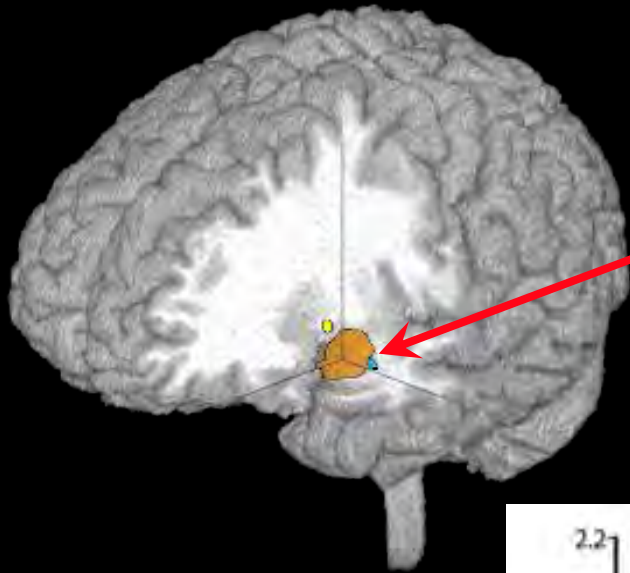


\* p<0.05

Standard deviations from normal



1. Carper et al. 2002 3.4 years
2. Bloss & Courchesne, 2007 3.8 years
3. Kates et al. 2004 7.6 years
4. Palmen et al. 2005 11.1 years
5. Hazlett et al. 2005 19.1 years  
(left cerebrum only)
6. Schumann, Pierce et al. 2010 2 years

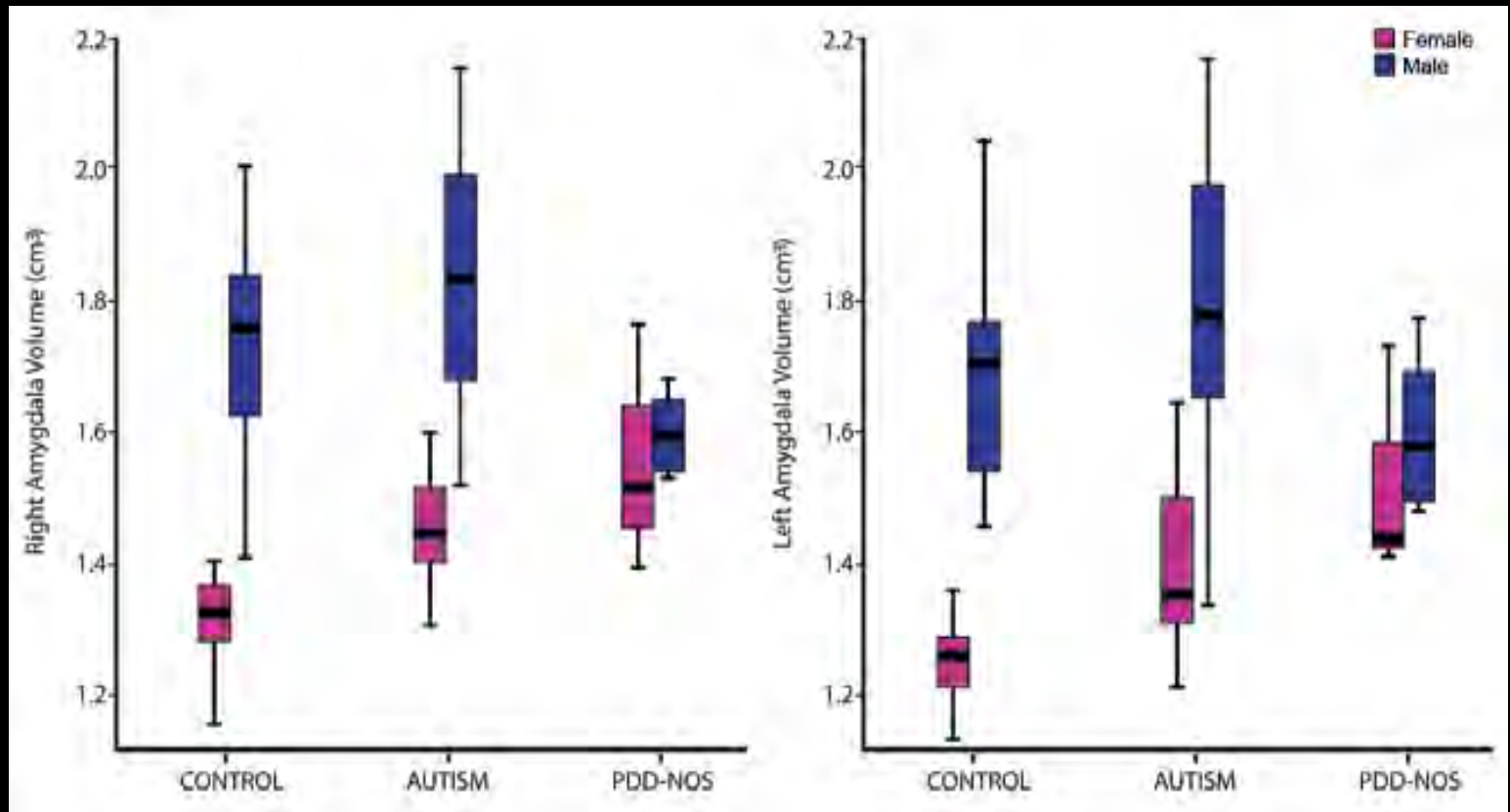


# Amygdala Overgrowth in Autism by 2 to 4 Years of Age

Schumann, Courchesne & colleagues 2009

First Reported by  
Sparks et al., 2002

Also reported by  
Munson et al., 2006  
Mosconi et al 2009



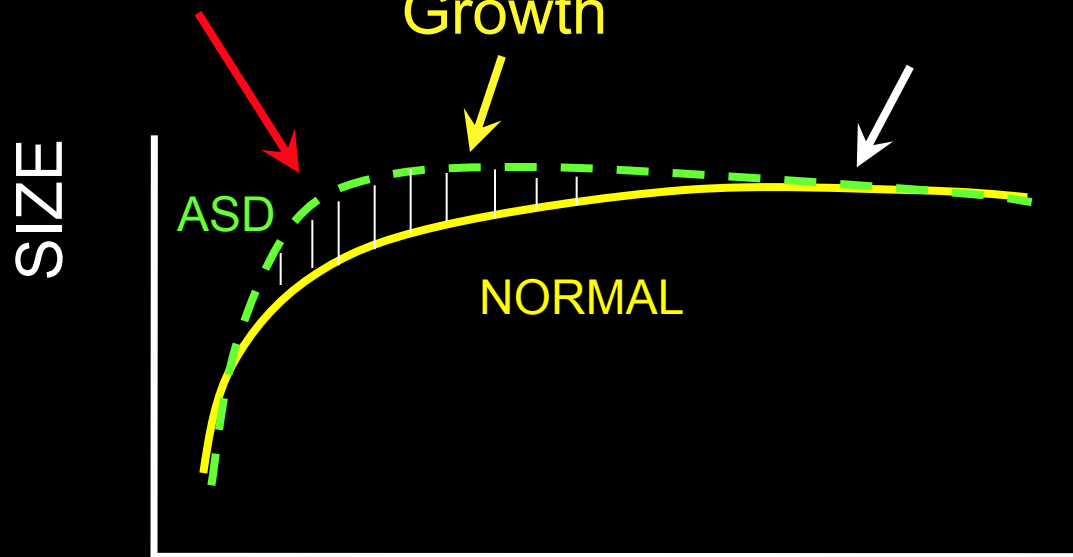


# Three Phases of Growth Pathology in ASD

Overgrowth

Arrested Growth

Possible Decline/Degeneration



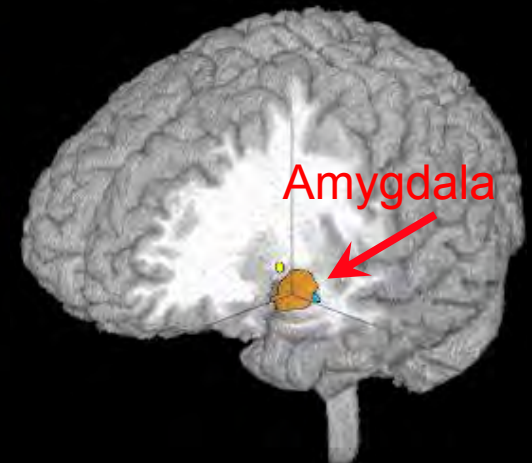
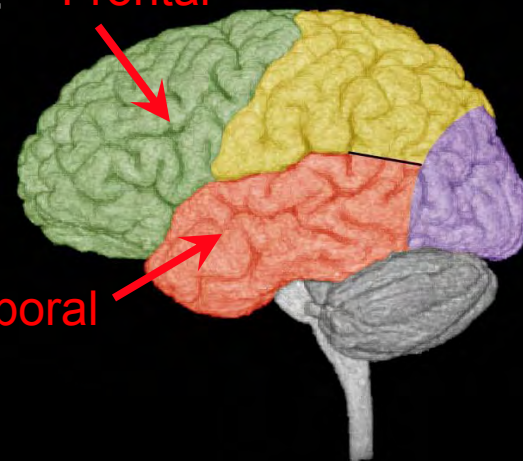
AGE

Frontal

Temporal

Amygdala

Courchesne et al 2001  
Courchesne & Pierce 2005  
Courchesne et al., 2007





# **Autism in the First Years of Life**

**Eric Courchesne and Karen Pierce  
Neurosciences, UCSD  
NIMH Autism Center of Excellence**

# The UCSD-ACE Prospective Study of Autism

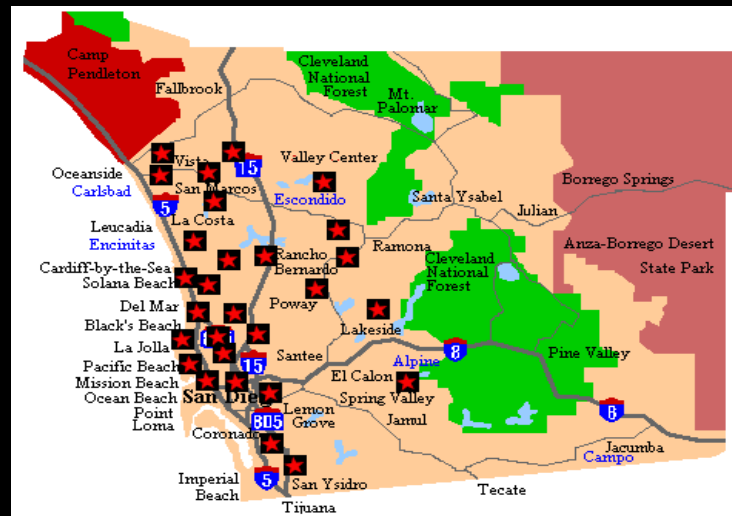
## 1 Yr Well-Baby Check-Up Approach



- Fast
- Easy
- Investigates autism as it occurs in the population

***Karen Pierce et al., in manuscript***

# UCSD-ACE PEDIATRICIAN NETWORK N=150



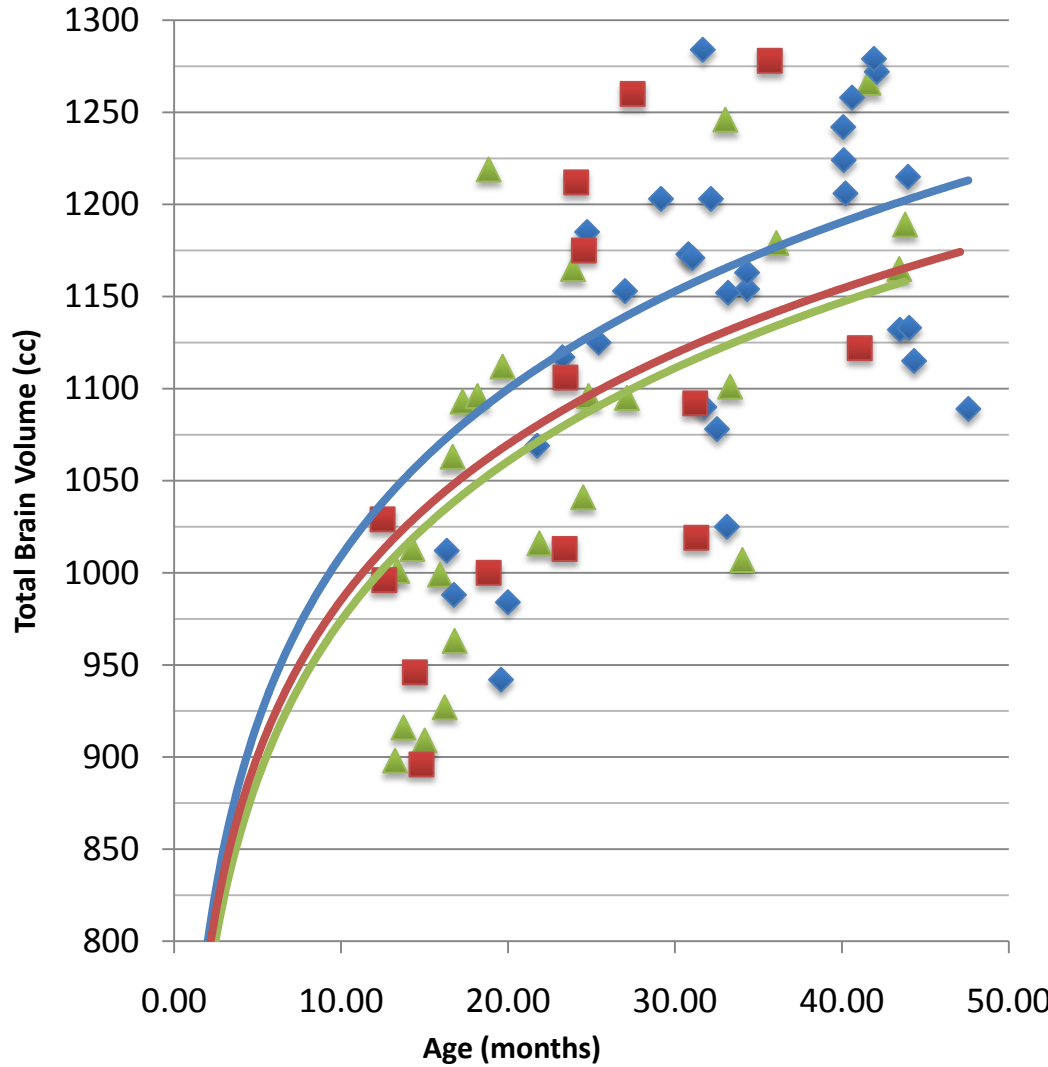
Dr. Robert Bjork, Dr. Michael Nelson, Dr. Cheryl Jennett  
Dr. Dr. John Kafa, Dr. Douglas Wilson, Dr. Crystal De Freitas  
Dr. Martin Gilboa, Dr. Patricia Juarez, Dr. George Madany,  
Dr. Seven Brody, Dr. Ingrid Martinez-Andree, Dr. Irene Chang  
Dr. Stephanie Powell, Dr. Adam Breslow, Dr. Patricia Pisinger  
Dr. Isabel Baratta, Dr. Sheila Cason, Dr. Thomas Neglia  
Dr. Stephen Balch, Dr. Randall Metsch, Dr. David Schmottlach  
Dr. Sonja Brion, Dr. Anna Mendenhall, Dr. Nancy Clementino  
Dr. Marshall Littman, Dr. Leslie McCormick, Dr. Sharon Sternfeld  
Dr. Cara Cohen, Dr. Nicholas Tsoulos, Dr. Elena Fishman  
Dr. Hilary Bowers, Dr. Albert Martinez, Dr. Genevieve Minka

Dr. Wendy Chacon, Dr. Leon Kelley, Dr. Victor Lipps, Dr. Jeffrey Selzer, Dr. Lynn Herring, Dr. Teresa O'dea, Dr. Richard Walls, Dr. Vivian Tung, Dr. Christian Archambault, Dr. Veronique James, Dr. Stuart Cohen, Dr. Nancy Shiau, Dr. Linda Smith, Dr. Tevor Henderson, Dr. Cheryl Morrell, Dr. Josef Zwass, Dr. Lon Dubeye, Dr. Andrea Siano, Dr. Aida Martinez, Dr. Rachel Ireland, Dr. Louis Luevanos, Dr. Laurie Tyrrell, Dr. John Cella, Dr. Jill Gustafson, Dr. Rosemary Page, Dr. David Steele, Dr. Carlos Quiros, Dr. Brian Chu, Dr. Kathleen Jones, Dr. James Moseman, Dr. Laurence Ashbacher, Dr. Theresa Dailey, Dr. Frederick Frumin, Dr. Nicholas Levy, Dr. Julie Snyder Block, Dr. Lori Taylor, Dr. Rosalind Dockweiler, Dr. Christine Wood, Dr. William Hitchcock, Dr. Robert Warner, Dr. Sheetal Gandhi, Dr. Suzanne Mills, Dr. Mona Sobel, Dr. Craig Duck, Dr. James Hay, Dr. Georgine Jorgensen, Dr. Richard Payne, Dr. James Quigley, Dr. Richard Buchta, Dr. Ann Marie Engfelt, Dr. Benjamin Siegel, Dr. Lori Gould, Dr. Micelle Sanford, Dr. Annie Kupelian, Dr. Paula Grayson, Dr. Raha Shaw, Dr. Gary Chun, Dr. Matilda Remba, Dr. Janna Cataldo, Dr. Nicole Gorton, Dr. Bret Gerber, Dr. Denise Brownlee, Dr. Stuart Rubenstein, Dr. Peggy Manuel, Dr. Veda Wu, Dr. Michael Berent, Dr. Gargi Kubal, Dr. Norman Gollub, Dr. Teresa Hardisty, Dr. Jeanne Montal, Dr. Katrina Durkee, Dr. Kamei Tolba, Dr. Carol Hart, Dr. Dennis Butler, Dr. Howard Mehl, Dr. Marta Awdykovych, Dr. Uma Narayan, Dr. Richard McNeal, Dr. Marta Awdykovych, Dr. Richard McNeal, Dr. Jennie Ou, Dr. Howard Smart, Dr. Neethi Ratnesar, Dr. Fujii, Dr. Mattson, Dr. Norman, Dr. Sauer, Dr. Gabriela Mogrovejo, Dr. Julie Keeler, Dr. Liz Hourihan, Dr. Dania Lindenberg, Dr. Dori Mortimer, Dr. Marvin Zaguli

# Total Brain Volume:

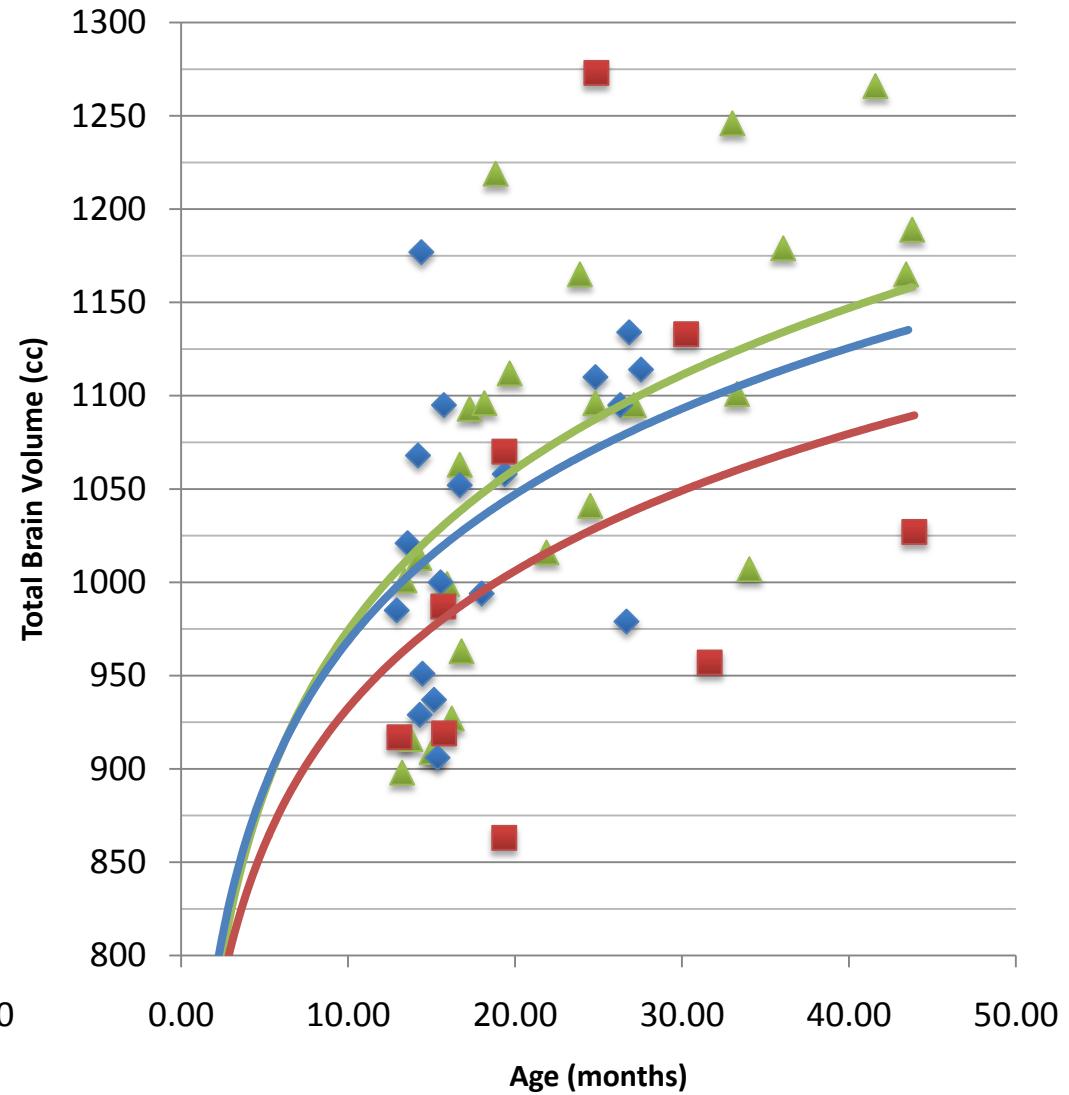
## Simplex vs. Multiplex

- ▲ Control
- ASD multi
- Log. (ASD single)
- ◆ ASD single
- Log. (Control)
- Log. (ASD multi)



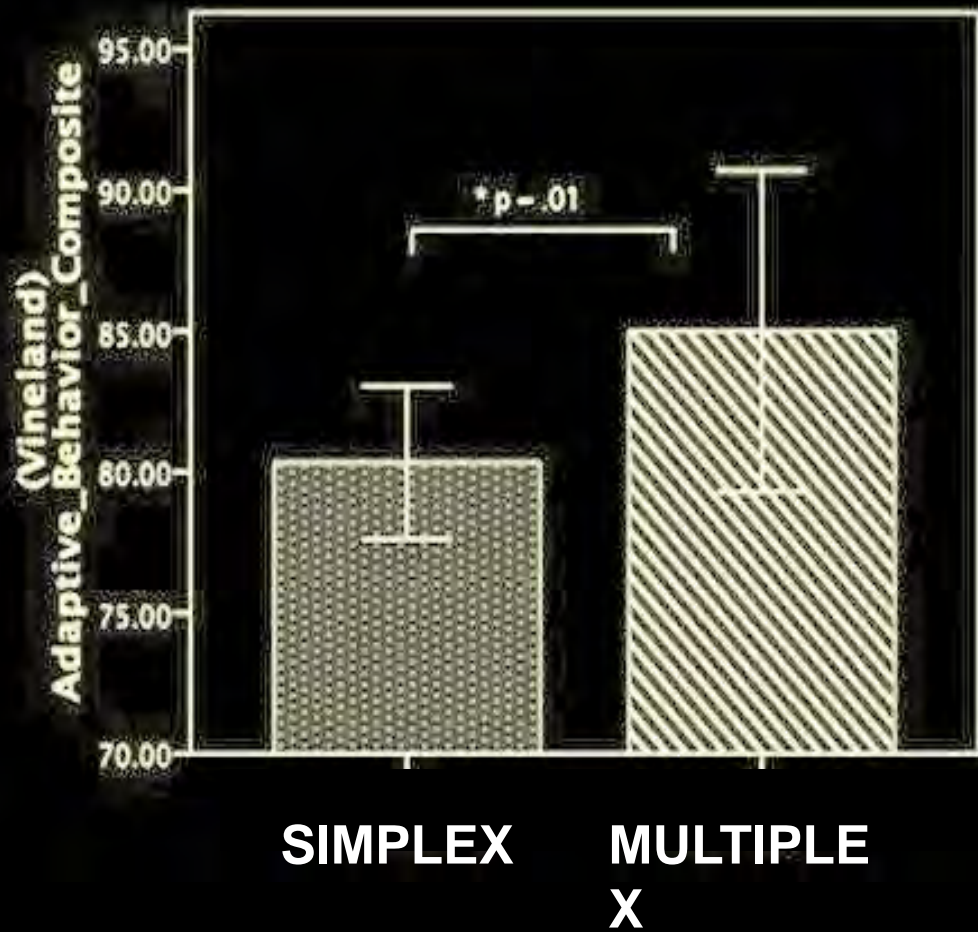
## LD vs. DD

- ▲ Control
- DD
- Log. (Control)
- ◆ LD
- Log. (LD)
- Log. (DD)

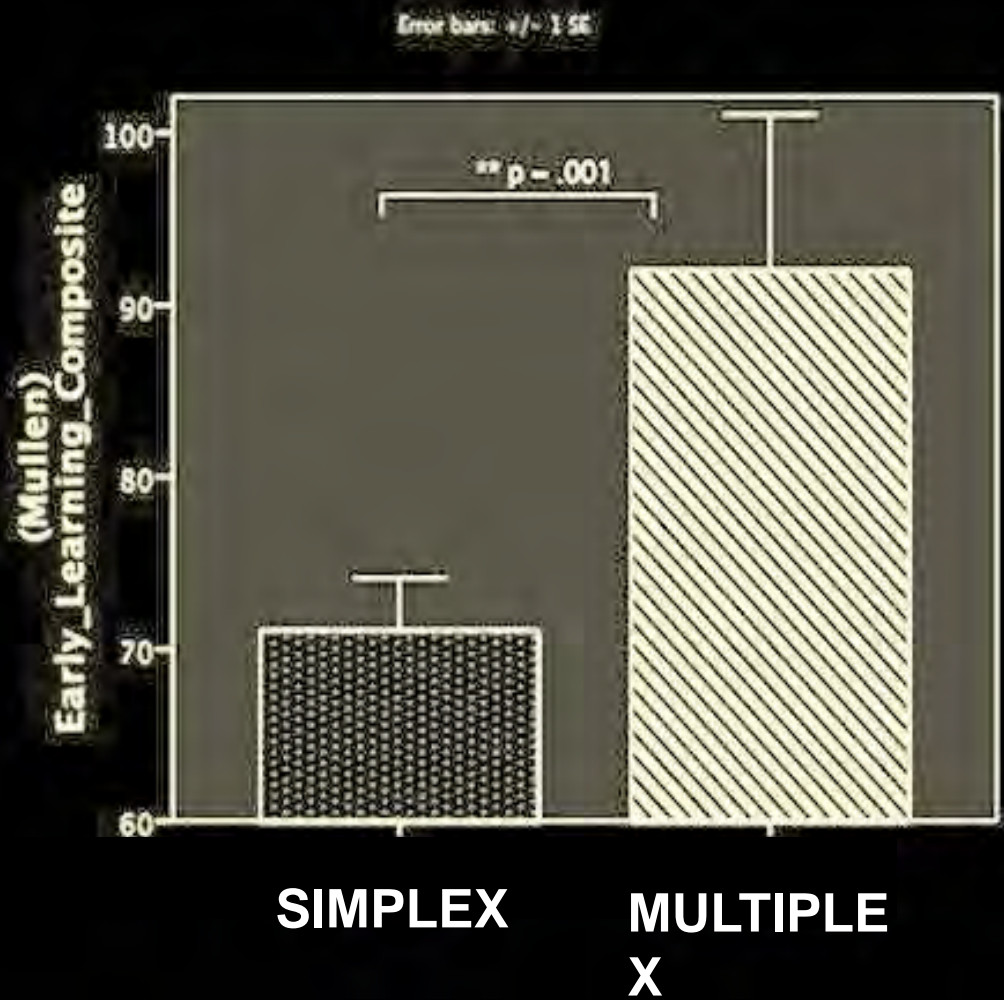


CLINICAL CHARACTERISTICS: Simplex More Severe

# VINELAND



# MULLEN: ELC



# **RED FLAGS of Autism Spectrum Disorder by 12- 24 Months**

## **Reduced social interest and affect**

**lack of warm, joyful emotional expressions**

**lack of sharing emotional enjoyment or interest**

**lack of response to name**

**lack of showing and interacting**

## **Abnormal language development**

**Lack of coordination of gaze, facial expression, gesture & sound during interactions**



DOG

CUTE HAT

WOW

How ...

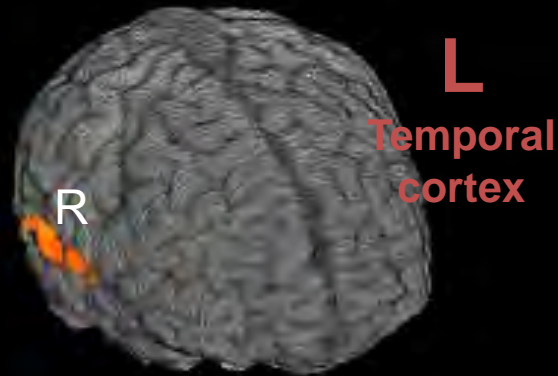


# Abnormal Laterality to Language in ASD Infants & Toddlers

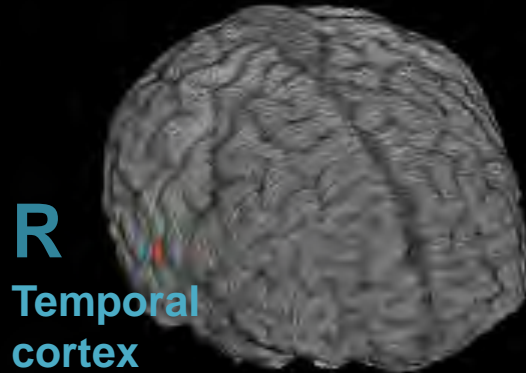
Eyler, Pierce and Courchesne



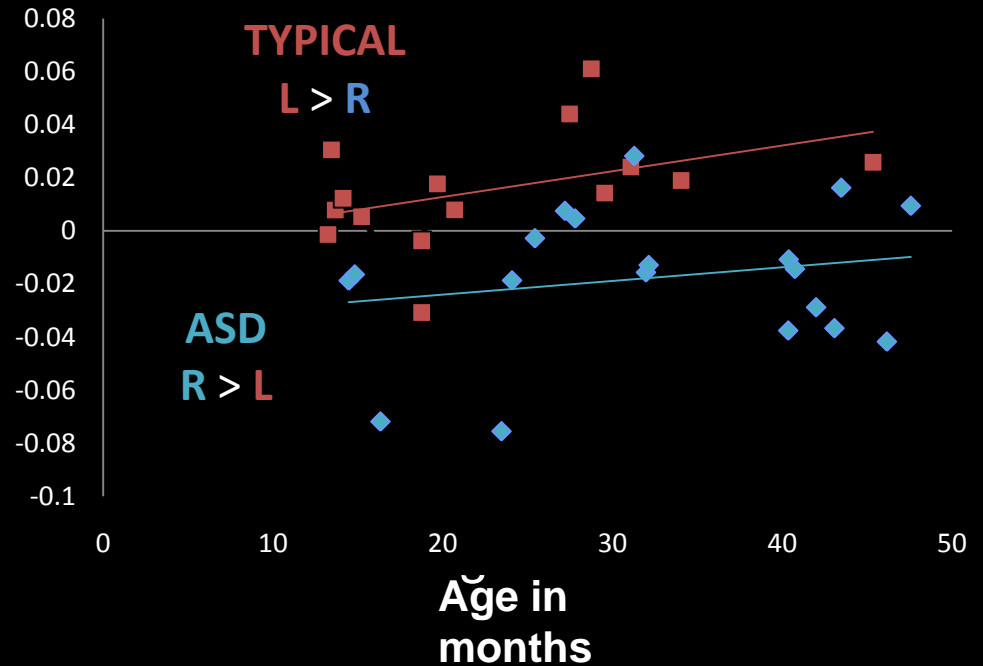
**TYPICAL**  
13 to 45 months



**ASD**  
14 to 47 months

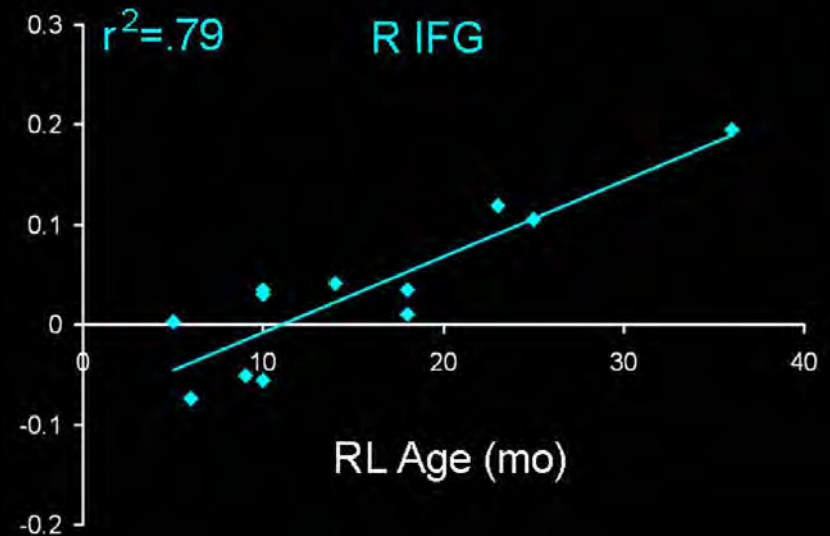
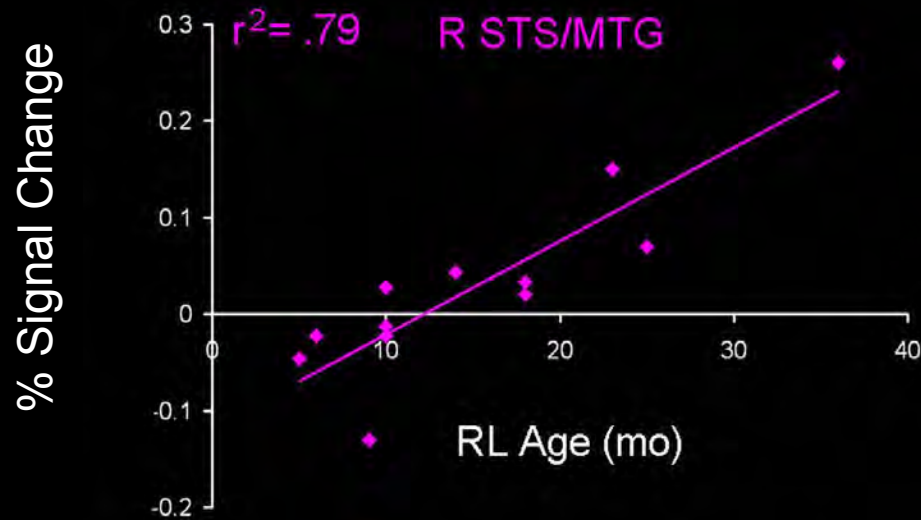
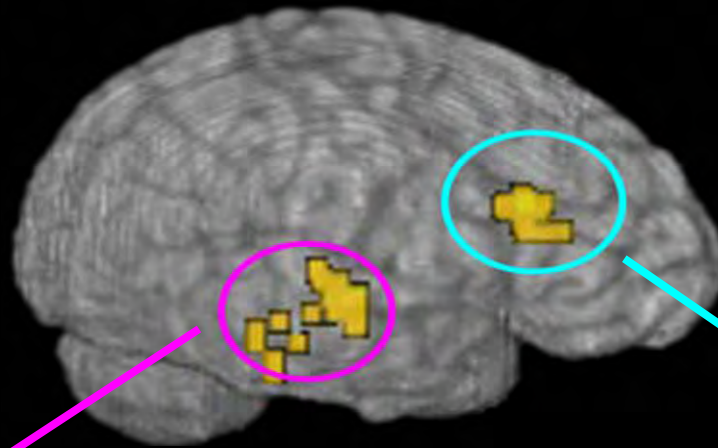


Left-Right Difference in Mean Fit Coefficient



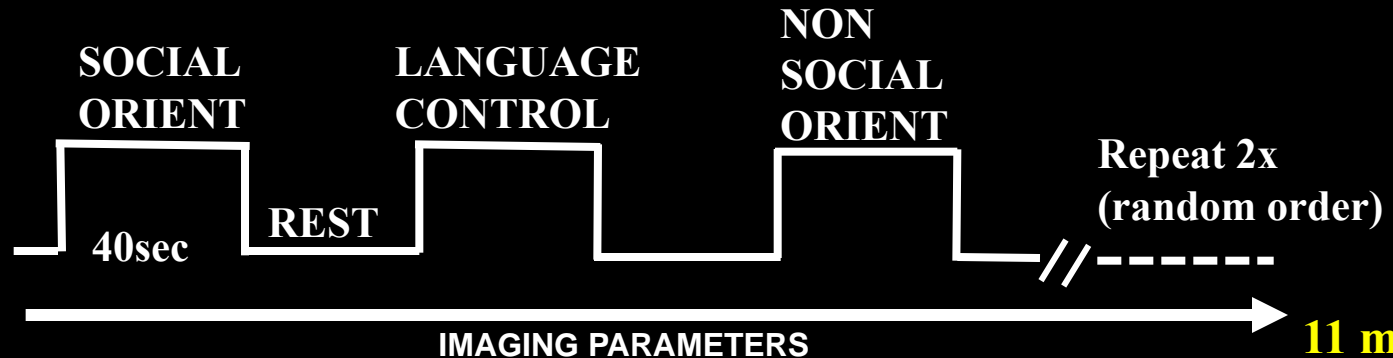
# RH recruitment may be advantageous in ASD

Reday & Courchesne, 2008



$p < .005$ , cluster 640 mm<sup>3</sup>

# SOCIAL ORIENTING EXPERIMENT



## IMAGING PARAMETERS

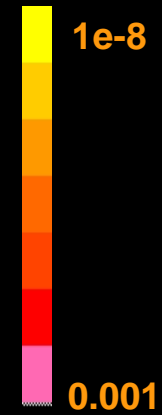
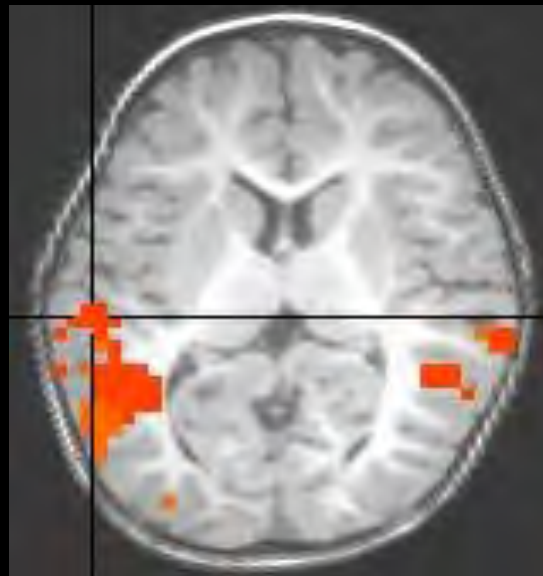
TR = 2.5 sec

# of TRs = 270

TE = 30 msec

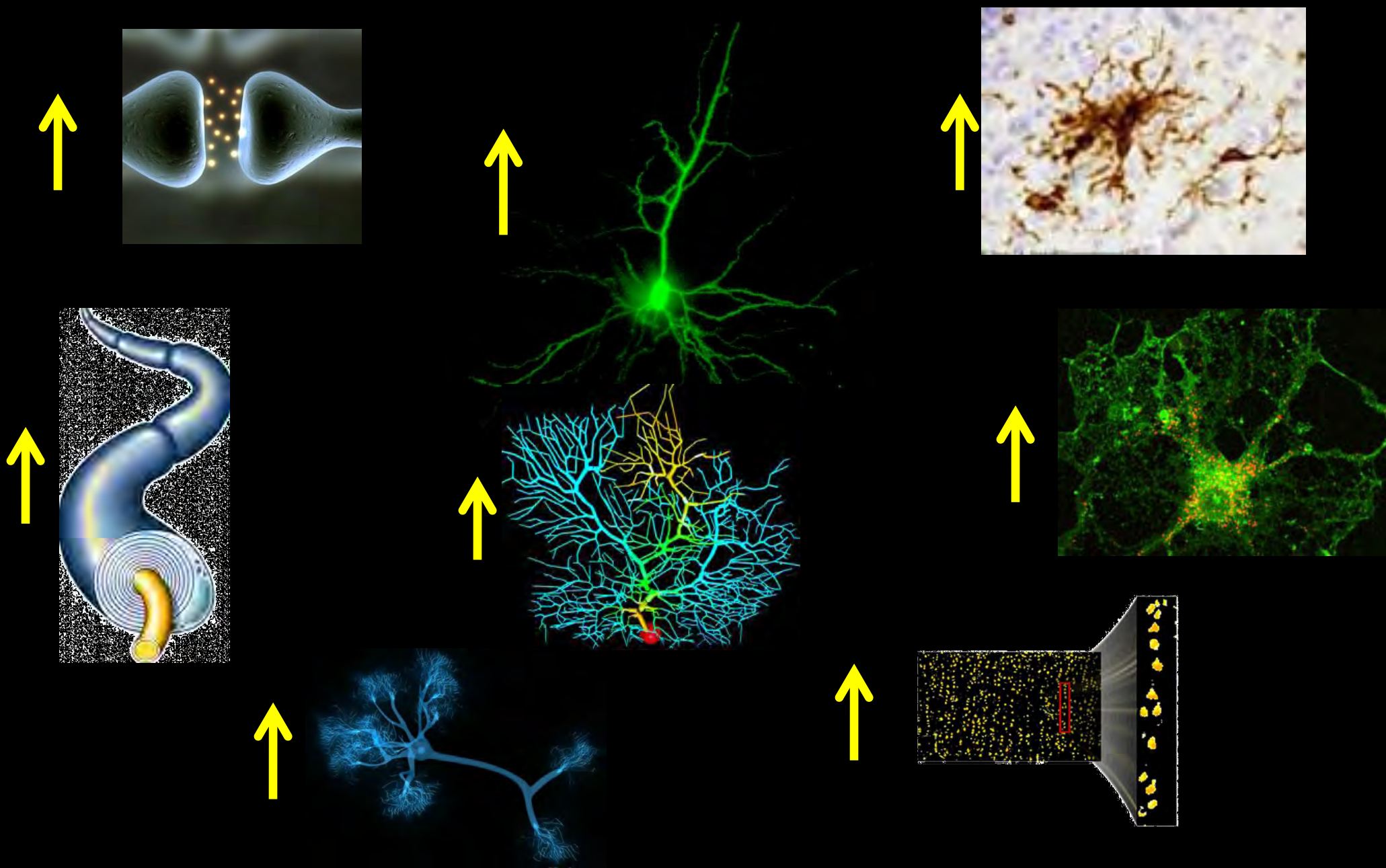
**Typical Toddlers > Autistic Toddlers**

L

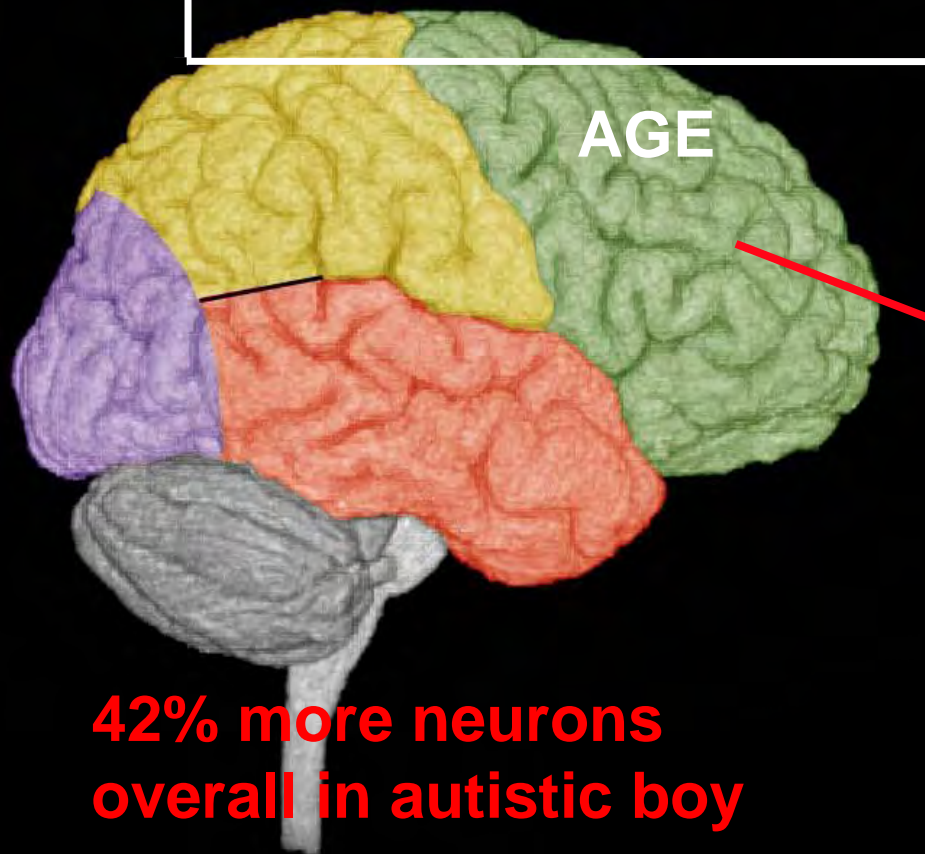
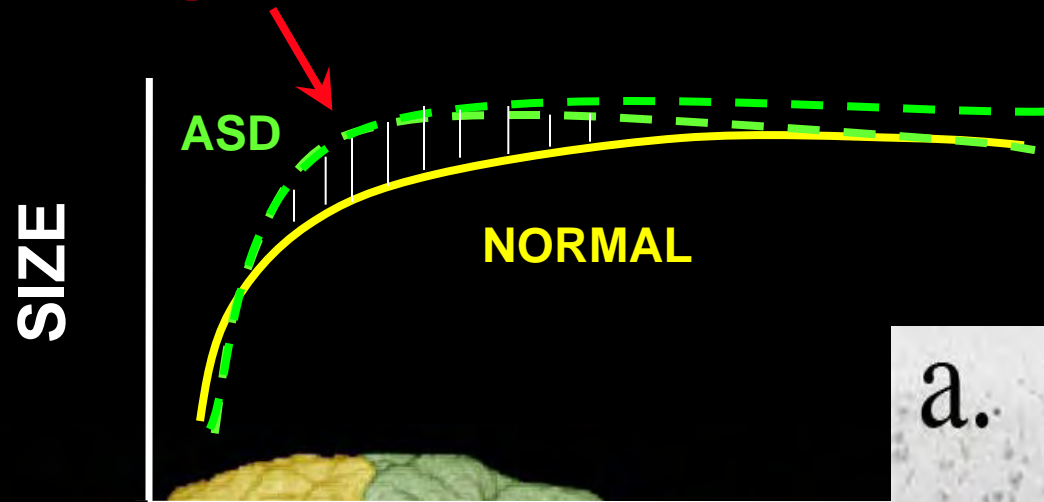


**Karen Pierce et al,  
in manuscript**

# Early Brain Overgrowth May Be Caused By:



# Overgrowth



**42% more neurons overall in autistic boy**

