

### **Meeting of the IACC**

### **ASD Science Update**

#### Thomas Insel, M.D.

Director, National Institute of Mental Health and Chair, IACC IACC Full Committee Meeting – July 10, 2012



**Predictive diagnostics:** Biomarkers (MEG, DTI, EEG), Cognitive (eye gaze, video tasks), Screening (1 yr check up)

#### PEDIATRICS Six Developmental Trajectories Characterize **Children With Autism** May 1, 2012

Christine Fountain, Alix S. Winter and Peter S. Bearman

#### Differences in White Matter Fiber Tract Development THE AMERICAN JOURNAL OF PSYCHIATRY Present From 6 to 24 Months in Infants With Autism

Jason J. Wolff, Hongbin Gu, Guido Gerig, Jed T. Elison, Martin Styner, Sylvain Gouttard, Kelly N. Botteron, Stephen R. Dager, Geraldine Dawson, Annette M. Estes, Alan C. Evans, Heather C. Hazlett, Penelope Kostopoulos, Robert C. McKinstry, Sarah J. Paterson, Robert T. Schultz, Lonnie Zwaigenbaum, Joseph Piven, the IBIS Network Am | Psychiatry 169:6, June 2012

#### **BMC Medicine**

A stable pattern of EEG spectral coherence distinguishes children with autism from neuro-typical controls - a large case control study

Frank H. Duffy and Heidelise Als

BMC Medicine 2012, 10:64

**Defining the problem**: Synaptic pathology, Circuit disorder, Whole body issues (immune, GI, etc)



### Brain enlargement is associated with regression in preschool-age boys with autism spectrum disorders

Christine Wu Nordahl<sup>a</sup>, Nicholas Lange<sup>b</sup>, Deana D. Li<sup>a</sup>, Lou Ann Barnett<sup>a</sup>, Aaron Lee<sup>a</sup>, Michael H. Buonocore<sup>c</sup>, Tony J. Simon<sup>a</sup>, Sally Rogers<sup>a</sup>, Sally Ozonoff<sup>a</sup>, and David G. Amaral<sup>a,1</sup> PNAS | December 13, 2011 | vol. 108 | no. 50 |

#### Developmental Trajectories of Resting EEG Power: An PLoS one Endophenotype of Autism Spectrum Disorder

Adrienne L. Tierney, Laurel Gabard-Durnam, Vanessa Vogel-Farley, Helen Tager-Flusberg, Charles A. Nelson

June 2012 | Volume 7 | Issue 6 | e39127



#### Mutations causing syndromic autism define an axis of synaptic pathophysiology Benjamin D. Auerbach, Emily

Nature. 2011 Nov 23;480(7375):63-8.

K. Osterweil & Mark F. Bear



# What caused this to happen and can it be prevented?

**Genomic risk factors**: New candidates, de novo mutations, rare events

#### PNAS MAY 22, 2012 A common X-linked inborn error of carnitine biosynthesis MAY 22, 2012 May be a risk factor for nondysmorphic autism

Patrícia B. S. Celestino-Soper<sup>a,1</sup>, Sara Violante<sup>b,c,1</sup>, Emily L. Crawford<sup>d</sup>, Rui Luo<sup>e</sup>, Anath C. Lionel<sup>f</sup>, Elsa Delaby<sup>g</sup>, Guiqing Cai<sup>h</sup>, Bekim Sadikovic<sup>a</sup>, Kwanghyuk Lee<sup>a</sup>, Charlene Lo<sup>a</sup>, Kun Gao<sup>e</sup>, Richard E. Person<sup>a</sup>, Timothy J. Moss<sup>a</sup>, Jennifer R. German<sup>a</sup>, Ni Huang<sup>i</sup>, Marwan Shinawi<sup>a,j,2</sup>, Diane Treadwell-Deering<sup>j,k</sup>, Peter Szatmari<sup>1</sup>, Wendy Roberts<sup>m</sup>, Bridget Fernandez<sup>n</sup>, Richard J. Schroer<sup>o</sup>, Roger E. Stevenson<sup>o</sup>, Joseph D. Buxbaum<sup>h</sup>, Catalina Betancur<sup>g</sup>, Stephen W. Scherer<sup>f,m</sup>, Stephan J. Sanders<sup>p</sup>, Daniel H. Geschwind<sup>e</sup>, James S. Sutcliffe<sup>d</sup>, Matthew E. Hurles<sup>i</sup>, Ronald J. A. Wanders<sup>b</sup>, Chad A. Shaw<sup>a</sup>, Suzanne M. Leal<sup>a</sup>, Edwin H. Cook, Jr.<sup>q</sup>, Robin P. Goin-Kochel<sup>a,j,r</sup>, Frédéric M. Vaz<sup>b,1</sup>, and Arthur L. Beaudet<sup>a,j,r,1,3</sup>



*De novo* mutations revealed by whole-exome sequencing are strongly associated with autism Sanders, et al.

Sporadic autism exomes reveal a highly interconnected protein network of *de novo* mutations

April 5, 2012

O'Roak, et

#### Patterns and rates of exonic *de novo* mutations in autism spectrum disorders Neale, et

These slides do not reflect decisions of the IACC and are for discussion purposes only.

al.



## What caused this to happen and can it be prevented?

Environmental risk factors: Results from CHARGE study

Is Maternal Influenza or Fever During Pregnancy Associated with Autism or Developmental Delays? Results from the CHARGE (CHildhood Autism Risks from Genetics and Environment) Study

Ousseny Zerbo • Ana-Maria Iosif • Cheryl Walker • Sally Ozonoff • Robin L. Hansen • Irva Hertz-Picciotto

Journal of Autism and Developmental Disorders May 2012 [epub]

#### **PEDIATRICS** April 9, 2012 [epub] Maternal Metabolic Conditions and Risk for Autism and Other Neurodevelopmental Disorders

Paula Krakowiak, Cheryl K. Walker, Andrew A. Bremer, Alice S. Baker, Sally Ozonoff, Robin L. Hansen and Irva Hertz-Picciotto

Maternal periconceptional folic acid intake and risk of autism spectrum disorders and developmental delay in the CHARGE (CHildhood Autism Risks from Genetics and Environment) case-control study<sup>1–3</sup>

Rebecca J Schmidt, Daniel J Tancredi, Sally Ozonoff, Robin L Hansen, Jaana Hartiala, Hooman Allayee, Linda C Schmidt, Flora Tassone, and Irva Hertz-Picciotto American Journal of Clinical Nutrition, July 2012



# Which treatments and interventions will help?

### New initiatives in medication development: biomarker driven trials, public-private partnerships, leveraging on results w FraX and Rett

#### **FNIH Biomarkers Consortium**

• Autism Speaks, Simons Foundation, FDA, NIH, 5 companies

#### FAST Fail Trials in Autism Spectrum Disorders (FAST-AS) Initiative

• An NIMH initiative to implement rapid Proof of Clinical Mechanism (POCM) and Proof of Concept (POC) trials in order to quickly test and analyze novel interventions

#### Autism Treatment Network (ATN)

• Autism Speaks, HRSA, NIMH developing best practices, RCTs, biobank



# Which treatments and interventions will help?

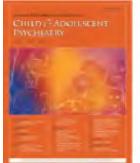
### New findings w behavioral treatments:

Longer term effects, generalizability, pre-emptive Rx



#### Making the connection: randomized controlled trial of social skills at school for children with autism spectrum disorders Apr 2012

Connie Kasari,<sup>1</sup> Erin Rotheram-Fuller,<sup>2</sup> Jill Locke,<sup>3</sup> and Amanda Gulsrud<sup>1</sup>



#### Longitudinal Follow-Up of Children With Autism Receiving Targeted Interventions on Joint Attention and Play

Connie Kasari, Ph.D., Amanda Gulsrud, Ph.D., Stephanny Freeman, Ph.D., Tanya Paparella, Ph.D., Gerhard Hellemann, Ph.D.

JOURINAL OF THE AMERICAN ACADEMY OF CHILD & ADOLESCENT PSYCHIATRY VOLUME 51 NUMBER 5 MAY 2012



ORIGINAL PAPER

Pivotal Response Treatment for Infants At-Risk for Autism Spectrum Disorders: A Pilot Study May, 2012

Amanda Mossman Steiner, Grace W. Gengoux, Ami Klin and Katarzyna Chawarska



## **Economic and health issues:** Effects on caregivers, costs of medical care

#### **PEDIATRICS** March 19, 2012 [epub] Implications of Childhood Autism for Parental Employment and Earnings

Zuleyha Cidav, Steven C. Marcus and David S. Mandell



Volume 33, Issue 2, March-April 2012, pages 467-476

#### Concurrent medical conditions and health care use and needs among children with learning and behavioral developmental disabilities, National Health Interview Survey, 2006–2010

Laura A. Schieve<sup>,</sup>, Vanessa Gonzalez, Sheree L. Boulet, Susanna N. Visser, Catherine E. Rice, Kim Van Naarden Braun, Coleen A. Boyle

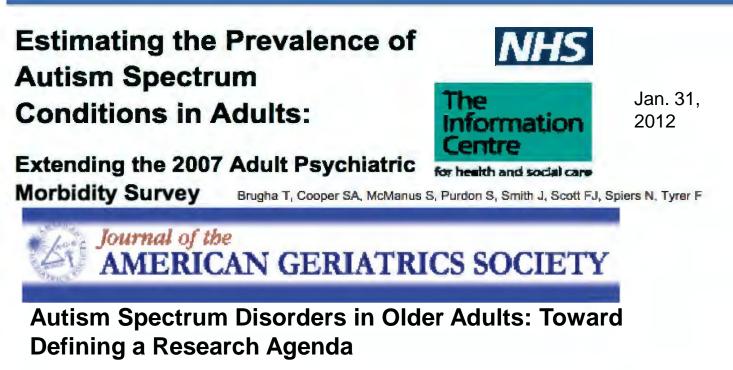
#### Service and Wider Societal Costs of Very Young Children with Autism in the UK

Barbara Barrett, Sarah Byford, Jessica Sharac, Kristelle Hudry, Kathy Leadbitter, Kathryn Temple, Catherine Aldred, Vicky Slonims, Jonathan Green and PACT Consortium

Journal of Autism and Developmental Disorders, 2012, Vol. 42 No. 5, pgs. 797-804



# What does the future hold, particularly for adults?



Joseph Piven and Peter Rabins, on behalf of the Autism-in-Older Adults Working Group *November 2011* 

### Postsecondary Education and Employment Among Youth With anAutism Spectrum DisorderPEDIATRICSMay 14, 2012 [epub]

Paul T. Shattuck, Sarah Carter Narendorf, Benjamin Cooper, Paul R. Sterzing, Mary Wagner and Julie Lounds Taylor



What other infrastructure and surveillance needs must be met?

Prevalence and database: CDC reports 1 in 88 (1 in 54 boys) – 78% increase from 2002. NDAR expands to >30,000 subjects.



Prevalence of Autism Spectrum Disorders — **Autism and Developmental Disabilities Monitoring** Network, 14 Sites, United States, 2008

Sharing Heterogeneous Data: The National Database for **Autism Research** 

Neuroinformatics May 2012

Dan Hall, Michael F. Huerta, Matthew J. McAuliffe, Gregory K. Farber