Autism Today Is Not The Autism of Your Mother’s Day
ASD Today

- Wide range of IQs including superior
- Wide range of verbal abilities including complex sentence structure in half
- Manifestations are unusual social, communication, play, and thinking
- Often misdiagnosed as psychiatric disorders - usually many that don’t work
- Considerable variability person to person
“Cause”

- Etiology
- Pathophysiology
- Analysis of specific action for “cause”
Big News: Understanding Cause

- Really do understand a lot, relative to what was known which was worse than nothing
- Really have a lot to learn yet; brain is very complex
- Major features now identified from gene to behavior
- New understanding is generating new neurocognitive interventions in second year & second decade that are more effective
Etiologies

- 20-30 genes or chromosomal syndromes account for 15-20% of cases; genes scattered across chromosomes; genes code for proteins not diagnoses; overlapping brain basis-overlapping genes
- “New” genetic mechanism- CNV
- Environmental origins much discussed, rare supporting evidence except as below
- Fetal rubella infection & a few fetal drug exposures- operative word is “fetal”
Pathophysiology-Mechanisms

Biggest advances:
- Connections among higher brain regions
- Connectivity Theory began here
- Cortical neuron connections
- Integrative processing
- Disturbances in developmental neurobiological mechanisms
Cause Now Framed As

- Cortical underconnectivity - cortical origin of affected neurons explains syndrome
- Impaired integrative processing and speed of processing account provides common framework for all symptoms
- 20-25 genes coding for development of brain cell connections
- As neuronal organization and migration disorders and particularly axonal outgrowth
New Treatments

New neurocognitive interventions which include emotion component:
- Denver Model+: at 14 months of age
- Cognitive Enhancement Therapy- 2nd decade and older

Neuropharmacology:
- Rapamycin for prevention of ASD, ID, and epilepsy in tuberous sclerosis
Emerging Directions

- Advanced imaging: how the brain is connected, how it is organized, how it thinks consciously and nonconsciously
- Advanced studies of automatic information processes
- Developmental neurobiology mechanisms
- Gene hunt continues on steroids
Brain Connection Science

Technology to Read Out the Genetic Programs that Determine Brain Connectivity with Future Applications to Disorders Such As Autism. Walter Schneider
University of Pittsburgh wws@pitt.edu

Diffusion Acquisition

ODF & Streamline Reconstruction

Tract Segmentation

Cortical Gradients

Track Growth Operations

Genetic Growth Routine

Neurosurgery

Clinical

Traumatic Brain Injury

Track Quantification

Connection Disorders

Movement

Autism

<table>
<thead>
<tr>
<th>Neuron Growth Program</th>
<th>X1</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>IF X1=1 X1=- X3=+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>IF X3=0.75 Funnel = -</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>IF X3=1 Stop Divide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Connective Pipe Diagram

Growth Operations

Neuroscience

Traumatic Brain Injury

Cortical Gradients

Track Growth Operations

Genetic Growth Routine

Neurosurgery

Clinical

Track Quantification

Connection Disorders

Movement

Autism
General Overview
Mapping the Cable Harness of the Human Brain
Reading out the Genetic Grammar to Wire the Human Brain

Identify the Cable running programs of the human brain; what are the rules for connectivity; How is it engineered?

Airbus A320

Aircraft Cable Harness with drop points for different Instruments

9 Crossings
11 Splitting
Mapping Brain Wiring Diagram and Genetic Specification

- Identify fiber tract/bundles, get number of micro tracts connecting brain areas
- Get 500,000 streamlines
- Identify key manifolds
Example Genetic Bugs

- Missing gradient - all seeking that gradient confused neurons don’t know where to go
- Missing sensor – neurons of given tract do not make turn
- Missing If statement – no change in expected turn
- Differential proportion of cells divided between programs
  - e.g., decussation
Making The Future Happen Now

• Funding for those students who help develop technology as they are learning the tools

• Math, neuroscience, neuroanatomy undergrads, pre-docs and post-docs

• Growing technical skills to make these advances
Fundamentals

- NIH Motto: When God speaks, we listen.
- FDA Corollary: From everyone else we expect data.

- Science is a process in progress
- The plural of anecdotes is not data.
- Progress based on technology is exponential.