



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 s & s
- 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

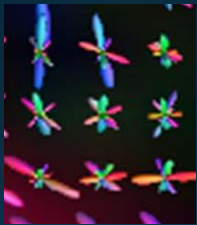


Emerging Directions

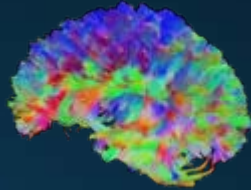
- Advanced imaging: how the brain is connected, how it is organized, how it thinks consciously and nonconsciously
- Advanced studies of automatic information processes
- Developmental neurobiology mechanisms
- Gene hunt continues on steroids

Brain Connection Science

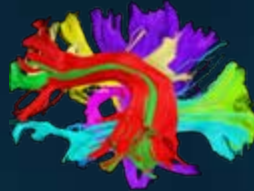
Diffusion Acquisition



ODF & Streamline Reconstruction



Tract Segmentation



Neurosurgery

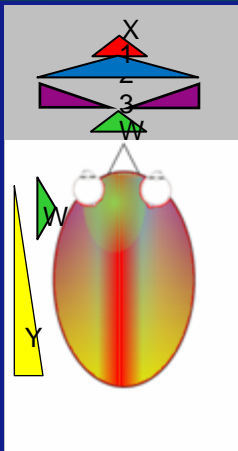


Clinical

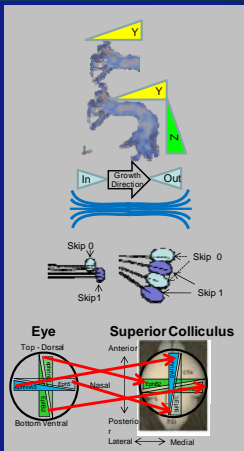
Traumatic Brain Injury



Cortical Gradients



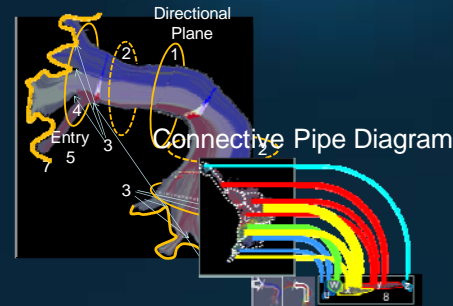
Track Growth Operations



Genetic Growth Routine

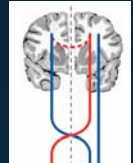
Neuron Growth Program	X1
Start	+
If X1=1 X1=- X3=+	-
If X3=0.75 Funnel = -	-
If X3=1 Stop Divide	

Track Quantification

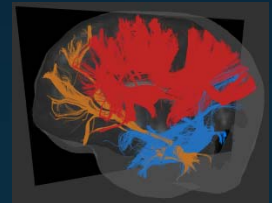


Connection Disorders

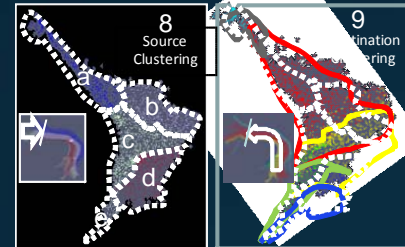
Movement



Autism



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



General Overview

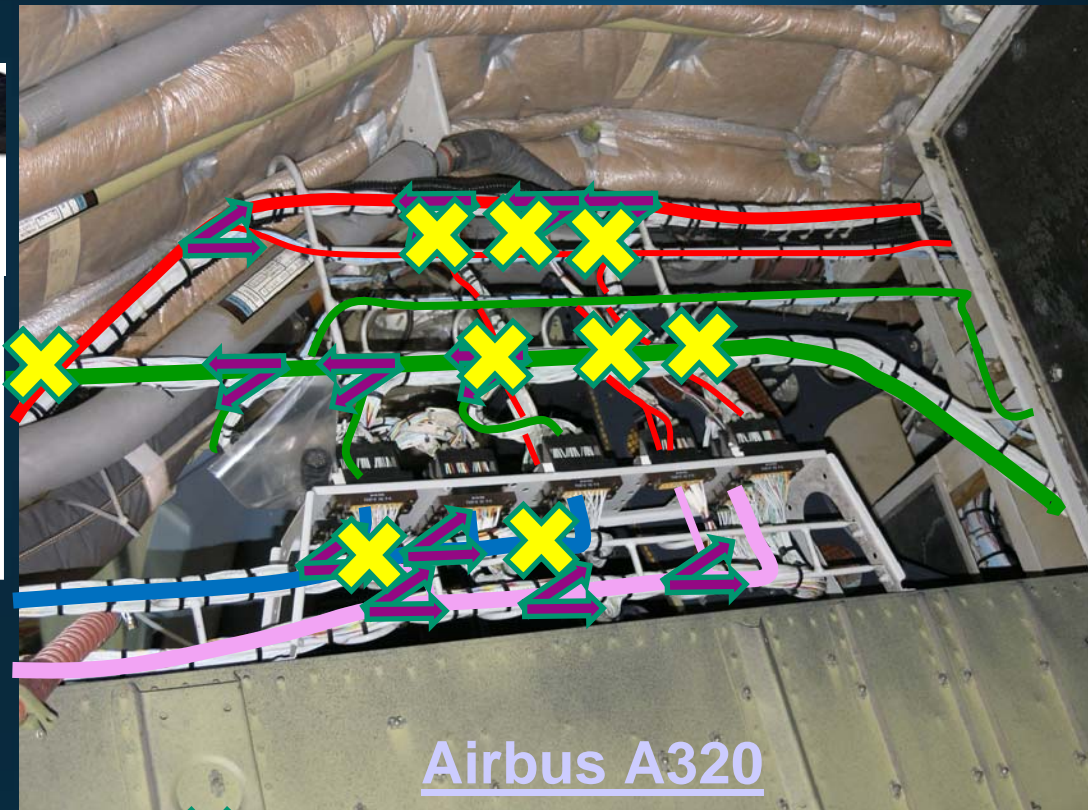
Mapping the Cable Harness of the Human Brain

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?



Aircraft Cable Harness with drop points for different Instruments



Airbus A320

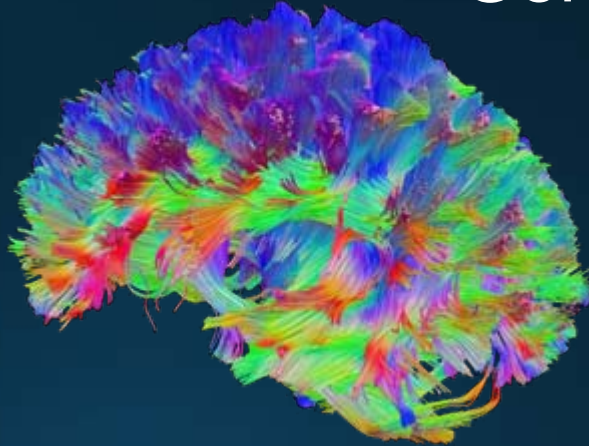


9 Crossings



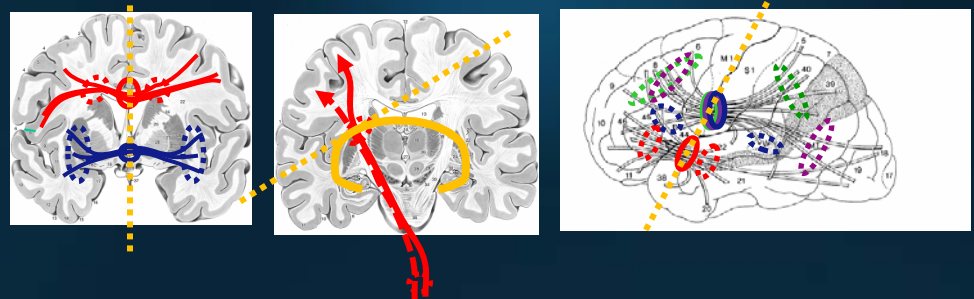
11 Splitting

Mapping Brain Wiring Diagram and Genetic Specification



Get 500,000 streamlines

Identify key manifolds



Identify fiber tract/bundles, get number of micro tracts connecting brain areas



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:
- Science is a
process in progress
- From everyone else
we expect data.
- The plural of
anecdotes is not data.
- Progress based on
technology is
exponential.