Unravelling Autism

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Learning Objectives

• Describe essential features of autism spectrum disorders
• Overview of genetic factors in the disorder
• Understand brain function related to core features of autism
• Review features of epidemiology—is there an epidemic or not
• Role of science/education vs. Myth/meme
Autism Spectrum Disorders

• Autistic Disorder
• Pervasive Developmental Disorder NOS
• Asperger’s Syndrome
• Rett’s Disorder
• Child Disintegrative Disorder
• ALL become ASDs in DSM-V
Historical Perspective

- Feral children
- Kanner-1943 Infantile Autism
- Asperger-1944 Autistic Psychopathy
- Rank-1949 Atypical Personality
Autism Defined

The Great Autism Researcher--Dr Seuss

Thing One: Social Disability-intuitive understanding of others, feeling their feelings, social understanding, intersubjectivity

Thing Two: Early Onset of neuro-developmental disorder

(Stolen from Ami Klin)
Core Features ASDs

- Social impairment
- Communication Deficits
- Restricted interest/Repetitive Behaviors
- Deficit/Deviance beyond IQ/developmental
- Core Feature is SOCIAL
Areas of Concern

Social Impairment

Communication

Restricted and Repetitive
M-CHAT screening

- Pediatrics - all 18 and 24 month olds
- Does your child take interest in other children?
- Does your child ever use his/her body to point, to indicate interest?
- Does your child smile in response to your smile?
- Does your child respond to his/her name when called?
- Does your child imitate you?
- Does your child ever pretend, e.g., to talk on the phone or take care of dolls?
Early Warning Signs Autism

• Social: abnormal eye contact, limited social interest, little affect, anticipation pickup, happy to be alone, limited play
• Communication: poor response to name, doesn’t look at objects held by others, limited babbling/late words, fail to respond to gesture
• Behavior: averse to touch, hand/finger movements, unusual sensory behaviors
Infant Observation
Autism Diagnostic Observation Schedule

- Social and communicative presses or bids
- Play session with set structures/interactions
- Social response
- Communication response
- Developmentally oriented
- Clinical Interview
Joint attention, Shared emotion
Bid for Attention
On the Way, but holding back
Social Engagement and Reciprocity
Asperger’s Syndrome

- Original Case series - all male
- Marked social problems
- Normal to above average IQ, VIQ >> PIQ, NLD
- Motor clumsiness, talks before walks
- Restricted interests - train schedules
- Positive FH, dads less social
- Good language but poor communication, hyperlexia
Asperger’s Syndrome

• No language delay, hence later diagnosis
• Language NOT normal though-pedantic, poorly modulated, literal, concrete, miss the point, verbosity, circumstantial
• Very poor non-verbal pragmatic communication
• Usually unable to form friendships
• Social isolation, despite social hunger
• Little Professors
Asperger Myths Disspelled

• NOT “Autism-Lite”
• NOT mild social skills impairment
• NOT whatever you just read on the Internet
• ??? Not what a lot of people who say they have “mild” Asperger’s—Michael Palin, Dan Ackroyd, Tom Arnold
• IS Lifelong severe social disability/impairment
Cognitive Abnormalities in ASDs

- Face Processing: encoding facial features and eye gaze
- Social Affiliation: joint attention, sensitivity to reward
- Motor Imitation: body actions
- Language Ability
- Theory of Mind
Deficits in Learning and Memory

- Delay in spoken language
- Deficits in intelligence (75% Dev Dis)
- Majority of genes known to cause autism:
  - Synaptogenesis
  - Neuronal migration
- Disorder of Learning and Memory is social intelligence?
Cortical Abnormalities

- Increased Brain Volume
- Enlarged head circumference
- Possible accelerated head growth neonatal period
- Learning and Memory: Cerebral Cortex, hippocampus, amygdala
Face Processing

- Learning and memory social function
- Fusiform gyrus lights up in normal fMRI
- Autistic in light in fusiform gyrus
- Activate object processing areas when looking at faces in autism
- Face=Objects
- Included familiar and unfamiliar faces
Eye Contact and Gaze

- Eye tracking devices
- People with ASDs looks at chin and mouth, not eyes
- Reduced amount of time fixating on eyes
- Reduced eye contact responsible for lack of activation of fusiform gyrus
Social Awareness

- Words are Social Concepts
- Auditory Input, voice, Sensory Aspect
- Facial Processing, Sensory Aspect
- Many triggers
- Activates Superior Temporal Sulcus
Mirror Neurons

- Awareness of actions of others
- Visuomotor Neurons prefrontal cortex, parietal lobe, and STS
- Active when performing action or watching someone perform same action
- Requires seeing effective organ of action, the object, and the motion
- Imitation ability, self and other action
Social Language

• Prosody - the music of speech
• Temporal lobes superior portion
• Social = superior temporal sulcus
• Overlap between prosody and social areas
• Prosody conveys emotional and social context
• Tone of voice, emails
Theory of Mind

- Action monitoring
- Self-knowledge
- Person perception
- Mentalizing
- Outcome monitoring
Genetic evidence for Autism

- Twin studies-concordance identical 70% vs. fraternal 35%, previously 90/10
- Sibling recurrence 15%, up to 35% or more if >2 children affected
- 15-40% children with ASDs have chromosomal or Medelian cause or predisposition
Known Genetics Causes

- Fragile X
- Tuberous Sclerosis
- DNA for Fragile X
- Chromosomal Microarray-detects chromosomal deletions and copy number variants
Fragile X

- So-called because in 70s and 80s, chromosomal or cytogenetics testing identified a fragile site or narrowing at end of X chromosome.
- X-linked recessive, but more complicated.
- If mother is carrier, boys have 1 in 2 chance of having gene and disorder.
- If mother is carried, girls have 1 in 2 chance of having gene, being carrier and partial expression.
Fragile X

- Causes by CGG (code word or triplet) repeat expansion mutation (>200 repeats = full mutation) in the promoter of Fragile X mental retardation gene FMR1
- Leading inherited cause of Intellectual Disability
- Most common single gene disorder associated with ASDs
Fragile X Broad Phenotype

- Men: Intellectual Disability in 100%
- Speech delay and motor skills delay
- Behavioral and emotional issues
- Medical issues: cardiac
- Physical issues: large ears, long face, large testes, loose joints, scoliosis, braid forehead
Fragile X and ASDs

- 20-30% of men with Fragile X have ASD
- 40-70% have some feature of ASDs
- 50-90% may have symptoms of ASD: perseverative speech, poor eye contact, unusual hand motions
- Flip Side: of all individuals with ASDs, 3-6% have Fragile X
Is Autism Increasing?

• Are we counting better?
• Are we diagnosing better?
• Are we screening better?
• Young Shin Kim study: 1 in 38
• 2.6% prevalence
Risk of Recurrence

• Younger Sibs have 20% chance
• Much higher than previous estimates of 3-10%
• Baby brothers: 25% risk
• Infants with more than one sib with autism, multiplex families; 1 in 3