Unravelling Autism

- Preston Wiles M.D.
- Professor, UTSWMC
- Senior Attending, Autism Center

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

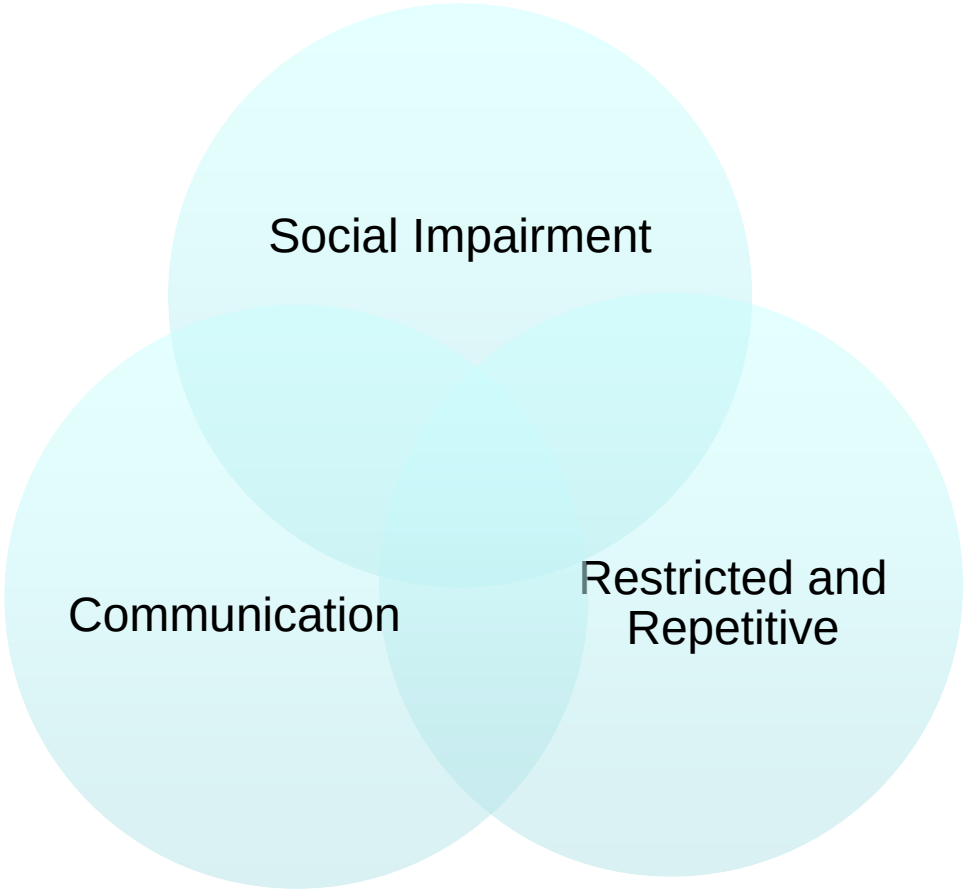
(Stolen from Ami Klin)

Core Features ASDs

- Social impairment
- Communication Deficits
- Restricted interest/Repetitive Behaviors

- Deficit/Deviance beyond IQ/developmental
- Core Feature is SOCIAL

Areas of Concern



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 familes; 1 in 3