Pervasive Developmental Disorders

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Questions 1

- A 3 year old girl presents with impaired receptive and expressive language. She has stereotyped hand movements although her parents say that up to the age of 18 months she seemed to be have purposeful hand skills. Her height and weight are age appropriate but her head growth has decelerated after she passed her second birthday. The most appropriate diagnosis is:
  - A Autistic disorder
  - B Rett's disorder
  - C Asperger's disorder
  - D Childhood disintegrative disorder
  - E Pervasive developmental disorder NOS

Question 2

- Which of the following statements is true
  - A-Some children with Asperger's disorder have mental retardation
  - B-The gene for autistic disorder is found on chromosome 7q
  - C-The evidence supports a link between the MMR (measles/mumps/rubella) vaccination and autism
  - D- The chance of having a child with Autistic disorder is 1 in 500
  - E-If a couple have a child with autistic disorder the chance of having a second child with that diagnosis is 1 in 100

Question 3

- The RUPP study on the treatment of aggression in Autism presents evidence on the use of which atypical antipsychotic for this presentation?
  - A Haloperidol
  - B Quetiapine
  - C Olanzapine
  - D Risperidone
  - E Aripirazole

Question 4

- Which of the following is a semi-structured interactive assessment that can be conducted with a during an evaluation for an autism spectrum disorder?
  - A Autism Diagnostic Observation Schedule (ADOS)
  - B Autism Diagnostic Interview Revised (ADI-R)
  - C Childhood Autism Rating Schedule (CARS)
  - D Pervasive Developmental Disorders Screening Test (PDDST)
  - E Checklist for Autism in Toddlers (CHAT)

Question 5

- All of the following statements about the prognosis for a child with autism are true except?
  - A-Seizures effect about 25% of those with a generalized learning disability
  - B-The peak age for onset of seizures is 11-14 years of age
  - C-About 10% go through a phase in adolescence when they lose some language skills
  - D-By adulthood approximately 10% of individuals with full autistic syndrome will be working and able to look after themselves
  - E-They are at increased risk for developing schizophrenia in late adolescence and adulthood

*The goals of the presentation

- Using the information in this presentation will be able to describe:
  - Diagnosis, evaluation, assessment of Pervasive Developmental Disorders
  - Treatment planning for Pervasive Developmental Disorders
  - The use of psychopharmacological agents in children and young people with Pervasive Developmental Disorders with emphasis on RUPP study and aggression interventions

PDDs: Historical Overview

- Kanner 1943: Early Infantile Autism (n=11)
  - Autism, resistance to change, congenital
  - False leads: high SES, no organicity or MR
- Asperger 1944: Autistic Psychopathy
- Diagnostic confusion
  - Early DSM lumped autism and psychoses
  - 1971 (Kolvin) first delineated criteria based on onset of symptoms
- APA 1980: Pervasive Developmental Disorder

*PPDs

- “Pervasive” differentiates from “Specific” developmental disorders (e.g., reading, expressive language)
- Disorders of early childhood
- Significant deviations in social interactive skills , language and communication
- Restricted interests
- Repetitive behaviors

*PDDs: Classification

- Autistic Disorder (AD)
- Asperger's Disorder(AspD)
- Rett's Disorder
- Childhood Disintegrative Disorder
- PDD-NOS

*Autistic Disorder (AD, Classic Autism)

- Deficits in social relatedness, communication (both verbal and non-verbal), imaginative play
- Engages in repetitive stereotyped behaviors (e.g., twirling, toe-walking) and becomes upset with changes in routine

*AD-II

- Social interaction / reciprocity
  - Deficits in mutual gaze, joint attention, Theories of Mind (ToM)
- Communication / language
  - ~ 1/2 mute
  - Echolalia, pronoun reversal, prosody deficits
  - Poor non-verbal communications
- Repetitive behaviors
  - Similar, but distinguished from OCD

*AD-III

- Early onset
  - 50% of parents worried by age 1; 90% by 2
    - Language delay, concerns over deafness
    - Aloof, not anticipating being picked up
    - Not follow pointing by parent
    - Doesn’t bring toys for parents to enjoy
  - Diagnosis often missed until later
    - All deviance attributed to development’s bell curve
  - Key role of early intervention to improve outcomes

AD-IV-Associated genetic conditions

10-11% of AD (Cohen et al 2005)

Those with “pure autism”

- Tuberous sclerosis-1-4% pf AD;-ectodermal abns shagreen patches and café-au-lait spots; periungal fib, renal, card lesions; MRI brain “tubers”
- Fragile x- 5% of AD, mild-mod MR, ADHD, long face, large jaw, large ears
- Duplication of long arm chrom. 15: severe MR, seizures, hypotonia
- Down syndrome

Those with autistic traits

- San Filippo-1% of AD-paroxysmal laughter and crying
- Angelman syndrome (UBE3A, 15q11-q13, look for paroxysmal and excessive laughter, temper tantrums)

*AD-V

- 10% macrocephaly
- Cognition
  - ~3/4 function in the MR range
    - Rough distribution of IQ scores:
      - 50% IQ < 50, 70% have IQ<70, 90% have IQ< 90
  - Occasional islets of ability “autistic savants”

*Asperger's Disorder-I

- Misuse of term for high-functioning individuals with AD or PDD-NOS
- DSM-IV Criteria requires normal IQ and normal language development although they may have subtle language problems (e.g., "flat"prosody, poor modulation, Schriberg et al 2001)
- Special areas of interest; talk incessantly about it despite disinterest of others-"little professors"
- Want friends but no "social savoir-faire"
- Motor clumsiness

Asperger's -II

- Proton magnetic resonance spectroscopy shows pre-frontal lobe abnormalities (Murphy et al 2002)
- Coexistent with Tourette's Disorder, OCD, ADHD; may develop depression in teens (Klin 2003)

*Rett's Disorder

- Normal development for the first 6 months
- Then, loss of acquired hand skills with stereotypy, head growth deceleration, development of ataxia or truncal movements, intermittent abnormal breathing
- Autistic symptoms may be transient or permanent
- Later, mental retardation, sz, language impairment
- Mutations in the MECP2 (Methyl-CpG-binding protein) gene-> ?alterations in neuronal dendrites
- Rare disorder (1/10,000) usually girls

Childhood Disintegrative Disorder (Heller's Syndrome)

- Very very rare, etiology unknown
- Normal development for at least 2 years
- Loss of acquired skills:language, social, motor or bladder/bowel control
- Severe MR
- More in males
- May be associated with other genetic conditions (e.g., Schilder's disease)

*PDD-NOS

- Term used when there is “severe and pervasive impairment” in communication, reciprocal social interaction or restricted interests and/ or stereotypies present but symptoms are subthreshold, or late onset or does not meet criteria in all 3 areas,

*PDDs: Epidemiology and Etiology

- Epidemiology
  - AD: increasing prevalence from 1980's-from 3-4/10,000 - true or better case finding and changes in diagnosis (Wing and Potter 2002) rates from 6-54/10,000 (Fombonne 2005)
  - Aspergers 2-16/10,000 (Fombonne 2005)
  - All PDD spectrum disorders may be as high as 58/10,000 (around 1/200) (Chakrabati and Fombonne 2005)
- Etiology PDDs as a final common pathway
  - Genetics
    - Interest in 7q, serotonin transporter gene
  - Early insults, neurological comorbidity (e.g., seizures)
    - Infection, "double hit", immune theories

*Autism and Inheritance

- A monozygotic twin of a child with autism has a 50-60 % chance of Autistic disorder and a 90% chance of a PPD spectrum disorder
- The dizygotic twin of a patient and a full sibling have about the same risk of autism: about 4.5%
- The general population's risk is about 0.2% (1/500)

Vinstra-Vanderweele and Cook JAACAP 42:1 2003 (a review of the genetics of autism)

Do vaccinations cause AD?

- Measles, mumps and rubella (MMR) vaccines have not been shown to be linked to AD and bowel problems (Elliman and Bedford 2002)

*PDDs: Assessment I

- Medical work-up
  - Audiological
  - Neurological (seizures in ~1/3)
  - Genetic screening
    - Fragile X in ~1%: CGG repeats in Xq27.3
    - Rett: X-linked, rare boys, mutations in the MECP2 (Methyl-CpG-binding protein) gene
    - Amino/organic acid metabolism
    - Other genetic diseases associated with autism include: Angelman syndrome, duplication of 15q11-q13, Down syndrome, San Filippo syndrome, phenylketonuria, Smith–Magenis syndrome, 22q13 deletion, adenylosuccinate lyase deficiency, Cohen syndrome, and Smith–Lemli–Opitz syndrome) see Cohen, D et al, Journal of Autism and Developmental Disorders, Vol. 35, No. 1, February 2005
  - Physical examination with close attention to skin and dysmorphology

*Assessment II

- Family history
- Developmental milestones
- Syndromal vs non syndromal autism
- Genetic testing for rare syndromes should be based on clinical findings
- For isolated autism with moderate mental retardation consider:
  - karyotyping,
  - Check for Fragile X mutation,
  - FISH for 15q11-q13 duplication (Angelman's) and 22 q13 deletion (VCFS)
  - Bratton-Marschall test (adenylosuccinate lyase deficiency)
  - check for mucopolysaccharides in urine (San Fillipo disease)

PDDs: Assessment III-Diagnostic Assessment

Screening instruments:

- Checklist for Autism in toddlers (CHAT)
- Childhood Autism Rating Scale (CARS) observational assessment-15 items-score of 30-36=mild-mod Autism
- Pervasive Developmental Disorders Screening Test (PDDST)
- Autism Behavior Checklist (57 item checklist)

*PDDs: Assessment III- Diagnostic Assessment

Structured Evaluation- ‘gold standard’

- ADI-R (Autism Diagnostic Interview - Revised) a comprehensive parent interview
- ADOS (Autism Diagnostic Observation Schedule) a semi structured interactive assessment conducted with the child

PDDs: Assessment III

- Neuropsychological & Language
  - Developmentally Appropriate Instruments: **WISC-IV, Leiter International Test of Intelligence-revised, Mullen Scale of Early Development, Bayley**
- Rating Scales
  - **Aberrant Behavior Checklist** (Aman et al 1985)

  58 items: Subscales:
    - Irritability/Lethargy/Stereotypy/Hyperactivity/Speech
    - Normative data, reliable, valid, sensitive to change (Scahill 2005)
  - **Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS, version for PDD (McDougle in press)**
    - Repetitive behaviors

*Prognosis For Autistic Disorder

- Three consistent outcome factors:
  - IQ
  - The presence or absence of speech
  - The severity of the disorder
- Up to 28% of children with no neurologic disorder in early childhood develop a seizures in adolescence or later. Peak age of onset is 11-14 years old
- A small number of children with autism show intellectual and language decline in adolescence
- While a significant number of children with autism may have coexisting psychiatric disorders there is no increased risk for schizophrenia

*PDDs: Treatment Planning

- Multidisciplinary treatment interventions to improve communication and social development
  - Psychoeducational: Autism Society of America http://www.autism-society.org
  - Therapy/educational (e.g., Treatment and Education of Autistic and Communication Handicapped Children (TEACCH) program, Applied Behavioral Analysis (ABA)
  - Speech and language (e.g., augmentive communicative systems, picture exchange communication system (PECS), sign-language
  - Vocational

*PDDs: Treatment Planning-II

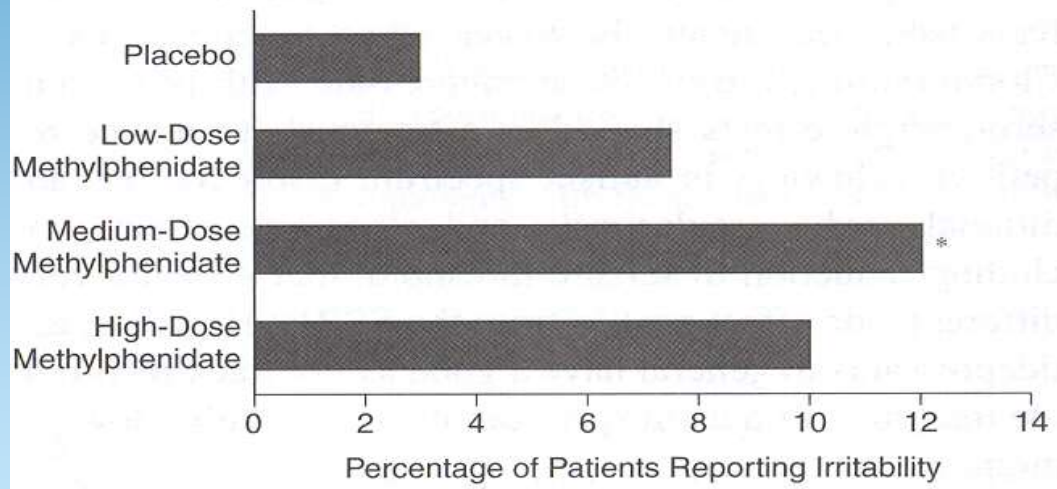
- Pharmacotherapy: target symptoms that interfere with development of language and social skills that fail to respond to behavioral interventions
  - Aggressive / disruptive behaviors
  - Self-injurious behaviors
  - OC, repetitive behaviors, stereotypies ?Autistic OCD syndrome, “the broad autism phenotype” (Gross-Isseroff et al 2001 and Micali, Chakrabati and Fombonne Autism Vol 8 #1 2004)
  - Hyperactivity

*PDD and ADHD/Psychostimulants

- 50% of kids with AD have ADHD (Posey 2005) but little research base
- Only 25% of children with PDD and ADHD had good response (except Asperger which is better, Stigler 2004)
- DB placebo crossover study with differing doses of MPH-> 49% response in RUPP study, ES=small to medium size, AEs especially irritability led to discontinuation in 18%; highest dose worsening social w/d (RUPP 2005)

RUPP Study 2004

Figure 2. Irritability in Patients With Autism Spectrum Disorders Treated With Methylphenidate[a]



Data from Research Units on Pediatric Psychopharmacology Autism Network.[11]

[a]$p < .01$ (medium dose).