Pervasive Developmental Disorders

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Pre-Lecture Exam Question 1

1. **A child of age 2-1/2 years is not yet speaking single words. He has no imaginative plan, but pulls his mother's hand to show what he wants. He does not shake his head to indicate "yes" or "no". Which one of the following statements is true?**

A. One of the Pervasive Developmental Disorders is unlikely because he has no imaginative play.

B. One of the Pervasive Developmental Disorders is unlikely because he uses his mother's hand as a tool.

C. One of the Pervasive Developmental Disorders is unlikely because he does not shake his head.

D. One of the Pervasive Developmental Disorders is likely because he is not able to do any of the above.

E. One of the Pervasive Developmental Disorders is unlikely because he is too young to make a diagnosis.

Question 2

2. **If a child has a diagnosis of Autistic Disorder, which one of the following statements is true?**

A. He is likely to have normal intelligence.

B. He is unlikely to have any coexistent medical condition.

C. It is very likely that a sibling will have the same condition.

D. If he learns to speak, he is likely to have a better outcome.

E. He has a “refrigerator mother”.

Question 3

3. **The "gold standard" for diagnosis of Pervasive Developmental Disorders is which of the following?**

A. Childhood Autism Rating Scale and Aberrant Behavior Checklist.

B. WISC or WIPPSI

C. Childhood Autism Rating Scale and Leiter

D. Autism Diagnostic Interview and Autism Diagnostic Observation Schedule

E. WIPPSI and Childhood Autism Rating Scale

Question 4

4. **A child of 9 years has a confirmed diagnosis of Autistic Disorder. He is non-verbal. Which one of the following statements is true?**

A. He has a 1 of 3 chance of developing seizures as an adolescent.

B. He has 1 of 10 chance of developing seizures as an adolescent.

C. There is no reason to give him speech and language interventions since he is non-verbal.

D. He should be treated with fenfluramine to improve his IQ.

E. He should be placed in a residential treatment facility.

Question 5

5. **Which one of the following statement is true about pharmacotherapy in childhood Autistic Disorder?**

A. Drug studies show that fluvoxamine is the drug of choice in the treatment of aggression in children with Autistic Disorder.

B. Drug studies show that risperidone can improve aggression and increase IQ in children with Autistic Disorder.

C. Drug studies show that risperidone can improve repetitive behaviors and self-injurious behaviors in children with Autistic Disorder.

D. Drug studies show that fluvoxamine can improve aggression in children with Autistic Disorder.

E. There are no clinical studies that show that risperidone is useful in the treatment of repetitive behaviors in children with Autistic Disorder.

Question 6

6. **A child of 8 years has a diagnosis of Autistic Disorder. He is very aggressive and you are considering the use of risperidone. You are discussing the possibility of using this drug with his parents. Which one of the following statements is true?**

A. He is very unlikely to gain weight.

B. He is unlikely to gain weight since he is not yet a teenager.

C. He is unlikely to gain weight because he has Autistic Disorder.

D. He is likely to gain weight because he has Autistic Disorder.

E. He is likely to gain weight because he is in a high risk group because of his age.

Question 7

7. **A parent of a child with normal intelligence, normal language development, but poor social skills asks if it is possible that their children has Asperger Syndrome. You reply:**

A. Definitely not, since children with Asperger do not have normal intelligence.

B. Definitely not, since children with Asperger do not have normal language development.

C. Definitely not, since children with Asperger do not have poor social skills.

D. Possibly, since children with Asperger have normal intelligence, normal language development, and poor social skills.

E. Possibly, since children with Asperger have normal intelligence and poor social skills but abnormal language development.

Question 8

8. **A parent of a child with Pervasive Developmental Disorder NOS is concerned about the fact that their child is receiving clomipramine (CMI) because of possible side effects. They ask you which side effects they should be concerned about. Which one of the following statements is true?**

A. Children who take CMI have a high incidence of pancreatitis.

B. Children who take CMI are at special risk to develop Stevens-Johnson syndrome.

C. Children who take CMI frequently develop polycystic ovaries.

D. Children who take CMI frequently develop mitral valve prolapse.

E. Children who take CMI are at risk for the development of seizures.

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 syndrome (AspS)
- Rett syndrome
- Childhood Disintegrative Disorder
- PDD-NOS

Autistic Disorder (AD, Classical 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 conditions: 10% have Tuberous sclerosis, Neurofibromatosis,Angelman syndrome, intrauterine rubella, Fragile X etc
- 10% macrocephaly
- Cognition
  - ~3/4 function in the MR range
  - Occasional islets of ability “autistic savants”

Aspergers Syndrome-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

Aspergers Syndrome-II

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

Rett 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 to 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 impairments” in communication, reciprocal social interaction or restricted interests and/ or sterotypies 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 20002)
  - PDD-NOS: as high as 1/200?
- Etiology PDDs as a final common pathway
  - Genetics
    - Sibling and twin risk studies : identical twins-AD-50%
    - Interest in 7q, serotonin transporter gene
  - Early insults, neurological comorbidity (e.g., seizures)
    - Infection, OXT "double hit", immune theories

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

PDDs: Assessment II

- Diagnostic Assessment
  - Screening instruments:Checklist for Autism in toddlers (CHAT), Childhood Autism Rating Scale (CARS)
  - Structured Evaluation-'gold standard'
    - ADI (Autism Diagnostic Interview)
    - ADOS (Autism Diagnostic Observation Schedule)

PDDs: Assessment III

- Neuropsychological & Language
  - Developmentally Appropriate Instruments: **WISC-III, Leiter International Test of Intelligence-revised, Mullen Scale of Early Development, Bailey**
- Rating Scales
  - **Aberrant Behavior Checklist** (Aman et al 1985) Subscales:
    - Irritability/Lethargy/Stereotypy/Hyperactivity/Speech
  - **Children's Yale-BrownObsessive Compulsive Scale (CY-BOCS, Scahill et al 1997)**
    - Repetitive behaviors

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 (Gross-Isseroff et al 2001)
  - Hyperactivity

Serotonergic Agents I

- Serotonin in autism: background
  - Hyperserotonemia (Schain & Friedman 1961)
  - mCPP and fenfluramine challenges
    - Blunted neuroendocrine response
  - Tryptophan depletion (McDougle et al 1996)
  - Serotonin transporter (HTT)
    - *l / s* polymorphisms - (Cook et al 1997)
  - Clomipramine and SSRIs

Serotonergic Agents II

- Fenfluramine
  - Early enthusiasm, no replication
  - Toxicity concerns: neural death, valvulopathy
- Clomipramine
  - Controlled and crossover studies >PLA, >DMI
  - Concern about side effects especially in younger children (e.g., sedation or agitation, taccycardia, QTc prolongation, seizures)