Objectives

1. Understand the diagnostic concept of childhood onset schizophrenia including clinical presentation and course of the disorder.
Objectives

2. Appreciate the differences between childhood onset schizophrenia and other psychiatric disorders in childhood that may present with psychotic symptoms.

Objectives

3. Understand the current evidence base regarding treatment options for childhood onset schizophrenia.

Childhood Psychosis

- Applied historically to heterogeneous group of children with pervasive developmental disorders
- Evidence emerged for a different clinical entity – childhood onset schizophrenia
  - Diagnoses formally separated in 1980s
What is Schizophrenia?

- Psychotic disorder characterized by the following:
  - Hallucinations
  - Delusions
  - Disorganized speech and behavior
  - Negative symptoms

Hallucinations

Delusions
Disorganization

Negative Symptoms

Childhood Onset Schizophrenia

- Characterized by an onset of psychotic symptoms before age 12
Childhood Onset Schizophrenia

- No modification of DSM-IV TR diagnostic criteria for children except functional decline could be met by failure to achieve expected level of interpersonal, academic, or occupational achievement

Epidemiology

- Occurs in less than 1 in 10,000 children
- Onset of schizophrenia in adolescence is 50 times greater than childhood onset
- Rarely diagnosed before age 5

Etiology
Neuroimaging

- Gray matter loss
  - Loss originating in parietal regions proceeding frontally (back to front)
  - Severe bilateral frontal gray matter loss occurring in a dorsal to ventral pattern (top down)

Clinical Features

- Onset frequently insidious
- Higher rates of premorbid language, social and motor development abnormalities

Clinical Features

- May take many months or years to confirm diagnosis
- Psychotic symptoms described in developmental context
Clinical Course

- Predictors:
  - Premorbid level of functioning
  - Age of onset
  - IQ
  - Response to pharmacological interventions
  - How much functioning regained after 1st episode
  - Family support

- Overall, tends to be a more malignant type of schizophrenia
- Often poor response to treatment; resemble poor outcome adult onset cases

Other childhood conditions with psychotic symptoms...
- Affective Disorders

Delusions of Grandeur
Other childhood conditions with psychotic symptoms...
- Psychosis due to GMC
- Substance-induced Psychosis

Other childhood conditions with psychotic symptoms...
- Pervasive Developmental Disorders

Other childhood conditions with psychotic symptoms...
- Conduct disorder
Other childhood conditions with psychotic symptoms…
- Multidimensionally impaired youth
  - Transient, stress induced psychotic sx.
  - Emotional lability
  - Impaired interpersonal skills
  - Cognitive deficits
  - No thought disorder
  - Comorbid ADHD

Treatment
- Psychosocial Treatments
- Biological Treatments

Psychosocial Treatments
- Family education and support
- Individual supportive therapy
- Social skills interventions
- Appropriate academic placement
Pharmacological Treatment

- Considered to be the mainstay of treatment
  - Typical Antipsychotic (1st Generation)
  - Atypical Antipsychotic (2nd and 3rd Generation)

Typical Antipsychotics

- Haloperidol
  - 16 children with dx. Schizophrenia
    - Ages 5-11
  - Effective in reducing positive symptoms of psychosis
  - High rates of EPS, sedation and elevated prolactin levels
    (Spencer et al., Psychopharmacol Bull 1992)
Typical Antipsychotics

- 2 other trials
  - Thiothixene and thioridazine
    - (Realmuto et al., Am J Psychiatry, 1984)
  - Loxitane
    - (Pool et al., Curr Ther Res Clin Exp, 1976)
- Similar results to haloperidol trial

Typical Antipsychotics - Summary

- Effective option targeting particularly positive symptoms
- Adverse effects particularly with chronic use (ie.,TD) limited the use of these agents

Atypical Antipsychotics
Atypical Antipsychotics

- Considered to be first line treatment for childhood onset schizophrenia
- Extension of findings from adult studies
- Few actual studies of the topic

Atypical Antipsychotics

- Adolescent onset schizophrenia
- Risperidone versus placebo
  - Ages 13 - 17
  - Randomized double blind trial
  - Both active treatment groups improved significantly versus placebo
  (Haas et al., *J Child Adolesc Psychopharmacol*, 2009)

Atypical Antipsychotics

- Adolescent onset schizophrenia
  - Risperidone (high, low dose) versus placebo
  - Risperidone significantly lower PANSS ratings than placebo at 8 weeks
  (Pandina et al., *Meeting of AACAP*, 2007)
Atypical Antipsychotics

- Adolescent onset schizophrenia
- Olanzapine versus placebo
  - Olanzapine greater reductions on BPRS and CGI; high placebo response rate
  - High rates of weight gain (Kryzhanoskaya et al., Meeting of APA, 2006).

- Aripiprazole (10mg and 30 mg day) versus placebo
  - Aripiprazole improvement in PANSS symptoms relative to placebo, 10 mg / day interestingly only group to improve negative symptoms (Robb et al., Meeting of AACAP, 2007)

Atypical Antipsychotics - Summary

- Effective option versus placebo in treating psychosis in children and adolescents
- Also limited by long term adverse effects (ie. weight gain, metabolic syndrome)
Comparative Studies

Atypical Antipsychotics
- COS patients and Adolescent onset
- Risperidone vs. Olanzapine vs. Molindone
  - No differences in symptom reduction
  - Atypical agents associated with greater weight gain
  (Sikich et al., *Am J Psychiatry*, 2008)

Atypical Antipsychotics
- Children and Adolescent patients with psychotic disorders
- Risperidone vs. Olanzapine vs. Haloperidol
  - No difference in symptom reduction; significant weight gain and EPS in all groups
  (Sikich et al., *Neuropsychopharmacology*, 2006)
Atypical Antipsychotics

- Treatment refractory COS patients
- Clozapine versus Haloperidol
  - Double blind – not placebo controlled trial
  - Clozapine more effective than haloperidol
    (Kumra et al., Arch Gen Psychiatry, 1996)

Atypical Antipsychotics

- Treatment refractory COS patients
- Clozapine versus Olanzapine
- 2 Studies
  - Both treatment groups improved; clozapine group greater improvement in negative symptoms
    (Shaw et al., Arch Gen Psychiatry, 2006)
    (Kumra et al., Biol Psychiatry, 2008)

Comparative Studies - Summary

- Evidence base does not support greater rates of adverse effects of typical agents in the short term
- Clozapine demonstrates superiority in head to head clinical trials with typical and atypical agents BUT….
Clozapine – Adverse effects.

- Sedation
- Siallorhea
- Weight gain
- Risk for agranulocytosis – requiring regular blood monitoring (deep breath)

Clozapine – Adverse effects...

- Dose dependent lowering of seizure threshold
- Potential for myocarditis
- Cumbersome start up procedures
- Lack of appropriate clinics to monitor children treated with clozapine…

Take Home Points

- Childhood onset schizophrenia is a severe and rare mental health condition
- Characterized by similar symptoms to adults but exhibits a course typical of poor outcome cases
Take Home Points

- Other more common mental health conditions in childhood should be ruled out prior to diagnosing schizophrenia in children
- Medication management considered the mainstay of treatment
  - Pros and cons with specific agents
  - Small evidence base in children

Questions?