

Update on First Psychotic Episodes in Childhood and Adolescence

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Childhood-Onset Psychosis

- 8% of psychiatrically referred youth in the US (age ~ 11) have psychosis (Biederman 2004).
- High comorbidity with disruptive, mood and anxiety disorders; i.e. for childhood-onset schizophrenia (Russell et al 1989)
 - 31% with CD/ODD
 - 37% with depressive disorders
- Chronic course and significant impairment

Differential Diagnosis for Psychotic Symptoms in Childhood

- Childhood-Onset Schizophrenia (spectrum)
- Multidimensional Impairment (brief psychotic symptoms, poor affect regulation, difficulty with attention and impulse control)
- Mood disorders
- Dissociative Disorders
- Emerging Personality Disorders
- Psychosis Due to a Medical Condition
- Substance-Induced Psychosis



Childhood-Onset Schizophrenia Criteria

- A** ≥ 2 symptoms ≤ 1 month or less if treated:
delusions, hallucinations, disorganized speech and behavior, negative symptoms
OR 1 bizarre delusion OR running commentary OR ≥ 2 voices in conversation
- B** Function (failure to achieve expected interpersonal or academic achievement)
- C** 6 month duration (continuous)
- D** Mood symptoms, if present, are brief relative to other symptoms
- E** Not secondary to substance or medical condition
- F** If PDD, need hallucinations or delusions.

Negative Symptoms



- Social isolation and withdrawal
- Avolition
- Decreased expression of emotion
- Decreased experience of emotions and self
- Decreased ideational richness
- Deterioration in role functioning

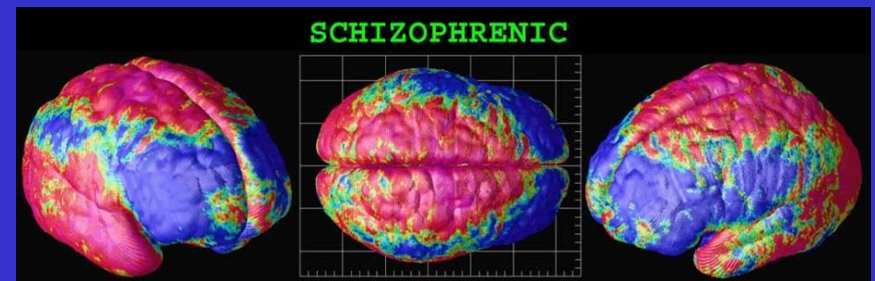
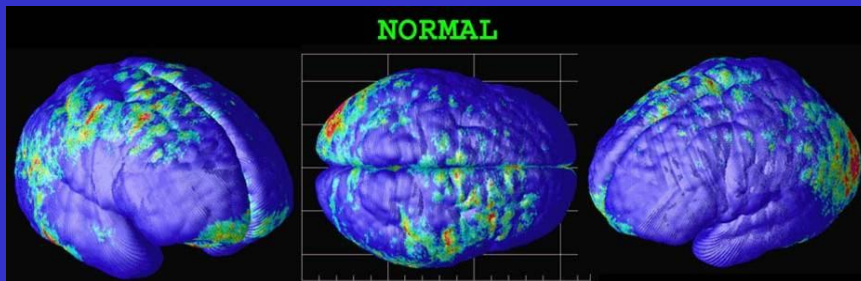
Childhood-Onset Schizophrenia



- 1 in 40/000 children; onset before age 13
- 90% with continued schizophrenia as adults, half with deteriorating course (Asarnow 2004)
- Adulthood – many still psychotic, also unemployed, long-term care, few friends
- 50% with severe impairment 16 years later (Eggers et al 2002)
- High mortality rate (13% within 5 years: risk-taking and suicides; Werry et al 1991)

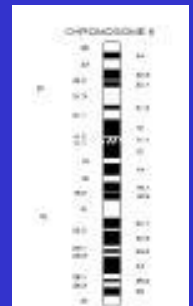
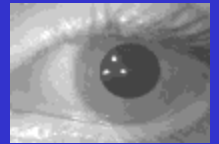
Comparisons with Adult-Onset Schizophrenia: Differences

- Harder to treat, worse prognosis
- More familial: 33% (vs. 10-20% in adults) has a 1st degree family with schizophrenia spectrum disorder
- More chromosomal abnormalities
- Characteristic progressive loss of gray matter (back to front, ages 14-18) (Rapoport)



Similarities to Adult-Onset Schizophrenia: Biology

- Physiology - Smooth pursuit eye-tracking abnormalities
- Brain structure - Enlarged ventricles, reduced grey matter, and cortical thinning
- Brain metabolism (MRS) – abnormal energy metabolism and phospholipid turnover
- Schizophrenia susceptibility genes , i.e. Dysbindin (6p22.3)
- Most responsive to Clozapine



Similarities with Adult-Onset Schizophrenia: Behavior

- Premorbid speech and language impairment (even more so with childhood-onset)
- Poor motor coordination
- Cognitive impairment: Global deficit (1-2 standard deviations below normal), esp. psychomotor speed, executive function
- Poor school performance
- Social function : few friends, isolated play
- Attentional dysfunction with impulsivity
- Insidious onset with anxiety

Premorbid features of COS (Muratori et al., 2005)

- 23 early-onset schizophrenia pts (age = 15.3)
- Childhood Behavioral Checklist given to mothers (retrospective)
- Ages 4-11: More social, thought, attention and school problems
- Ages 4-11: 1/3 with high “total problem” score
- Ages 2-3: “Internalizing” profile evident that worsened in subsequent epochs

Overlap with Autism Spectrum Disorders: Premorbid Developmental Abnormalities in Childhood-Onset Schizophrenia

Study	Subject No.	Age of Onset	Premorbid Developmental Abnormalities
Kolvin et al 1971	33	<15	87%: social abnormalities; 49%: major milestone delay; 46%: speech delay
Asarnow and Ben-Meir 1988 (UCLA)	17	<13	Very poor scores on PAS (4.1 ± 1.0); poor premorbid social functioning
Watkins et al 1988 (UCLA)	18	<12	Premorbid language deficits: 72%; Motor deficits: 72%; Symptoms of infantile autism: 39%; PDD NOS: 17%
Russell et al 1989, 1894 (UCLA)	35	<12	PDD features: 26%; transient premorbid autistic symptoms (hand flapping, echolalia, unusual interests): 40%
Green 1992 (NYU)	38	<12	Poor premorbid intellectual functioning; insidious onset in 79%
Alaghband-Rad et al 1995 (NIMH)	23	<13	Language delay/disorders: 43%; motor impairment: 36%; Social impairment: 50% (PAS = 2.3 ± 1.6); PDD features: 36%; infantile autism or Asperger syndrome: 13%; transient motor PDD features: 30%
Hollis 1995 (UK)	18	7-13	Language impairment: 44%; motor impairment: 28%; social impairment: 50%; more social and language impairment than in adolescent onset

From Sporn et al., 2004

Pervasive Developmental Disorder and Childhood-Onset Schizophrenia: Comorbid Disorder or a Phenotypic Variant of a Very Early Onset Illness?

Alexandra L. Sporn, Anjené M. Addington, Nitin Gogtay, Anna E. Ordoñez, Michele Gornick, Liv Clasen, Deanna Greenstein, Julia W. Tossell, Peter Gochman, Marge Lenane, Wendy S. Sharp, Richard E. Straub, and Judith L. Rapoport

- 25% of COS pts had PDD – 1 autism, 1 Asperger, and 17 PDD NOS
- COS +/- PDD: Same age of onset, IQ, medication response, outcome, family history and MRI findings. No difference in candidate genes.
- COS + PDD: More premorbid social impairment, language delay and motor problems. 17% (vs. 0%) had siblings with autism.

Schizotypy and Schizophrenia in Children: Similarities (Asarnow 2005)

- Schizotypy— social and interpersonal deficits, behavioral oddities, cognitive and perceptual disturbances; similar to schizophrenia “prodrome” or clinical high risk state
- Comorbid ADD, CD/ODD, and depression
- 17% deteriorate; ¼ with good outcome
- Outcomes for schizotypy at 3 years include schizophrenia or schizoaffective disorder (30%), schizotypy (50%), bipolar (10%) and other (10%) disorders.

Treatment of childhood-onset schizophrenia

Clozapine is superior to both (double-blind RCT)

1) Haloperidol (Kumra et al., 1996); 6 weeks; N = 21

Clozapine led to greater improvement in symptoms, but was associated with neutropenia and seizures.

2) Olanzapine (Shaw et al., 2006); 8 weeks; N = 25

Clozapine led to greater improvement in symptoms, in particular negative symptoms but was associated with lipid abnormalities and seizures.

Effective treatment for adolescent-onset schizophrenia

- More similar to adult-onset schizophrenia than childhood-onset schizophrenia
- Olanzapine is superior to placebo (Kryzhanovskaya et al., 2005)
- Risperidone (Haas et al., 2009)
- Aripiprazole (Findling et al., 2008)
- TEOSS study (Olanzapine, risperidone and molindone); Ages 8-19 (childhood and adolescent-onset)

Treatment of adolescent-onset schizophrenia (ages 13-17): 8 week double-blind RCT of 2 doses of Risperidone (Haas et al 2009)

Dose	1.5-6.0 mg/d	0.15 – 0.6 mg/d
PANSS	96 → 73	93 → 81
Adverse events	74%	65%
Weight gain	3.2 kg	1.7 kg

Treatment of adolescent-onset schizophrenia (ages 13-17): 6 week double blind RCT of 2 doses of Aripiprazole and PBO (Findling et al., 2008)

Both 10 mg/d and 30 mg/d doses of Aripiprazole had superior efficacy to PBO in terms of reduction in total PANSS scores

Both doses were associated with extrapyramidal symptoms, somnolence and tremor

There was no difference in changes in prolactin or weight compared to placebo.

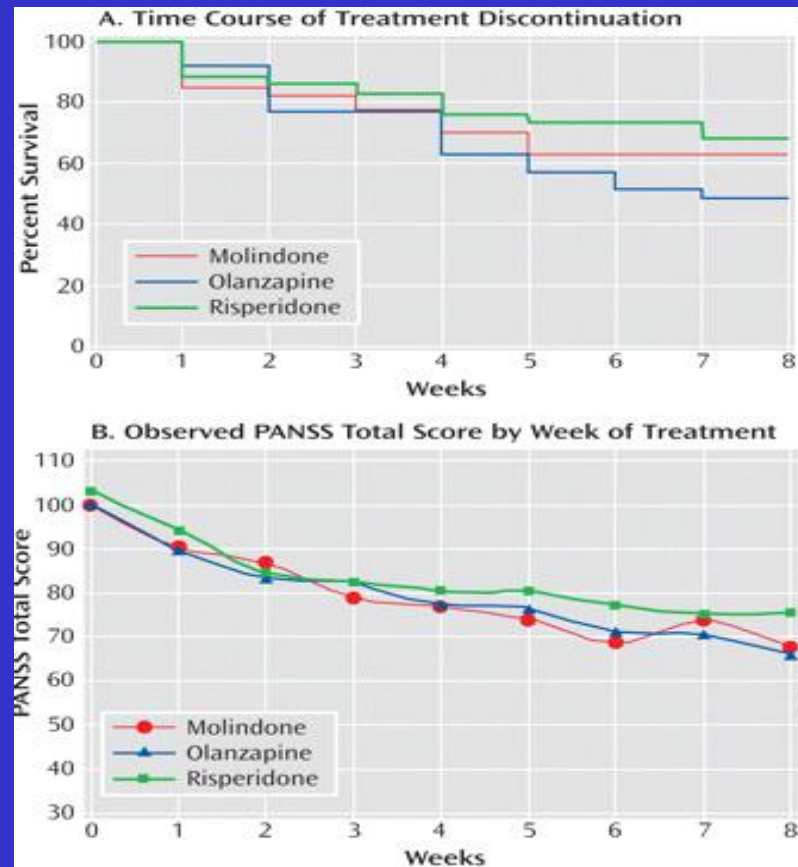
Treatment of early-onset schizophrenia spectrum disorders (TEOSS); Sikich et al. 2008

N = 116; Ages 8-19; 8 weeks; no substance abuse

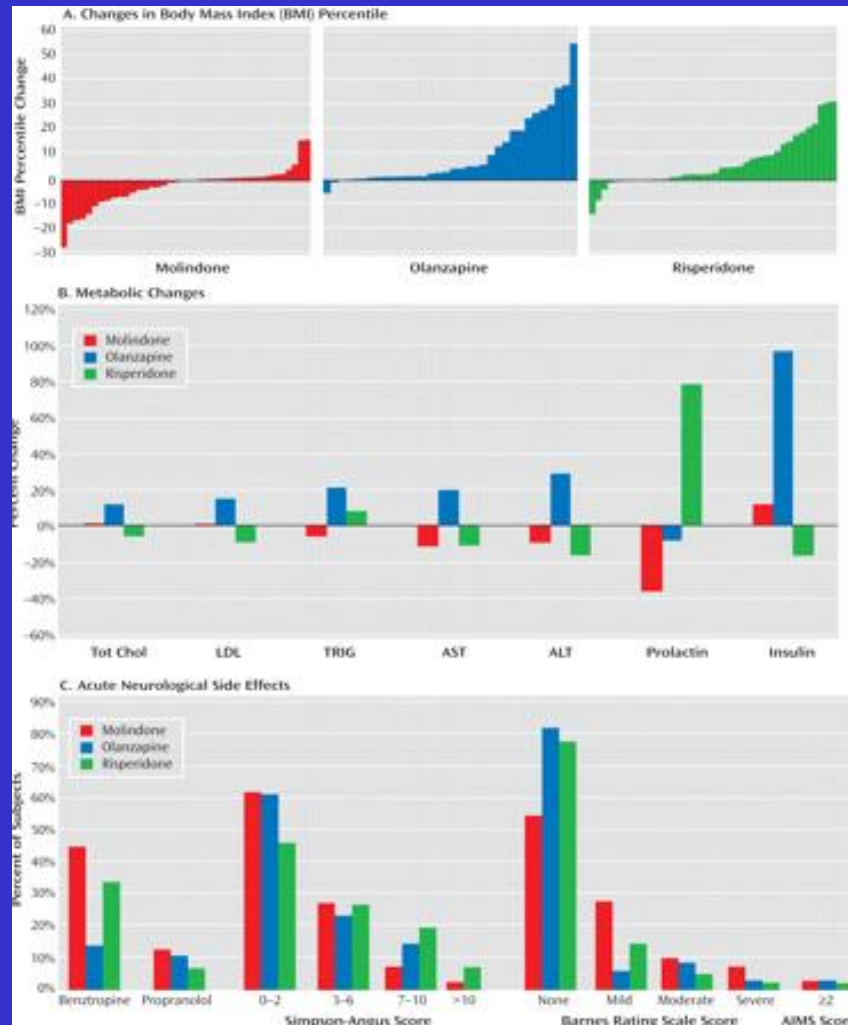
Response to Rx = CGI improved by 1 or 2 points and/or 20% reduction in PANSS total symptom score

Olanzapine	2.5 - 20	11.4	34%	Weight gain, fasting cholesterol, LDL's, insulin, liver enzymes
Risperidone	0.5 - 6	2.8	46%	Constipation
Molindone (w/ benztropine)	10 - 140	59.9	50%	Akathisia

TEOSS study: Clinical Improvement

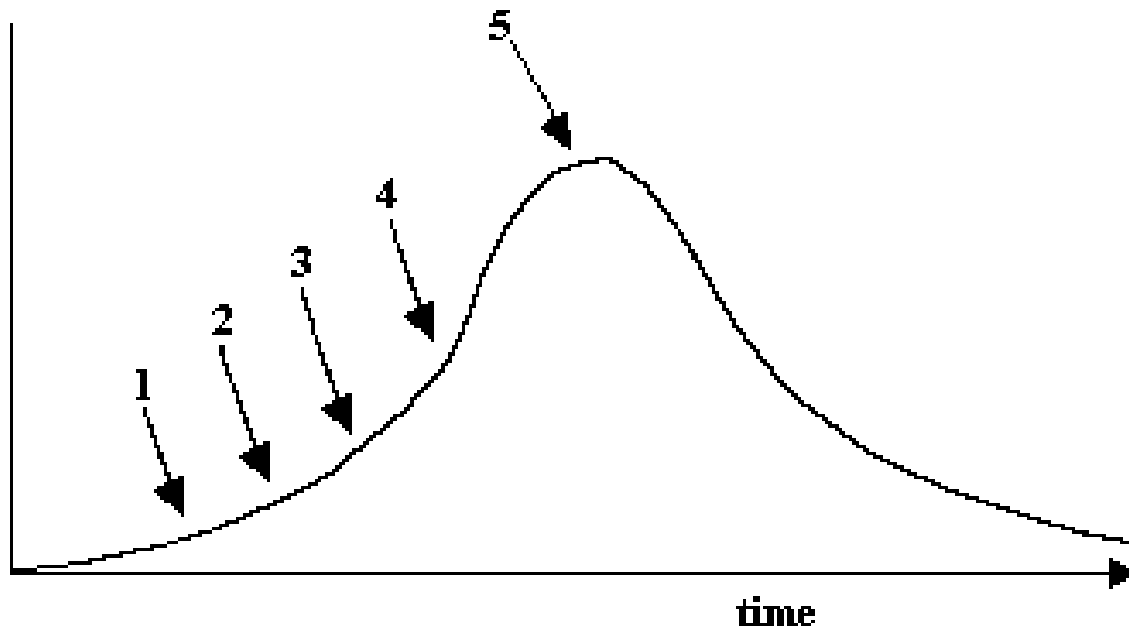


TEOSS study: adverse events



Before the First Psychotic Episode: The Schizophrenia “Prodrome”

Figure 1. Development of psychosis over time, with arrows indicating points of change noted by the patient or informants



Arrow points: 1 = patient first notices some change in self, 2 = family or friends first notice some change in patient, 3 = patient first notices psychotic symptoms in self, 4 = family or friends first notice psychotic symptoms in in patient, 5 = first psychotic intervention. See text for amplification.

Before the First Psychotic Episode: The Schizophrenia “Prodrome”

- Social isolation and anxiety
- Deterioration in role function (school)
- Attenuated or brief psychotic symptoms (illusions, overvalued ideas, suspiciousness)
- Nonspecific symptoms (anxiety, depression, irritability, apathy, withdrawal, lack of initiative and sleep disturbances)
- Estimated length of prodrome = 4 years
- Prodromal patients have a 30-40 % risk of developing psychosis in ~2 years



Interventions to try to Prevent the First Episode of Psychosis

- Antipsychotics may have some efficacy in preventing psychosis onset but are associated with side effects (olanzapine: weight gain; aripiprazole: akathisia; risperidone: prolactin increases)
- Psychological treatments (CBT) are well-tolerated but may only be effective for the duration of administration
- Neuroprotective strategies (omega fatty acids) are promising but require replication.



GRACIAS!

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Center of Prevention and Evaluation

Columbia University/ NYSPI

Prodromal Research Program in NYC that
offers consultation and treatment

