Module 3: Diagnostic Dilemmas: Psychosis and Autism Spectrum

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Is it just a mood disorder?  
(Simoncini, et al, 2014)

• 23 yo man with suicide attempt after break up in relationship
• 2 weeks of depression and mania and increase paranoia that led to jumping off porch and hospitalization
• Improved psychotic symptoms with medications but continued to have odd speech, restricted to eating foods in a pattern and little interest in others
Is it just Autism?

• 17 yo, Vietnamese teen with genetic defect, 22q11, “DiGeorge syndrome”
• Pt diagnosed with Autism and ID functional at baseline; attends school, cooperative
• Over several weeks, noted to have decreased verbal communication, more irritable, seemingly paranoid
• Pt eventually is almost mute, with little movement or response; loses some of milestones including toileting and ambulation
• Dx: Catatonia

• What is the diagnosis?
Learning Goals

• Understand history of relationship between diagnosis of Autism and Schizophrenia
• Understand key developmental history for a diagnosis of Autism
• Understand the similarities and differences between schizophrenic syndrome disorders and autism disorders
• Consider differential diagnosis of psychotic symptoms in a person with autism including mood and anxiety disorders and schizophrenia
History of Autism

1905, Bleuler noted Autism to be a core symptom of Schizophrenia.

1943: Kanner diagnosed disturbed children with, what would now be considered COS, as Autistic.

1970: Kolver and Rutter differentiated presentation social and communication disturbance in infancy (ASD) vs those that develop later.

1977: ICD9, first time Autism was listed as separate diagnosis from Schizophrenia.

Now considered separate diagnosis with some common genetic, neurobiological underpinning.
Autism Spectrum Disorder

• DSM5: Neurodevelopmental Disorder
• Frequency: 1/88
• Core symptoms
  – impairment of social communications and interactions
  – Restrictive and repetitive behaviors
• Types
  – With and without ID
  – With and without language deficits
  – Mild, Moderate and severe: defined by level of function/support needed
Social Communication Deficit

• 1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.

• 2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.

• 3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.
Restricted and Repetitive Behaviors

- 1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypes, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
- 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
- 3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
- 4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).
Schizophrenia Spectrum Disorders (SSC)

- SSC disorders – DSM5
  - Schizophrenia
  - Delusional disorder
  - Schizoaffective disorder

- Prevalence
  - Childhood onset schizophrenia: 1/40,000
  - Adolescent onset (13-18): 1/20,000
  - Schizophrenia: 1/100 (1%)
Core Symptoms of Schizophrenia

- Positive symptoms for over one month
  - AH, VH
  - Delusions
  - Disorganized thinking

- Negative symptoms:
  - Apathy
  - Social withdrawal

- **Decline** in function or failure to progress
Schizophrenia: Development

- Very Early Onset Schizophrenia: less than 13 y
- Early onset: before age of 13
- Schizophrenia: after age 18
## Symptoms Overlap

<table>
<thead>
<tr>
<th>Schizophrenia</th>
<th>Autism</th>
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</thead>
<tbody>
<tr>
<td>Social withdrawal/Negative symptoms</td>
<td>Communications deficit/poor social skills</td>
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<tr>
<td>Affective flattening</td>
<td>Poor reciprocity</td>
</tr>
<tr>
<td>Disorganized speech</td>
<td>Stereotype use of language</td>
</tr>
<tr>
<td>Disorganized behavior</td>
<td>Little spontaneous play or imaginative play</td>
</tr>
<tr>
<td>Delusions</td>
<td>Preoccupations /Obsessions</td>
</tr>
<tr>
<td>Catatonic abnormal movements</td>
<td>Stereotypes</td>
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</tbody>
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Is Autism a Risk Factor for Schizophrenia?

• 30 year Autism follow up: 35% of patients had comorbid schizophrenia (Mouridsen, 2008)
• Early Autism features may be related to severity of schizophrenia (Barneveld, 2011)
• Childhood onset schizophrenia (Rapoport, 2009)
  – Likely to have history of Autism spectrum
  – Range 30-50 % had ASD before schizophrenia
  – Progression from ASD to schizophrenia (10 %)
• Comparison of 14 men with Autism and 14 with Schizophrenia (Konstantareas, 2001)
  – 50% of autistic subjects met criterion for schizophrenia
ASD and Psychosis

• Found that ASD + anxiety more likely to have psychotic symptoms than anxiety alone
• ASD with mood disorders more likely to have psychotic process
• Konstantareas and Hewitt (2001), compared sample with autism and schizophrenia
  • Overlap of symptoms but ASD subject did NOT report hallucinations or delusions
Prevalence of ASD in Psychotic Adults (Kincaid, 2017)

• Literature review of studies looking at ASD, Autistic like traits (ALT) in individuals with psychosis
• 7 studies reviewed; 3 included individuals with ID
• ASD and ALT more common than general population; ALT more common than full ASD in psychosis
• When studied, diagnostic prevalence of ASD increased among those with psychosis
• Is this comorbidity or misdiagnosis?
Are Patients with ASD at Risk of Psychosis?
(Larson, 2017)

- Examined (adult) individuals with ASD alone, ASD with Psychosis (ASD-P), and Psychosis alone
- Those with ASD-P present differently
- Hypothesize that ASD may be more linked to Psychotic mood disorder than schizophrenia
  - Compared to ASD alone, ASD-P had less restricted interests and stereotypes
  - Compared to those with Psychosis alone, ASD-P less likely to progress to schizophrenia
Autism Traits in Schizophrenia (Kastner, 2015)

• Developed a tool to differentiate ASD and Schizophrenia
• PAUSS- Used the Positive and Negative Severity Scale to develop a PANS Autism Severity score
• Correlated with ADOS- 4
• Pts with this comorbidity may be less responsive to standard antipsychotic regimens
Genetics

• Recurrent copy number variants:
  – Excellent model of comorbidity: 22q11.2 (DiGeorge syndrome)
  – Chromosome 17q12 (Renal cysts and Diabetes syndrome):
  – Chromosome 16p.11.2
    • Associated with autism
    • Approximately 1% of pts with autism have this variant

• Neurixin: presynaptic protein that connects neurons
  – Deletions, mutations and copy number variants implicated in autism
    and schizophrenia

• Oxytocin: noted gene mutations and polymorphism at this site correlated
  with autism and schizophrenia
  – Possible benefit of oxytocin for social interaction
Clinical Overlap: Theory of Mind

• Describes ability to understand another person’s point of view
• Those with ASD and Schizophrenia may have impairments in accurately understanding another person
• Misunderstand social cues and may seem insensitive to other people’s reactions
• Unable to describe own emotions and experiences
• Some believe this may be linked to increased criminal behavior in some on the spectrum
Complex Neurodevelopmental Disorders
(Towbin, Jaacap 1993; Kumra, JAACAP, 1998)

- MCDD - Multiple Complex Developmental Delay
  - Impaired regulation of affect
  - Impaired social behavior and sensitivities
  - Impaired cognitive processing (e.g., poor reality testing)

- MDI - Multidimensional impaired children – categorized from group referred to NIH for evaluation of COS
  - Did not have COS, but did have severe impairment
  - This group did NOT progress to schizophrenia
  - Early isolated psychosis may be more predictive of mood/anxiety disorder
  - The clinical profile cohort may be less stable than ASD only population
Can we tell the difference?
Consider Developmental Differences

- **ASD:**
  - Social /Communication disorder
  - Sensory integration problems
- **Schizophrenia:**
  - may be more specific to receptive language
  - Neuromotor/developmental delays
Brain Differences

• Autism: notable for increased head size and total brain volume early on

• Schizophrenia: Decrease in cortical grey matter
  – Adult pattern: prefrontal and superior temporal cortical grey matter

• If have both ASD and SSD, may have more severe grey matter loss
Differences in History and Thought Form

**ASD**
- Present before age 3
- Relatively stable presentation since early childhood
- Disorganized thoughts but no clear delusions or hallucinations
- Delusions c/w preoccupations or obsessions
- Generally little change in baseline
- Possible developmental regression

**Schizophrenia**
- Delusion or hallucination for at least one month
- Poor reality testing that is a change from baseline
- Thought disorder that is change from baseline
- Decline in function
Measures to Consider to Screen for Autism and/or Psychosis

- PAUSS- Positive and Negative Syndrome Scale- used with patients with schizophrenia to diagnose autistic phenotypes (Kastner, 2015)
- Brief Psychiatric Rating Scale (BPRS-C) (Overall and Gorham, 1962)
- Prodromal Questionnaire Brief Version (PQ-B)- screen for early onset psychosis (Loewy, 2011)
- ADOS-4- Autism Diagnostic Observation Scale for older children and adolescents with verbal capacity
- ASI-R – Semi-structured interview for children and adults autism (2.5 - 3 hours; harder to use for severe cognitive delay)
- **Most tools have overlap for negative symptoms and communication deficit in autism**
Autism Traits in Schizophrenia
(Kastner, 2015)

• Developed a tool to differentiate ASD and Schizophrenia
• PAUSS: Used the Positive and Negative Severity Scale to develop a PANS Autism Severity score
• PAUSS Correlated with ADOS-4 for diagnosis of Autism
• Patients with positive symptoms of schizophrenia and significant scores on PAUSS are less responsive to standard antipsychotic regimens
Summary

- Schizophrenia, even COS, is NOT the same as ASD; although symptoms and genetic risk may overlap.
- Thought ‘disorder’ of ASD may be disorganized, but usually do not have delusions and hallucinations of schizophrenia.
- Autism appears to be a heterogeneous disorder with varying phenotypes that may represent variable risks and outcomes.
- Important to look for psychotic features in autism and for ASD features in those who present with psychosis with or without mood disorder.
References


• Kincaid, D. What is the prevalence of autism spectrum disorder and ASD traits in psychosis? A systemic review. Psychiatry Research, 250 (2017)