

Intersections Between Autism & Clinical High Risk for Psychosis

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HISTORY & CONTEXT



AUTISM & PSYCHOSIS: BRIEF HISTORY

Early conception of schizophrenia:

1. **Association** – loose connections leading to illogical thinking
2. **Affectivity** – “emotional deterioration”
3. **Ambivalence** – conflicting emotions
4. **Autism** – “self-absorption” / “withdrawal from reality”



AUTISM & PSYCHOSIS: BRIEF HISTORY

- Autism features used to be formally termed “**childhood schizophrenia**”
- Autism conceptualized as precursor to / synonymous with schizophrenia until 1970's



PREVALENCE & THEORY



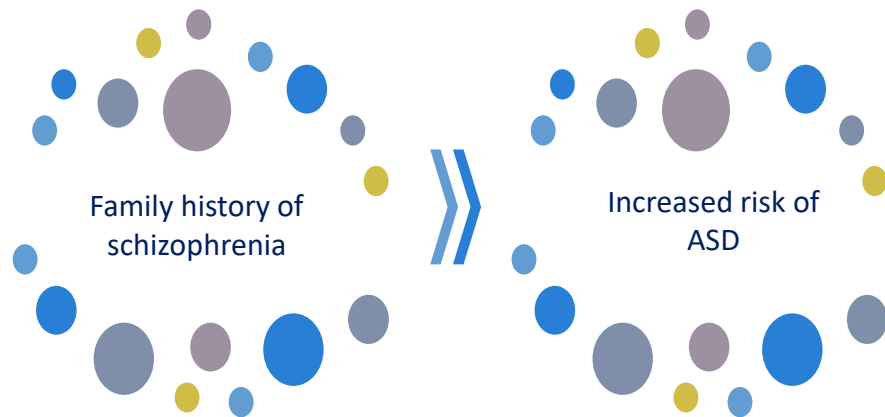
ASD/CHR PREVALENCE

- Approximately 1.5% of population in developed countries are diagnosed with **ASD**
- **CHR** prevalence rates average around 2.4% of the general population
- Individuals with ASD are at increased risk for developing psychosis
 - Rates ranging from 7-34%
- DeGiorgi et al (2019) review: **9.5%**

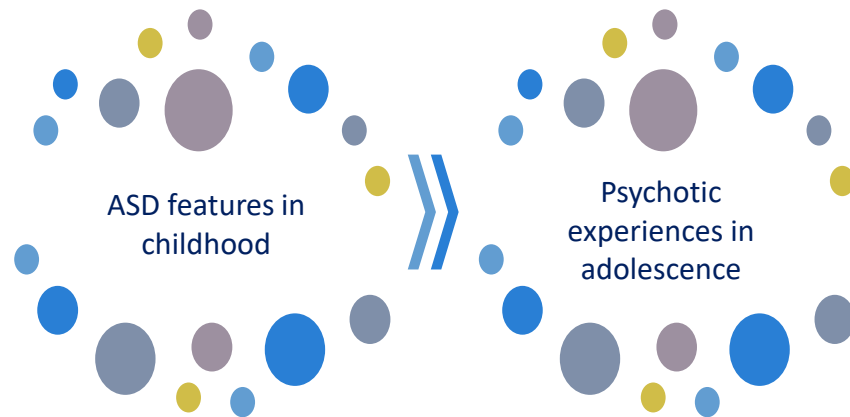


OVERLAP

BIOLOGICAL LINK



DEVELOPMENTAL LINK



MODELS OF ASSOCIATION BETWEEN AUTISM & PSYCHOSIS

1) Increased Vulnerability Model

2) Associated Liabilities Model

3) Multiple Overlapping Etiologies Model

4) Diametrical Model



SHARED ASSOCIATED FEATURES

- **Brain Function & Structural Abnormalities**
 - Areas associated with processing of social/emotional information (e.g., fusiform face gyrus, amygdala, regions of prefrontal cortex)
 - Areas associated with multisensory integration (e.g., corticothalamic circuitry)
- **Basic Sensory Perception**
- **Neurological Soft Signs** (e.g., early motor abnormalities)



SHARED ASSOCIATED FEATURES

- **Neurocognitive & Social Cognitive Performance**

- *Impairments in all domains of MATRICS battery*

- **Face Processing**

- **Emotion Recognition**

- **Theory of Mind**

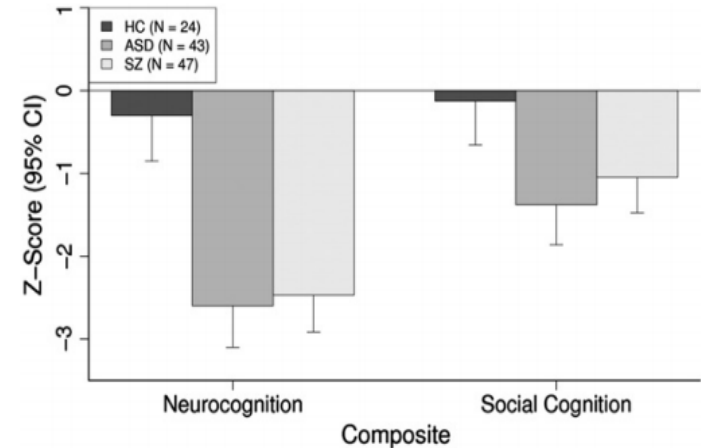


Fig. 1. Performance on composite indexes of neurocognition and social cognition among adults with autism, schizophrenia, and healthy individuals.



DIAGNOSTIC CRITERIA

ASD and CHR



DIAGNOSTIC CRITERIA

Autism

- Social communication/Interaction
 - Social-emotional reciprocity
 - Back/forth convo
 - Sharing interests, emotions
 - Initiation/response
 - Nonverbals
 - Verbal / Non
 - Eye contact
 - Gestures
 - Developing/maintaining relations
- Restricted behaviors/interests
 - Stereotyped movements
 - Routines, ritualized behavior
 - Preoccupation
 - Sensory input issues
- Cause impairment

Clinical High Risk for Psychosis (CHR/APS)

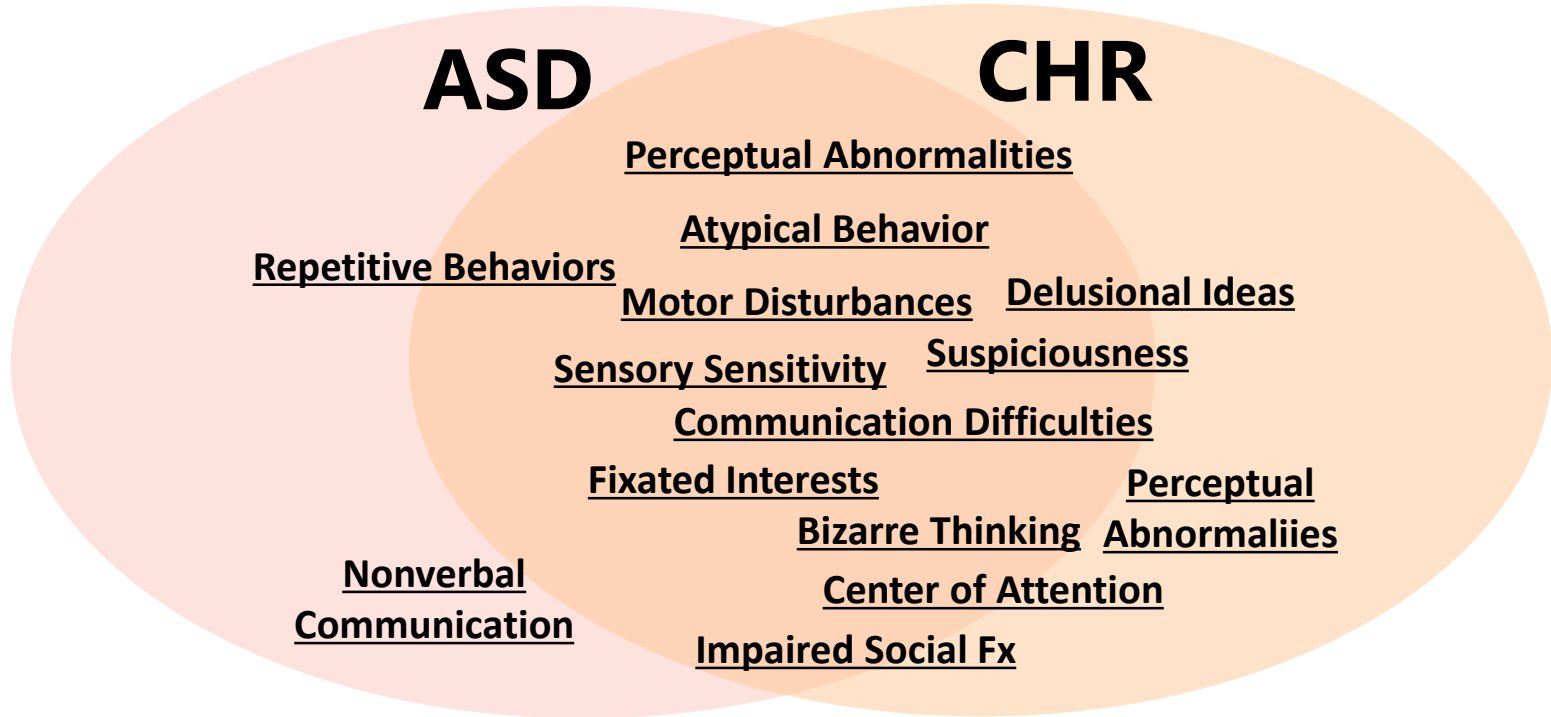
- At least one of following symptoms present in attenuated form, w/ intact reality testing and is of severity or frequency to warrant clinical attention
 - Delusions
 - Hallucinations
 - Disorganized speech
- Symptoms must have been present at least 1x/week in last month
- Symptoms must have begun or worsened in past year
- Symptoms are sufficiently distressing and disabling to warrant clinical attention, not better explained by another mental disorder.
- Criteria for any psychotic disorder have never been met



Pretty distinct on the surface,
but...



OVERLAP BETWEEN ASD & CHR



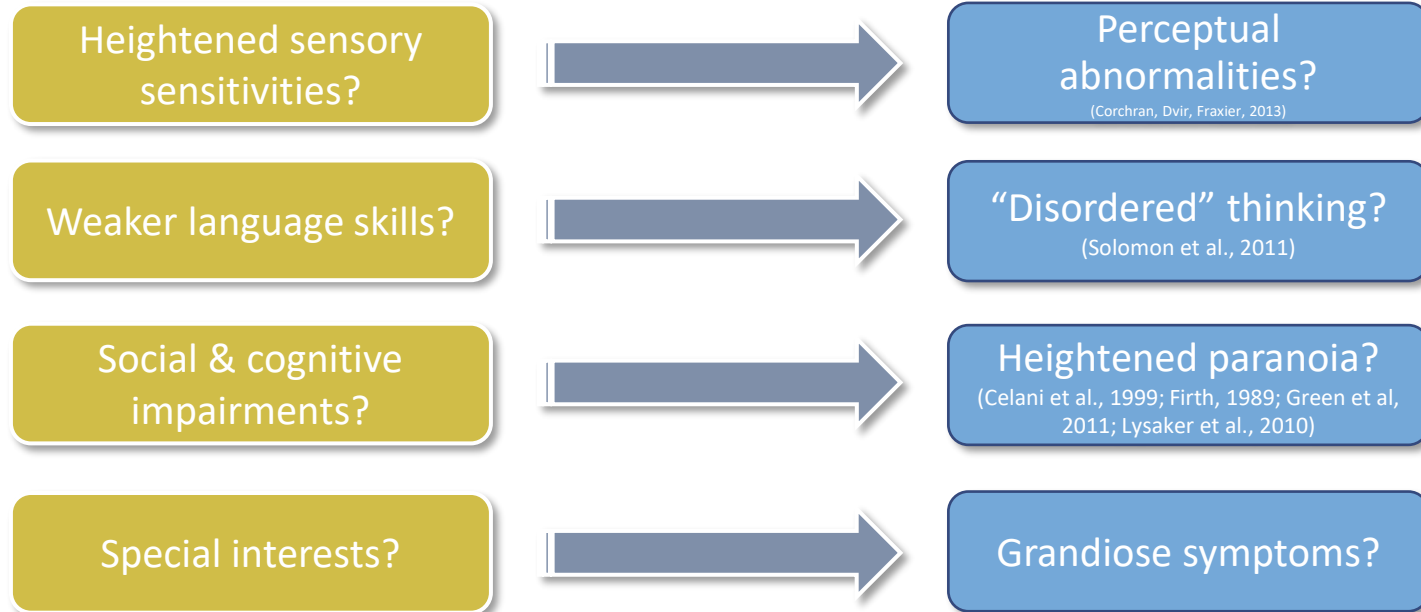
OVERLAP BETWEEN ASD & CHR

Overlap between core features of ASD and SIPS criteria

Core Features of Autism	Autism	SIPS Criteria
Social-Emotional Challenges	<ul style="list-style-type: none">• Lack of social-emotional reciprocity• Misreading social cues• Restricted or flattened affect	<ul style="list-style-type: none">• Social anhedonia• Impaired experience of emotions and self• Dysphoric mood• Avolition
Communication Challenges	<ul style="list-style-type: none">• Language delay• Echolalia	<ul style="list-style-type: none">• Disorganized communication• Reduced expression of emotion• Impaired ideational richness
Unusual Thought Content	<ul style="list-style-type: none">• Restricted interests• Perseveration• Concrete thinking• Problems with perceptual processing	<ul style="list-style-type: none">• Delusional ideas• Suspiciousness/persecutory ideas• Perceptual abnormalities• Bizarre thinking• Grandiosity
Behavioral Features	<ul style="list-style-type: none">• Repetitive behavior/movement	<ul style="list-style-type: none">• Motor disturbances• Odd behavior or appearance



POSSIBLE CONFUSION?



ASSESSMENT



THE STRUCTURED INTERVIEW FOR PSYCHOSIS-RISK SYNDROMES (SIPS)

Commonly used assessment in CHR

- Attenuated positive symptoms of CHR
- Distinguishes between low & high risk, and psychosis

SIPS positive symptoms map on to hallmark characteristics of psychosis

- P1: unusual thought content/delusional ideas
- P2: suspiciousness or persecutory ideas
- P3: grandiose ideas
- P4: perceptual abnormalities/hallucinations
- P5: disorganized communication



EXPERT REVIEW OF THE SIPS: OVERVIEW

- Surveyed 13 experts in autism
- Identified 85% SIPS P items as possibly problematic for adolescents with ASD
- Challenges for assessment of CHR in ASD:
 - 1) Differentiating ASD and psychotic symptoms
 - 2) Valid symptom reporting
 - 3) True symptoms vs. secondary gain (e.g., attention)
 - 4) Lack of assessment tools or instruments in ASD



EXPERT REVIEW OF THE SIPS: CHALLENGES

- Difficulties understanding the wording of items: Valid Reporting
- Concrete or literal interpretation of items: Valid Reporting
- Symptom overlap / over-endorsement: Differentiation
- SIPS items misattributed to psychosis risk: Differentiation
 - E.g., sensory sensitivity / perceptual abnormalities



CLINICAL EXAMPLES FROM THE EXPERTS:

DIFFERENTIATION / VALIDITY

- I have worked with children who have very unusual expressive language that can resemble the "word salad" one finds among individuals with schizophrenia.
- Sometimes kids with autism use idiomatic language and syntax-- these complicate standard historical questions.
- Sometimes it's difficult to tell whether language abnormalities are due to a developmental language disorder vs. psychotic thought disorder.
- Sometimes it is difficult to tell whether disorganized communication (that seems very much like psychotic thought disorder) has worsened recently (suggestive of recent-onset psychosis) vs. a stable, longstanding problems related to autism.
- I have seen some patients with autism spectrum with vivid imaginary lives. It's difficult to tell whether some of this represents psychotic symptoms.



SIPS ITEMS

- **P1 (Unusual thought content/Delusional ideas)**
 - Have you had the feeling that something odd is going on or that something is wrong that you can't explain?
 - *"I'm very interested in subway maps and my sister says I'm weird."*
 - Do familiar people or surroundings ever seem strange? (Mom's response)
 - *"I always have to drive him home from your office the same exact way. If we go another way home, he gets very upset."*
 - Does your experience of time seem to have changed? Unnaturally faster, unnaturally slower?
 - *"Yeah, I lose track of time a lot. I get lost in internet rabbit holes about vacuums."*
 - Do you daydream a lot or find yourself preoccupied with stories, fantasies or ideas?
 - *"I love Mario Brothers. I love being in Mario Brothers world."*



SIPS ITEMS (CONT.)

- **P2 (Suspiciousness/Persecutory Ideas)**
 - Have you had the sense that you are often the center of people's attention?
 - *"Yes. People are always staring at me, and my therapist is always with me."*
 - Do you ever feel that people around you are thinking about you in a negative way?
 - *"People call me names in my school."*
- **P3 (Grandiosity)**
 - Do you feel you have special gifts or talents?
 - *"My mother says I am very special."*
 - *"I know about LeBron James."* (memorized all stats)



SIPS ITEMS (CONT.)

- **P4 (Perceptual Abnormalities/Hallucinations)**
 - Have you been feeling more sensitive to sounds? Have sounds seemed different? Louder or softer?
 - Do you seem to feel more sensitive to light or do things that you see ever appear different in color, brightness or dullness; or have they changed in some other way?
- **P5 (Disorganized Communication)**
 - Are you aware of any ongoing difficulties getting your point across, such as finding yourself rambling or going off track when you talk?



OTHER SYMPTOMS FROM THE SIPS

Risk of improper differentiation...

- Do you usually prefer to be alone or with others?
- Do you find yourself having a harder time distinguishing different emotions/feelings?
- Do people ever say your ideas are unusual or that the way you think is strange or illogical?
- Do you think others ever say that your interests are unusual or that you are eccentric?
- Do you get thrown off by unexpected things that happen to you during the day?



Feasibility of psychosis risk assessment for adolescents diagnosed with autism

**Camille S Wilson¹ , Laura Anthony², Lauren Kenworthy³,
Rivka Fleischman⁴, Caroline Demro⁵, Nicole Andorko⁶,
Anna Chelsea Armour³ and Jason Schiffman⁶**

Autism
2020, Vol. 24(4) 834–850
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Interviewed 21 adolescents w/ ASD & 22 typically developing adolescents

- **Is the SIPS tolerable for youth with ASD?**
 - ASD group found instructions harder to follow
 - Although still acceptable
 - Too long

VALIDITY OF SIPS

- By and large, the groups were similar
- Limits of SIPS applied to those w/ & w/o ASD
- There were some differences, however...
- **Most problematic item:**
 - *“Do familiar people or surroundings ever seem strange?”*
- *Participants w/ ASD slightly more likely to:*
 - Ask for clarification
 - Say “I don’t know”
 - Refuse to answer

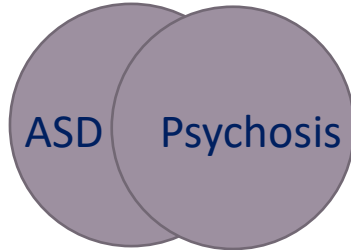


PSYCHOSIS IN AUTISM ASSESSMENT

- Autism Diagnostic Observation Schedule (ADOS-2)
 - Reliably distinguished between ASD, psychosis, and typically developing adults
 - High rate of false positives for ASD in psychosis group

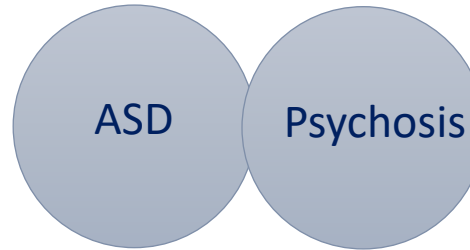
Negative Symptoms

More Overlap



Positive Symptoms

Less Overlap



**Positive symptoms of psychosis may be best
for distinguishing psychosis from ASD**

FUTURE DIRECTIONS FOR ASSESSMENT

- Need for instruments that reliably distinguish ASD and psychosis
 - Continue refining our understanding of *which* features of psychosis and autism are **truly shared**

VERSUS....

- Features that only **appear shared** due to artifacts of the assessment process



FUTURE DIRECTIONS FOR ASSESSMENT

- *Positive and Negative Syndrome Scale for Schizophrenia (PANSS)*
Autism Severity Scale (PAUSS)
 - Undergoing validation
 - Quantifies autism severity trans-diagnostically
 - “Autistic phenotype” associated with persistent symptoms



IMPLICATIONS OF COMORBIDITY



PATHWAYS TO PSYCHOSIS

Multiple Complex Developmental Disorders (MCDD) vs. Psychosis Risk

- Comparison of CHR symptoms in two groups at risk for psychosis
 - Psychosis Risk Only, $n = 80$
 - MCDD, $n = 32$
- 78% of sample with MCDD met criteria for risk
- Psychosis Risk group exhibited more severe positive and negative symptoms on SIPS



PREDICTING PSYCHOSIS RISK IN ASD

- **Psychosis risk & ASD (CHR/ASD+)**
 - No sig difference in tot. SIPs scores
 - Higher levels of social anhedonia
 - Lower levels of social functioning
- **ASD+CHR \neq increased psychosis**
- NAPLS Risk Calculator predicted transition rates equally well
 - <http://riskcalc.org:3838/napls/>

An Individualized Risk Calculator for Psychosis

For more information on Prodromal Risk Syndromes and risk assessment, see [NAPLS](#)

For more information on derivation and uses of this risk calculator, see [Cannon et al.](#)

Please check the box if your answer is yes

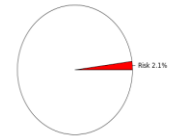
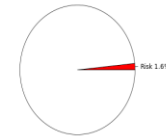
☒ Does the patient have an interview-based
SPS diagnosis of a prodromal risk
syndrome?

☒ Were the ratings and test scores obtained by
a professional?

Sum of rescaled SPS ratings for unusual thought content

Sum of rescaled SPS ratings for unusual thought content

1-year and 2-year probability of conversion to psychosis



This calculator was based on a Cox proportional hazards regression model that was developed from a cohort consisting 596 clinical high risk participants from the



AUTISTIC FEATURES & PSYCHOTIC SYMPTOMS

- **Autism Spectrum Quotient (ASQ)**
 - In people with FEP, 27.8% had elevated traits of autism
- *FEP + autism traits associated with:*
 - Lower employment at baseline (Zhang et al., 2020)
 - Less improvement in general psychological symptoms and functioning at one year follow up (Zhang et al., 2020)
 - Worse psychosis symptoms (Chisolm et al., 2019)
 - Poorer quality of life (Chisolm et al., 2019)
 - Lower functioning (Chisolm et al., 2019)



AUTISM FEATURES IN PSYCHOSIS

The combination of ASD and psychosis features may be associated with poorer functioning and outcomes compared to ASD or psychosis alone



CLINICAL CONSIDERATIONS



BREAK SILOS

- Behavioral Health Care Systems
- Schools
- Developmental Disabilities
- Adult First Episode
- CHRP Clinics
- Early intervention, warm handoffs, integrated care
- Future of CHRP Grants



UNCOMMON, BUT IMPACTFUL

- Independent functioning
- Quality of life
- Family functioning, burden & distress

Even having features of both is challenging...



ASSESSMENT IS WORTH IT

Given almost 10% of people with ASD have psychosis, assessment is clinically relevant

- Setting matters
 - Comorbidity higher in inpatient



TIPS FOR ASSESSMENT

- Temporal precedence
- Consider adjusting language in SIPS
- Assess for ASD and other disorders
- Take **context** into account



TIPS FOR ASSESSMENT

- Beware of interview fatigue
- Use parental reports
- Mindful of the distinction between functional decline (psychosis) and pervasive developmental deficits (ASD)
 - *Humility*... SIPS not validated



TIPS FOR DIAGNOSIS/CLINICAL CONCEPTUALIZATION

- Positive symptoms of psychosis seem to best differentiate
- Negative symptoms (social withdrawal, reduced facial affect) tend to not differentiate
- Disorganized (psychosis) vs. “scripted” speech (ASD)
 - To parse apart, inquire whether caregiver can comprehend youth
- Consider family history of psychosis vs. ASD



TIPS FOR DIAGNOSIS/CLINICAL CONCEPTUALIZATION

- Consider other comorbidities with shared symptoms
- Diagnostic categories are just our “best guess” -
carving nature at its joints
- As always, consider context and cultural background
 - SO MUCH MORE WORK TO BE DONE



TREATMENT CONSIDERATIONS

- **We're all more similar than different**
- Be client/family driven
- Know your client
 - Create an individualized approach
 - Strengths, what's worked in the past, goals
- Psychoeducation
- Social skills
- CBT
 - Relaxation, School, Family, Wellness, Safety



VIGNETTE

Chris is a 14 yr old diagnosed with high functioning autism at age 5. Symptoms included social difficulties, needing to line up his matchbox cars by color order, reluctance to make eye contact, tactile sensitivity to certain fabrics and an aversion to being touched or hugged. When puberty started at age 13, in addition to these long-standing symptoms, Chris developed hypersensitivity to light and noise and began to see shadows and movement out of the corner of their eye. Chris also started hearing noises in their head like “static” and footsteps. All of this confused Chris because they knew they weren’t real but couldn’t stop them.

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VIGNETTE (FOLGER ET AL. 2019)

Michael is a 13-year-old boy born in Vietnam to a mother with mental illness. In his first mental health evaluation when he was 10, Michael's psychiatric nurse practitioner diagnosed him with attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). Pragmatic language and syntax deficits were also noted from an early age.

Last year, while in 6th grade, Michael exhibited anxiety and perseverative beliefs. He began “talking to himself in his room” and using neologisms. A school-based evaluation resulted in educational diagnoses of ADHD and ASD based on social disconnectedness and invading others' personal space. Michael's parents felt “something else was going on” and sought a second opinion. Considering Michael's history, previous assessments, and their assessment battery (Behavior Assessment System for Children, Behavior Rating Inventory of Executive Function, Autism Diagnostic Observation Schedule, and Rorschach Inkblot Test), the team characterized his current symptoms as “Attenuated Psychosis Syndrome.”

A few months later, clinicians in the psychiatry department confirmed symptoms of functional decline, cognitive disorganization, and hallucinatory experiences. They prescribed him an antipsychotic at that time, but concluded that these symptoms were best explained by post-traumatic stress they inferred from his pre-adoption life.

Most recently, Michael was weaned off risperidone to manage a new side effect of tics. He subsequently manifested growing suspiciousness with reactive aggression toward peers for imagined slights and insults that he could “swear he heard.” A different school-contracted psychologist's re-evaluation concluded that a diagnosis of psychosis was warranted based on the several years of unfolding clinical observations. Acting from the supposition that early-onset psychosis was too rare and too stigmatizing a condition to apply to a “kid who's just having trouble paying attention,” the first school psychologist remained adamant that ADHD and ASD were the most appropriate diagnoses, and Michael would be ill-served “pumped full of neuroleptics.”

What would you do to try to bridge this impasse?

VIGNETTE (FOLGER ET AL. 2019): FLAGS FOR PSYCHOSIS

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THOUGHT QUESTIONS

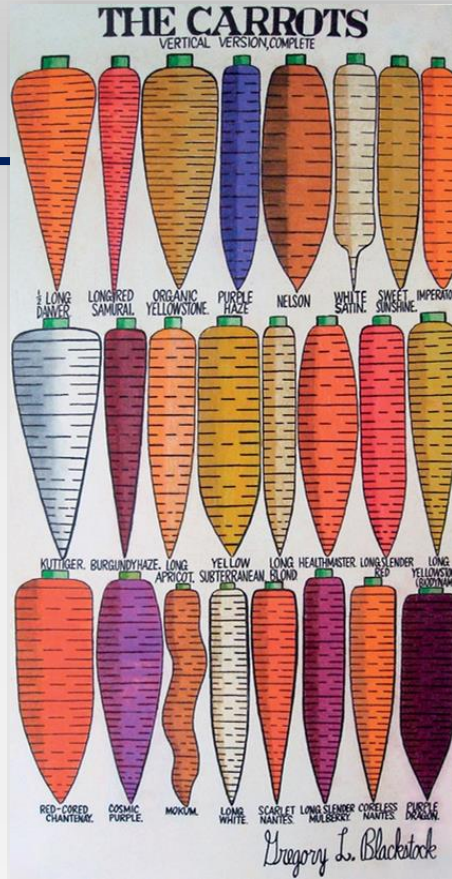
- What additional information would you like to know?
- How could you manage all the discrepant perspectives?
- How would you approach treatment planning?



SUMMARY

- ASD and psychosis/psychosis risk seem to overlap
- Assessment is possible but care should be taken
 - Assessment that is individualized is most helpful
- For individuals with features of both ASD and psychosis, the clinical picture can be more challenging
- Clinical care that spans across silos and prioritizes the needs of the family is always optimal... especially so youth with features of both ASD and psychosis

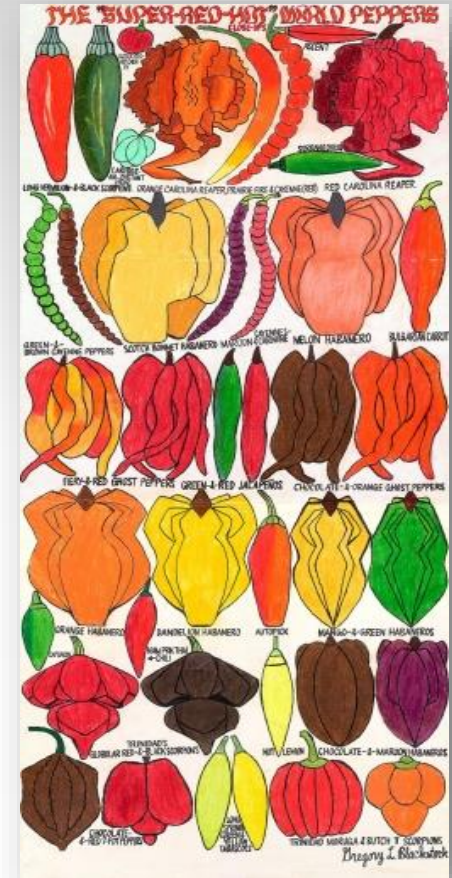




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Questions?

Drawings by artist Gregory
 Blackstock (b. 1946)
 Diagnosed with autism and
 schizophrenia





<https://screening.mhanational.org/screening-tools>
"Psychosis Test"

