# Psychosis In People with ID: Challenges in Differential Diagnosis

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"Of course, no man is entirely in his right mind at any time."

The Mysterious Stranger Mark Twain

## Psychotic Thoughts ...

- Believing your thoughts are being broadcasted on TV or radio -everyone can hear them
- Believing you are being controlled by outside forces, pursued or persecuted
- Thinking shows, songs etc. on media are directed specifically at you

\*For about almost seven years—
except during sleep —I have never
had a single moment in which I did not
hear voices. They accompany me to
every place and at all times; they
continue to sound even when I am in
conversation with other people, they
persist undeterred even when I
concentrate on other things, for
instance read a book or newspaper,
play the piano, etc.; only when I am
talking aloud to other people or to
myself are they of course drowned by
the stronger sound of the spoken
word and therefore inaudible to me."

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# **Psychosis**

- Very difficult to diagnose in people with moderate or greater ID
- ▶ In people with mild ID still very challenging
  - Rule out other explanations carefully

"Schizophrenia cannot be understood without understanding despair." — R.D. Laing

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# Schizophrenia

- Two or >:
  - Delusions
  - ▶ Hallucinations
  - ▶ Disorganized Speech
  - ► Grossly disorganized or catatonic behavior
  - ▶ Negative symptoms
- Social or occupational dysfunction
  - Not simply the disruption related to agitated behaviors in a person with ID
- ► Continuous signs for at least 6 months
  - ▶ No clear inter-episode recovery to baseline

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# Schizophrenia Symptoms

- Disorganized Speech
  - ▶ Must know baseline well
  - ▶ Recognize the impact of developmental features and developmental regression related to stress
- Grossly Disorganized or Catatonic Behavior
  - ▶ Must rule out encephalopathy, delirium or ADEs
- Negative Symptoms
  - Loss of motivation, anhedonia
  - ▶ Slowing of thoughts, movements, responses
  - ► "Flattening" of affect

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5

# Schizophrenia: Changes in DSM-5

- ▶ The criteria are more strict than before to reduce misdiagnoses
- Two major changes
- Criteria A Must have 2 of the listed symptoms
  - **Delusions**
  - **▶** Hallucinations
  - **▶** Disorganized Speech
  - ► Grossly disorganized or catatonic behavior
  - **▶** Negative symptoms
    - ▶ Previously, could be simply "bizarre delusions"
  - No more subtypes

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## Schizophrenia and Psychosis

- ➤ Findings indicate that the narrow definition of schizophrenia is significantly associated with greater morbidity (worse outcomes, few positive outcomes)
- Prevalence rates of subthreshold states vary @ 5-8%
- Psychotic experiences mostly --- @ 75% -- transient
- "The 'true' natural history of an illness cannot be determined from studies in treated populations."

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7

# Identifying the role of psychosis in MH disorders

- "...Psychosis can thus be considered as a marker for more severe psychopathology that negatively impacts outcome."
- ➤ You are more ill from whatever you are ill from when there are also psychotic symptoms present....Recent efforts to discriminate the DSM categories of bipolar disorder and schizophrenia using a multimodal set of biomarkers (cognition, evoked potentials, antisaccadic eye movement and neuroimaging) failed to yield a desirable outcome."
  - ► Guloksuz & Van Os, 2018

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### Schizoaffective Disorder

- Uninterrupted period of illness with BOTH
  - ► A mood episode
  - Symptoms of schizophrenia (2 or >)
    - Delusions
    - **▶** Hallucinations
    - ▶ Disorganized behavior speech
    - ▶ Negative symptoms
- ➤ At some point- at least 2 weeks of just psychotic symptoms without prominent mood disturbance

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9

## Prevalence of Schizophrenia

- < 1% general population, but 10% of people with first-degree relative with the disorder,
  - ▶ (parent, brother, or sister).
- Twins --- 40 to 65% concordance rate
  - have higher rates of rare genetic mutations.
  - ► Involves 100s of different genes
  - >>>> disruption to brain development

"Scientists think that interactions between genes and aspects of the individual's environment are necessary for schizophrenia to develop. Many environmental factors may be involved, such as exposure to viruses or malnutrition before birth, problems during birth, and other, not yet known, psychosocial factors."

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## Prevalence in IDD

- Best controlled studies that were population based and systematic
- ▶ Point prevalence rates of between 2.6% and 4.4%
  - Impacted by the classification system employed
  - ► About 5-10x > then gen population
    - ► (Cooper et. al., 2007)

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# Prevalence in Youth with ASD

- Modified K-SADs
  - ▶ In depth individualized assessment
- ▶ N=109 Children
- ▶ 5-17 y/o
- ▶ 68% FSIQ > 70, mean 83
- Unselected for psychiatric comorbidity
- ► ADR-I ADOS and DSM-IV-TR criteria for ASD met Leyfer et. al., 2006

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# Leyfer et. al., 2006

N = 109	PERCENT
Specific Phobia	44%
Manic Episode/BD	2%
Depression	10%
Psychosis/Schiz	0
Anxiety NOS	2%
OCD	34%
ADHD	31%

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13

# New Onset Psychiatric Disorders with Autism

- ▶ Followed 135 Children with ASDs until age 21
- Assessed new onset of psychiatric d/os
- Direct clinical assessments performed
- ▶ 16% had definite and 6% possible onset of a new psychiatric d/o
  - ▶ 5 OCD
  - ▶ 8 Affective do
  - ▶ 1 Anxiety d/o
  - ▶ 0 Schizophrenia
- ► Rates < Bipolar d/o Psychosis
  - v studies using less rigorous methods sample with < cognitive impairment

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Hutton, Goode, Murphy, Le Couteur & Rutter, 2008

# Schizophrenia

- ► Hallmark are "First Rank" symptoms or "positive" symptoms
  - **▶**Delusions
  - **▶** Hallucinations

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15

# Hallucinations in Schizophrenia (SZ)

- ► Hallucinations in Schizophrenia are usually AUDITORY
- ▶ If visual or tactile or olfactory:
  - ▶ Rule out neurological and other medical causes
  - ► Especially suspect drugs, delirium or drug-induced encephalopathy
  - ► When occurring in SZ, usually with a delusional association and occur during the day (not just at night)

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## **Hallucinations**

➤ "As many as two million people in the United Kingdom repeatedly see people, animals, and objects that have no objective reality. Hallucinations on the border of sleep, dementing illnesses, delirium, eye disease, and schizophrenia account for 90% of these. The remainder have rarer disorders."

Collerton, Perry & McKeith, 2005

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17

# CBS (Not the TV Station)

- ► Charles Bonnet's Syndrome (CBS)
  - ➤ Complex visual hallucinations in "psychologically normal people," used to be considered rare
  - Now know that CBS occurs frequently in elderly, visually handicapped patients
- ▶ 505 visually handicapped patients 60 met criteria for CBS
- "Sensory deprivation and a low level of arousal seemed to favour the occurrence of hallucinations."

Teunisse, Zitman, Cruysberg, Hoefnagels, & Verbeek, 1996

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### **Delusions**

- False, fixed beliefs
- ▶ Be very careful in people with ID to know developmental profile
  - ➤ At best baseline, is person able to distinguish reality from fantasy clearly
  - ► Knows that others can't hear their thoughts
  - ► Are not describing wishes

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19

# Capgras Syndrome

### Table. Examples of Capgras Syndrome

### **Physician Descriptions and Patient Comments**

Patient believes his wife has been replaced by an imposter.

Patient believes his daughter has been replaced by his dead sister.

Patient believes her husband is a lady or a stranger living in the house.

Patient will look at his wife and ask, "Where is my wife?"

Patient believes there are 6 people, including his wife, all named Shirley.

Patient said, "I am looking for Bob my husband, not him Bob."

Patient believes there are 2 daughters and 2 sons who look alike.

Patient said, "Someone homosexual is masquerading as my wife."

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# Newer thoughts about pathways in Capgras syndrome

- "There is a disconnect in the pathway between the temporal lobe, the area of the brain responsible for facial processing, and the limbic circuits associated with appropriate personal and emotional responses."
- May emerge after an infection i.e. UTI
- May have elements of a delirium

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21

# Adversity and Hallucinations

- ➤ Children who were abused or had 8 or more adverse life events had 5 x's the occurrence of hallucinations
- "...a history of childhood trauma should be looked for among persons with a history of hallucinations." (Whitfield, Dube, Felitti & Anda, 2005)

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# Differentiation of Auditory Verbal Hallucinations (AVH) in Healthy vs Psychotic Individuals

- Many more similarities than might be expected!
- 2 major factors that differed Included:
- ▶ The "emotional valence"
  - ▶ People who are healthy (not having other psychotics symptoms, not seeking or requiring MH care) did not report these as distressing
- Age of onset
  - ▶ Age of onset was younger in the "healthy" group
  - ▶ 12 v 21

Daalman et. al., 2011

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23

# Common Genetic Mechanisms in Multiple Neuropsychiatric Disorders

- Identified 10 genes commonly associated with ASD, SCZ (Schziophrenia), BD (Bipolar Disorder) and OCD (Obsessive Compulsive Disorder)
- ▶ These genes involved in:
  - dopamine and serotonin pathways
  - calcium ion channel networks
  - ▶ folate metabolism
  - regulation of gene silencing and expression
  - hippo signaling pathway (which regulates growth, differentiation, cell death)

O'Connell, McGregor, Lochner, Emsley & Warnich, 2018

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# Findings Related to Neurological Substrate

- ▶ Neurologic/brain imaging findings re schizophrenia:
  - ▶ Larger ventricles
  - Less gray matter
  - ▶ Variability in activity in different brain regions
- Changes seen in structure, location of cells formed before birth
  - Making it likely that problems arise during brain development
  - ► May provoke "faulty connections"
- Some problems may not show up until puberty

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"The problem may not show up in a person until puberty. The brain undergoes major changes during puberty, and these changes could trigger psychotic symptoms in people who are vulnerable due to genetics or brain differences."

75

# **ASD & Psychosis**

- Autism and schizophrenia share "overlapping genetic etiology, common changes in brain structure and common cognitive deficits."
- One hypothesis suggest that autism etiology commonly involves enhanced, but imbalanced, components of intelligence

Crespi, 2016

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# **ASD & Psychosis**

- ➤ Vitamin-D orchestrates innate immune responses, helps maintain "optimal antibacterial responses in humans"
- "An increasing body of evidence suggests that vitamin-D is an important player in mature brain function and brain ontogeny."

Kočovská, Gaughran, Krivoy & Meier, 2017

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27

# ASD & Schizophrenia

- Autism and schizophrenia are characterized by similar socialcognitive impairments..
  - may stem from different underlying abnormalities in the functional organization and communication of the social brain
- ► "Final Common Pathways" --- an important concept to reconcile these differences

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# **Auditory Hallucinations**

- Associated with increased activity in fronto-temporal areas
  - ► Areas involved in speech generation and speech perception
  - ► Also --- medial temporal lobe
    - ► Areas involved in verbal memory

Jardri, Pouchet, Pins & Thomas, 2011

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29

# **Epilepsy and Psychosis**

- 6% of individuals with epilepsy also have psychotic illness
- Patients with epilepsy have 8 x's > risk of psychosis
- Prevalence rate of psychosis is higher in temporal lobe epilepsy (7%)

"TLE and psychiatric symptoms coexist more frequently than chance would predict. Damage and deregulation among critical anatomical regions, such as the hippocampus, amygdala, thalamus, and the temporal, frontal and cingulate cortices, might predispose TLE brains to psychosis."

Kandratavicius et. al., 2012

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## Hallucinations and IDD

- Remember that these are almost always very distressing to people who are experiencing them
  - ► Developmental profile is key
  - ▶ At certain cognitive developmental stages, it is common to:
    - ▶ Process out loud (and not know it looks odd)
    - ► Have imaginary friends
    - ▶ Not understand the difference between reality and fantasy

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31

# Schizophrenia- Clinical Course

- Usual clinical course and history
  - ▶ Evolves slowly generally though there can be an acute break
  - ▶ Onset adolescence or early adulthood
  - ▶ May have what seems like an acute break, but looking back
    - ▶ Early signs of oddness, socially abnormal behavior
  - ▶ If onset is much later on....it may be something else

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### **Shared Risk Patterns**

- Shared environmental early risk factors have been observed for autism and schizophrenia
- Multiple studies have shown increased risk for both disorders related to:
  - ► Advanced paternal age
  - Pregnancy and birth complications

Strålin & Hetta, 2019

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33

# Convergence and Divergence in Developmental Pathways

- Genetic overlap between ASD and schizophrenia for rare copy number variants & rare de novo mutation events
  - > converging evidence for gene sets involved in synaptic function
- ► However genetic overlap between ASD and schizophrenia is small compared with overlap between psychiatric adult-onset only disorders
- ► This study examined social communication at various ages across development in samples of youth with ASD or schizophrenia

St Pourcain et al., 2018

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# Convergence and Divergence in Developmental Pathways

- "Genetic overlap with ASD was strongest for social communication difficulties during middle childhood (rg~33%) those with schizophrenia strongest for social communication difficulties during later adolescence (rg~18%)."
  - "Symptoms of ASD typically occur during early childhood, whereas most symptoms characteristic of schizophrenia do not appear before early adulthood."

St Pourcain et al., 2018

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35

# **Psychotic Symptoms - Differential**

- ▶ If there are psychotic symptoms, are these????
  - ► Mood congruent?
    - ► Morbid if depressed
    - Expansive if manic
  - ▶ "Bizarre"?
    - ▶ Be sure the cultural context is considered
    - ▶ Bizarre based on what standard?
  - ▶ Paranoid?
    - ➤ Rule out confusion, fear, social cognition challenges that have provoked anxiety re what others think

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# Rule Out Encephalopathy/Delirium

- ▶ Delirium develops over a short period of time
  - ► Hours to days
- Fluctuates across the day
  - Wax and wane
- ▶ Inability to focus or shift attention
  - ► Highly distractible
- Odd postures and odd motor behaviors, restlessness, picking at lint etc.
- ► Clear changes in level of arousal
  - "Clouded sensorium"

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37

# Misdiagnosis of Psychosis: What Informants Reported as Evidence of Psychosis

- ▶ His eyes bulged out
- ▶ He was VERY aggressive
  - ► A final common pathway!
- She talked about her children
- ▶ He kept referring to people not present
- He was constantly talking out loud and no one else was there
- ▶ He seemed to be responding to internal stimuli



"LET'S TALK A LITTLE ABOUT THOSE HALLUCINATIONS."

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# Misdiagnosis of Psychosis in ASD

- Odd use of words (or even made up words) when associated with externalizing behaviors can be confused as psychosis
- "Scripted speech"
- Conversation lacks give and take and speech content is idiosyncratic, worsened by stress —or anxiety
  - "Tangential thinking"
  - ▶ "Flight of ideas"

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39

# Treatment of Psychosis in ASD

- ► Four patients with ASD for whom authors felt confident of psychosis comorbidity
- ► Found that sustained use of antipsychotic medication was "objectively associated with an improvement in psychotic symptoms and quality of life." (Rai et. al., 2018)

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# Social Cognition and Psychotic Symptoms

- Current debate over what are the similarities and differences between ASD and psychotic disorders
- ➤ Tin et al. suggest..."social cognition may provide a broad marker of social disability"
- Youth with social-cognitive deficits are challenged in terms of integrating and processing social-interaction related sensory information

Tin et. al., 2018

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41

# Social Cognition and Psychotic Symptoms

- ▶ This in turn prevents rapid and accurate social information processing
- Further-this may lead to misinterpretations, mislabeling and potential paranoid thinking
  - ▶ "Impairments in social cognition may further reduce the capacity to engage in, and subsequently enjoy, social experiences....
  - ▶ "The loss of reward associated with social experiences may then exacerbate social withdrawal."

Tin et. al., 2018

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# CASE EXAMPLE J

- ▶ 40 y/o male with CdLS
- Obesity
- Constipation
- ▶ GERD
- Hiatal hernia
- Anemia

- ▶ Abilify 5 mg po qhs
- ► Effexor 150 mg po BID
- Depakote spkles 500 mg po BID
- Ativan 0.5 mg po qAM, 1 mg po qPM, 1 mg po qhs
- ► Trazodone 300 mg po qhs
- Nexium 40 mg po BID
- Zantac 150 mg po qhs
- Simvastatin 20 mg po daily
- ▶ Feosol 45 mg po daily
- ▶ Genteal 1-2 drops to right eye TID

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43

# "I think I swallowed battery acid"

# Cornelia DeLange Syndrome (CdLS): J.

- ▶ Very high rate of GI problems including GERD
- Skin problems
- Vision and hearing problems
- ASD
- Anxiety/phobias
- ► Attention problems
- Compulsions
- ► SIB

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# Psychosis & ASD

■ "Differentiating between the core symptoms of PDD and psychosis can be very difficult, as not only misinterpreting autistic behaviors as psychosis but also being unable to diagnose psychosis because of communication difficulties can occur."

Starling & Dossetor, 2009

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# Risks for nonaffective psychotic disorder and bipolar disorder in young people with autism spectrum disorder: a population-based study

- Found markedly increased risk for psychosis and bipolar disorder in youth with ASD
- Good news bad news, interpreting results...
- Good news:
  - Very large cohort, population based
  - ► Case controlled (Matched sample data for contrast)
- Bad news:
  - Diagnoses were recorded
    - ▶ How was it determined that individuals with ASD were actually psychotic?
    - Many pitfalls difficulty in differential is well recognized

Selten, Lundberg, Rai, & Magnusson, 2015

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# Psychosis and ASD

- ► Thought disorder and bizarre behavior
  - Unreliable indicators due to the fact that they are also core ASD symptoms
- Delusions
  - ▶ More reliable but cautiously useful as "unusual world view" and idiosyncratic obsessions also seen commonly in ASDs
- Auditory hallucinations
  - ▶ Should be differentiated from self-talk or pseudo- hallucinations

Starling & Dossetor, 2009

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# A Controlled Study Of Formal Thought Disorder in Children with Autism and Multiple Complex Developmental Disorders

- Examined multiple clinical groups and controls
  - ► Autistic Disorder
  - ▶ PDD nos MCDD
  - Anxiety d/os
  - **ADHD**
  - Controls
- ▶ Thought disorder was associated with verbal abilities
  - ▶ Highlighting the impact of developmental effects

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Gaag, Caplan, Engeland, Loman & Buitelaar, 2005

6

## Psychosis and ASD

- Compared adult males
  - ▶ 14 schizophrenia and 14 ASD
- > 50% of ASD group met criteria for schizophrenia
- Differences in symptoms noted between the two groups.
  - ▶ ASD group had limited language (affecting assessment)
  - ▶ 4/7 "bizarre behavior"
  - ▶ 1 -formal thought disorder
  - ▶ 6 -negative symptoms
  - 0 -hallucinations or delusions
  - 2 ? delusional without corroboration
    - then found that both were "merely stating accurate information in an immature way"

Konstantareas and Hewitt, 2001

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# Trauma, Sensory Over Responsivity & Dysregulation in ASD, IDD & SZ

- ➤ The triad may add risk for psychotic symptoms as transient and state dependent features
- Sensory over responsivity may also be common in schizophrenia (data are conflicting)
- Trauma may amplify sensory sensitivities through associative learning
- All may be tied together via anxiety

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51

## **Developmental Considerations**

- "The diagnosis of psychotic phenomena is not possible without considering the developmental limitations. The identification of symptoms of schizophrenia loses reliability in those with an IQ below 50 or a chronological age below 7 years."
  - Dossetor reviewed cases of mistaken identification of psychosis in children with ASDs
  - Most often, bizarre and delusional sounding constructions coupled with general dysfunction and anxiety provoked the misdiagnoses (Dossetor, 2007)

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# Impact Of Social Skill Challenges in ASD on Psychopathology

- ▶ Common misconception that all people with ASDs are absent social drive
  - ▶ This may change over the course of development
- Unusual or odd manner of trying to connect with others may lead to misdiagnosis of psychiatric symptoms
- ► Lack of understanding of social rules looks "bizarre"
- Lack of awareness of the impact of one's behavior on others seen as psychopathologic
  - ▶ Many formerly identified as having Asperger's syndrome:
    - ▶ Being right > being friendly

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# Communication and Emotional **Expression**

- Children with ASD
  - ▶ May have a more restricted range of emotional expression (but this varies!)
  - ▶ May have SOR (Sensory Over Reactivity)
  - Sudden laughing, smiling or crying can occur seemingly w/o connection to what is going on
    - ► More pronounced under stressful circumstances

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# Case Example

- ► Individual was
  - Screaming, yelling and non-compliant with request to leave event
  - ▶ Could not be redirected, many attempts
  - Expressed belief that characters who were in costume were real
  - ▶ Could not be shaken from this false belief
  - ▶ Had to be physically escorted to leave
  - ► QUICK DIAGNOSTIC HYPOTHESES?

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55

# Nicole Shows Evidence of Pre-logical, Magical Thinking



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# Cognitive Development

- Magical Thinking:
  - ► Fantasy reality distinctions are poor
  - Not due to psychotic thinking...
    - but to the nature of cognitive constructs
- ► Individual may be talking to people not present, not because of hallucinations, but because he or she is fantasizing
- Wishes may be expressed as beliefs, and can be misconstrued as delusions

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57

### Behavioral & Contextual Treatment

- ▶ Acutely psychotic individuals tend not to listen to "reason" so:
  - ▶ Respond to **affect** rather than content
  - ▶ Be soothing, agreeable, supportive, reassuring
  - ➤ Decrease stimulation, demands until person is better able to tolerate these
  - Maintain routines
  - Use approaches that work with anxiety!

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# CBT & Psycho-ed Groups

- Modified CBT can be a helpful intervention for people with IDD and psychosis. (Haddock, Lobban, Hatton & Carson, 2004)
- ▶ "Participants were able to understand the concept of psychosis, the need for medication, the role of stress and early signs of relapse. This approach may help participants to have a better understanding of their condition and prepare them to cope better in the future." (Cowley, Newton, Sturmey, Bouras & Holt, 2005)

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59

## **Antipsychotic Drug Treatment**

▶ "The 20-year data indicate that, longitudinally, after the first few years, antipsychotic medications do not eliminate or reduce the frequency of psychosis in schizophrenia, or reduce the severity of post-acute psychosis, although it is difficult to reach unambiguous conclusions about the efficacy of treatment in purely naturalistic or observational research."

Harrow, Jobe, & Faull, 2014

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# Clinical Antipsychotic Trial of Intervention Effectiveness in Schizophrenia in the U.S.A.

- ▶ In general, the newer drugs were no more effective or better tolerated than the older drugs.
- ► Clozapine outperformed other second-generation drugs
- ➤ 74% of patients were discontinued from their randomized treatment over 18 months

Lieberman, 2005

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61

# Medication SEs May Be Missed HEALTH in the ZIST CENTURY FEXOL guarantees weight loss but side effects attack ear canal. ODEETLE cures ear canal but enlarges prostate. NARXYL restores prostate but infects esophagus. BLPHM-2 disinfects esophagus but causes fettal lung kankle. ZARDO removes fettal lung kankle but results in uncontrolled weight gain.

# Psychosis in IDD: Things to Consider

- Misunderstanding, confusion and poor time concepts, neurocognitive features
  - Developmental effects
- Susceptibility to illness or drug induced encephalopathy
- ▶ Poor understanding of social contexts, "odd" ideas
  - "....individuals with ASD may experience some degree of delusions without the presence of any additional impairment, but that hallucinations are likely indicative of a distinct process." \*
- Paranoia at times = anxiety in the context of challenges to social cognition
- Desire to fit in and poor self-concept
  - "WISHFUL THINKING"

van Schalkwyk, Volkmar & Corlett, 2017

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# Great sadness and wishing to be "normal" can sometimes be mistaken for delusional thinking

