

Autism Spectrum Disorders and Co-Occurring Mental Health Conditions

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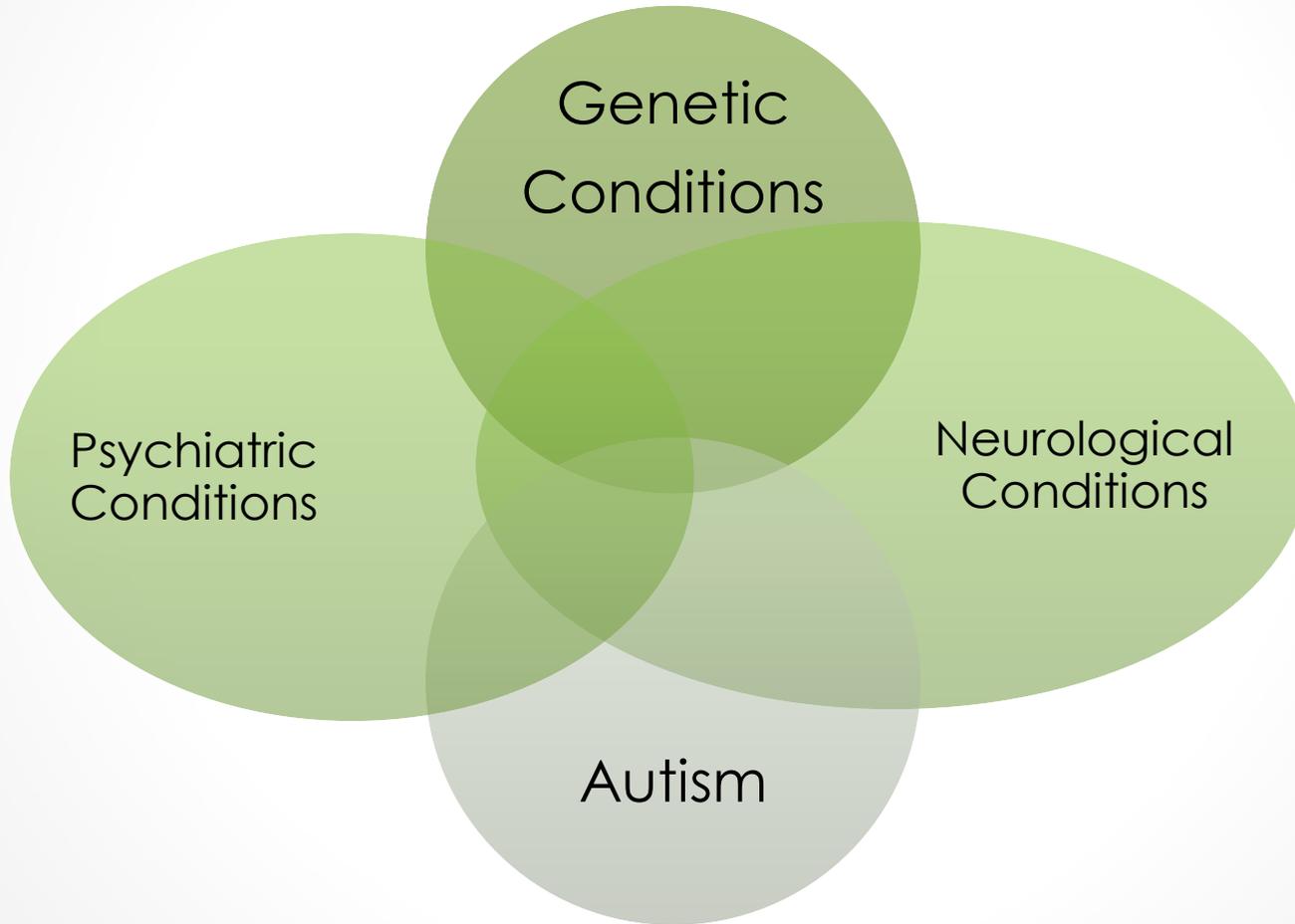
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Overview

- Children with autism are complex and at high risk for mental health conditions.
- We like to “keep it simple”, but this may not be possible
- Change in diagnoses with aging.
- Dual diagnosis:
 - DSMIV did not allow for dual diagnosis of

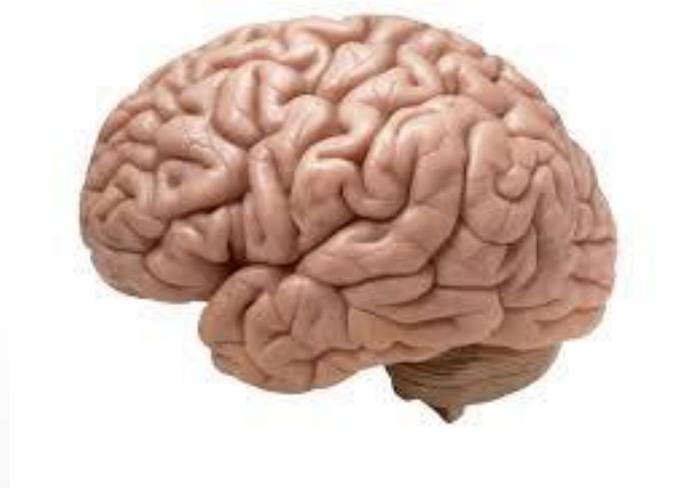


Autism Comorbidity



Why are Comorbidities Important?

- Targeted interventions based on comorbid condition
- Treatment of comorbid symptoms improves function.
- Improved understanding of biological underpinnings.



Case History:

A 4 year old boy presented with little interest in peers, compulsive behaviors, tantrums with transitions abnormal speech prosody. He had learning disabilities with difficulty with visual-spatial skills. He was diagnosed with autism and received educational and community services.

At 17 years of age, he had increasing behavior outbursts and it was determined that he had auditory hallucinations. His behavior deteriorated.

He was diagnosed with schizophrenia at 18 years.



Was the Diagnosis Wrong?

- Overlapping clinical symptoms can make diagnosis challenging
- Presentation of signs of psychiatric illness may be different in individuals with autism

Is this a common challenge?



Twin study: Sweden

- 9 year old twins born 1992-2001 (n=19,130)
 - 272 with ASD, 1.4% of population
- Recurrence rate 38% MZ, 8% DZ
- Half of individuals with ASD had 4 or more coexisting disorders, 4% did not have a comorbid diagnosis
- MZ twin pairs were frequently affected by a psychiatric disorder (boys 79%, girls 50%)
- DZ twin pairs were affected at 46% boys, 30% girls.



Case History

A 4 year old boy has autism and intelligence in at least the average range. He has increasing issues with attention in preschool and his teachers ask for further evaluation. Screening questionnaires for both ADHD and anxiety show elevated scores.



Children with ASD, with and without ID

- 101 children (57 boys, 44 girls, 4.5-9.8 years)
 - Anxiety disorder in 57%
 - Specific phobias 53%
 - ADHD 60%
- Higher IQ associated with anxiety disorders
- Older age associated with agoraphobia
- Night terrors associated with parental distress



Salazar F, Co-occurring Psychiatric Disorders in Preschool and Elementary School-Aged Children with **Autism** Spectrum Disorder.

Journal of Autism & Developmental Disorders. 45(8):2283-94, 2015 Aug.

Case History

A 13 year old boy has autism, Fragile X and mild intellectual disability. He has received supportive community and educational services and has done well in an inclusion educational setting.

He starts 8th grade and begins refusing to go to school because he is worried about varied aspects of his day. He develops insomnia and becomes very restrictive in his diet.

What do you do?



Anxiety and FXS

- The National Fragile X Survey was completed for 1,027 males with FXS
- Autism + anxiety= highest prevalence of ADHD symptoms, self-injurious behavior and aggressiveness

Hypotheses:

- Anxiety increases the severity of autism in FXS,
- Some neuropsychiatric and behavioral conditions are primarily related to comorbid anxiety, not autism;
- Prevalence of behavioral issues increases with age.

Talisa, V., Autism and anxiety in males with fragile X syndrome: an exploratory analysis of neurobehavioral profiles from a parent survey, Am Journal Med Gen, May, 2015

Case History

A 17 year old young man has autism and mild intellectual disability. He is increasingly hostile and aggressive and is becoming violent. He previously slept well, but now is sleeping only a few hours per night.

Concerns:

Change in behavior

Worsening behavior, now severe

New symptoms



When to Consider Comorbidity

- Signs of problems outside the autism spectrum are apparent
- An abrupt change from baseline
- A severe and incapacitating problem behavior
- Worsening of symptoms from baseline
- When the child does not respond as expected to treatment

- (Autism Spectrum Disorders: A research review for practitioners, edited by Sally Ozonoff, Sally Rogers, Robert Hendren, 2003

Bipolar Disorder in Adults with Asperger

- BD prevalence in adults with AS is 6-21%
- Symptoms usually start in adolescence
- Atypical presentation makes diagnosis difficult
 - Common: irritable, instable and dysphoric mood, hostility, restlessness, anxiety, aggression, violent behavior and insomnia
 - Uncommon: classic euphoric mood, elation and jocularity
- Relatives of individuals with AS are at higher risk of BD (almost 10%)

Vannucchi, G., et al, Bipolar disorder in adults with Asperger's Syndrome: A systematic review, *Journal of Affective Disorders* 168 (2014) 151–160

Treatments

- Therapy/Educational Models to treat the core symptoms of autism
 - ABA-based therapies (PRT, DTT,, Early Start Denver Model)
 - Play-based therapies
 - Relationship Development Intervention (RDI)
 - Floortime
 - TEACCH, SCERTS



Treatment of Psychiatric Disorders

- **Medication treatment** is favored by clinicians
 - Studies of psychosocial and behavioral treatment effectiveness are more complicated and difficult to do even in the non-autistic population.
 - Many psychosocial treatments such as psychotherapy are communication-based.
 - Children with autism typically have already received other non-medication interventions before they come to psychiatric treatment.
 - Autism is seen as a “biological” disorder, which biases clinicians towards “biological treatment.”
- However, there is a growing literature on the benefits of **cognitive-behavioral therapy** for anxiety in high-functioning people with autism

Medications

- THERE ARE NO MEDICATIONS THAT TREAT THE CORE SYMPTOMS OF AUTISM
- Medications used to treat psychiatric symptoms in autism:
 - Antipsychotics
 - Antidepressants
 - Sleep Medications
 - Psychostimulants
 - Alpha-Adrenergic Agonists

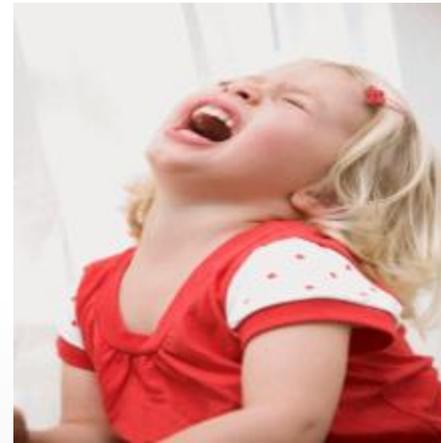


Medication Treatment: Antipsychotics

- One landmark study involving a multi-site, randomized, double-blinded trial of Risperidone compared with placebo in 101 children (ages 5-17 years old) with autism found that 69% of the Risperidone group improved on measures of irritability, stereotypies and hyperactivity compared to 12% of the placebo group (McDougle et al., 2002).
- This resulted in an FDA approval for the use of Risperidone (10/2006) for the treatment of irritable, aggressive and self-injurious behavior in children with autism. It is one of only two FDA-approved medications for autism. (The other medicine is Aripiprazole, also an atypical antipsychotic.)

Case Study

- A 29 month old Caucasian female diagnosed with Autism by ADOS presented with severe temper tantrums and anxiety. Her tantrums were causing her to harm herself and others. Despite her young age, Risperidone was started to stabilize the temper tantrums and decrease anxiety. The severity and dangerousness of her tantrums warranted a cautious medication trial. Within two weeks of starting Risperidone, she had added eleven vocabulary words and was participating in developmental interventions. Currently at age six, she is highly verbal and fully integrated into a mainstream regular education class with supports.



Medication treatments: Antidepressants

- Use based on cumulative data suggesting disruption in serotonergic mechanisms during early development in children with autism.
- SSRI's (Prozac, Luvox, Paxil, Celexa, Zoloft) are increasingly preferred due to their favorable side effect profile compared to other antidepressants.
- May help with anxiety, depression, repetitive behavior, mild aggression, irritability, social withdrawal.
- Not enough placebo-controlled trials.
- May be more “behaviorally activating” in autism spectrum disorders, causing more frequent side effects of insomnia, hyperactivity, agitation, aggression and anxiety.

Medication Treatments: Sleep Medications

- Evaluate need for changes in the sleep environment and improved sleep hygiene
- Consider whether sleep-disordered breathing may be present (overnight polysomnography).
- Behavioral interventions
- Chronotherapy
- Melatonin 1-3 mg thirty minutes before bedtime (not FDA approved). In children with ASD, 85% improved sleep with minimal adverse effects.

ASD with Bipolar Disorder

- Mood stabilizers are first line management
- Antipsychotics (second generation have serotonin and dopamine antagonism) and are preferred.
- SSRI medications helpful for anxiety, obsessive-compulsive symptoms and depression symptoms, but 54% have hypomanic or manic switches

Vannucchi, G., et al, Bipolar disorder in adults with Asperger's Syndrome: A systematic review, Journal of Affective Disorders 168 (2014) 151–160

Medication Treatment: Psychostimulants for ADHD symptoms in ASD

- IQ and gender are not a determinant of stimulant efficacy
- Effect sizes for the ASD population are somewhat smaller than the non-ASD population
- Fewer individuals in the studies are classified as 'responders' than in the non-ASD population
- Side effects are more common in the ASD population.

Antshel, K., The comorbidity of ADHD and autism spectrum disorder, *Expert Review of Neurotherapeutics*. 13.10 (Oct. 2013): p1117.

Alpha-Adrenergic Agonists

- Clonidine and Guanfacine
- Act by turning off norepinephrine release (decrease sympathetic nervous system tone)
- Wide range of uses in psychiatry—decreases impulsivity, decreases anxiety and agitation, can be sedating (sleep agent). Generally well-tolerated.
- Need to watch out for low blood pressure; can be dangerous at high doses.



Case History

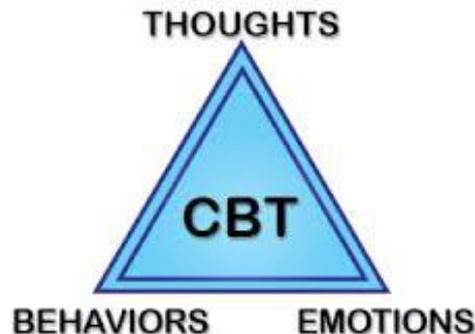
You see a 10 year old boy who has autism, mild intellectual disability and anxiety. His symptoms of anxiety are limiting his ability to participate in community activities and school. His parents do not want to use medication.

What do you tell them?



ASD and Anxiety: CBT

- Meta-analysis of 14 studies
- 14 studies involving 511 youth with high-functioning ASD
- Statistically significant pooled treatment effect for CBT with significant IQ heterogeneity.



Ung, D., A Systematic Review and Meta-Analysis of Cognitive-Behavioral Therapy for Youth with High-Functioning **Autism** Spectrum Disorders, *Child Psychiatry Hum D* 46(4):533-47, 2015 Aug.

Future Research Directions: New Experimental Treatments for Core Social Domains in ASD

- New paradigm shift in research
- NMDA Antagonists
- Oxytocin
- Insulin Growth Factor-1



Future Research Directions:

ClinicalTrials.gov

- Autologous Bone Marrow Stem Cells for Children With Autism Spectrum Disorders
- A Trial of CM-AT in Children With Autism- Open Label Extension Study
- Psychotherapy for Anxiety in Children With Autism Spectrum Disorder
- Neural Mechanisms of CBT for Anxiety in Autism
- Galantamine Versus Placebo in Childhood Autism
- Stem Cell Therapy in Autism Spectrum Disorders

Conclusions

- Psychiatric comorbidity in autism spectrum disorders is common
- Identification and treatment of psychiatric disorders and symptoms may substantially improve the overall quality of life in autism spectrum disorders.
- Psychiatric treatment should always be offered within an integrated, multi-disciplinary treatment plan

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