

USE OF PSYCHIATRIC MEDICATIONS FOR SERIOUS MENTAL HEALTH CHALLENGES

AXYS Family Conference
June 29th, 2019

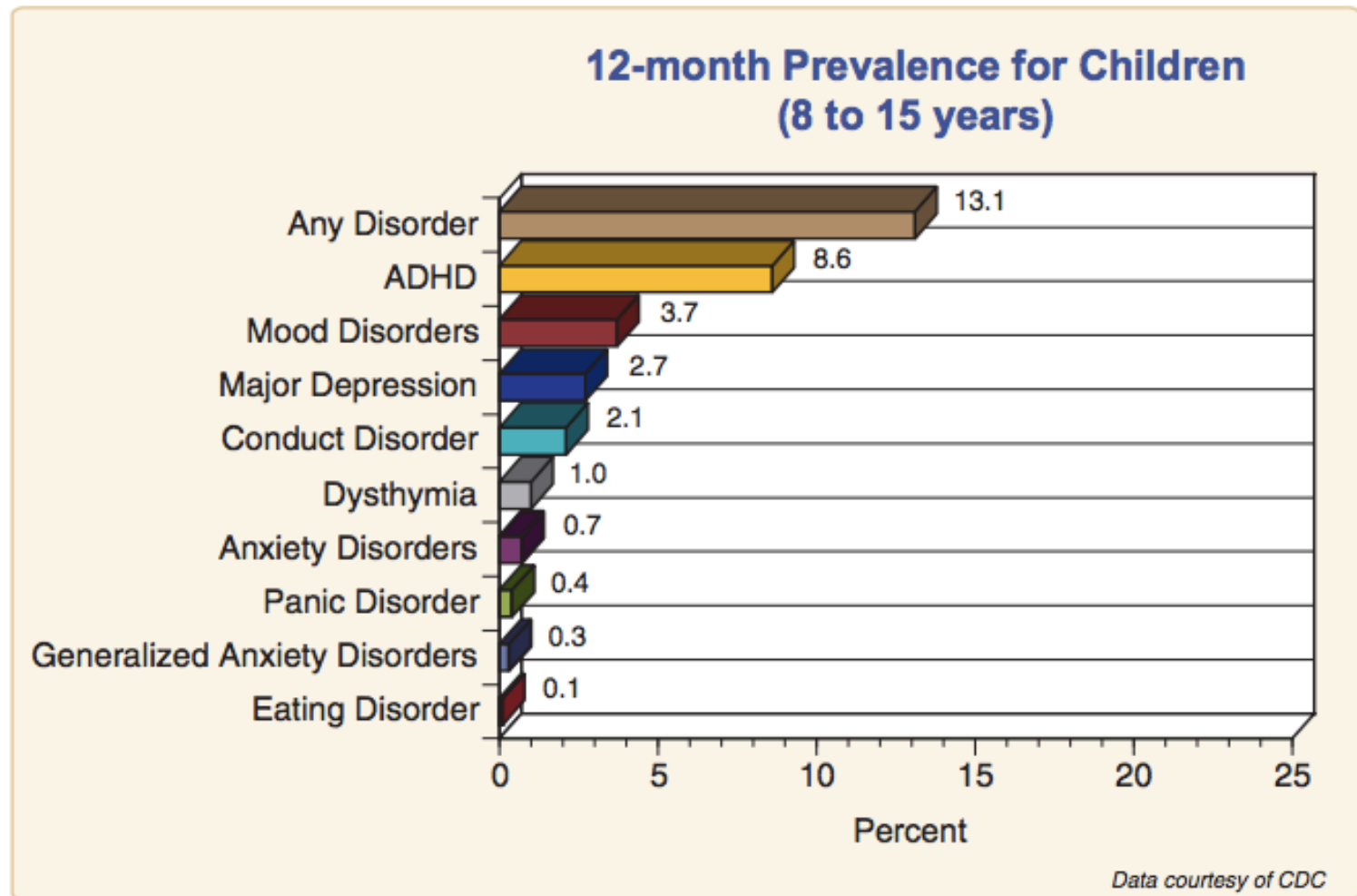
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ParentLab, Inc.

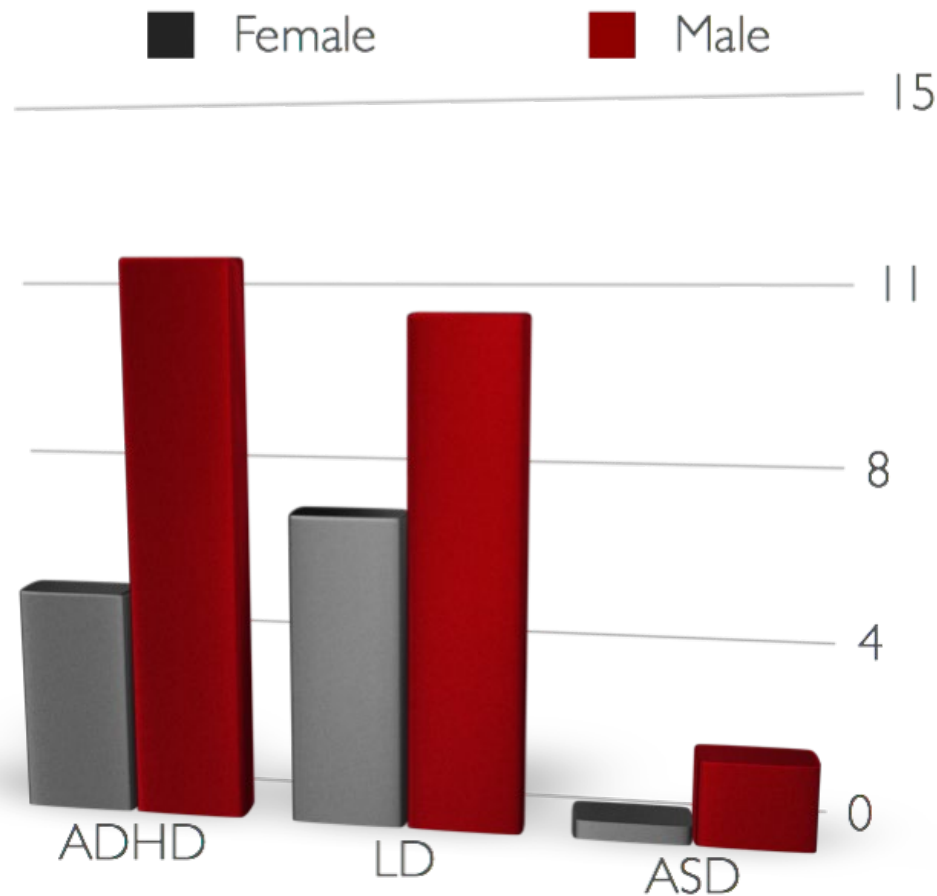
Agenda

- Gain a global understanding of psychiatric symptoms associated with X&Y variation
- Gain insight into the evaluation process for these conditions
- Get a snapshot of commonly used interventions if a diagnosis is given, which includes an overview of medications

How common are psychiatric disorders in children and adolescents in general?



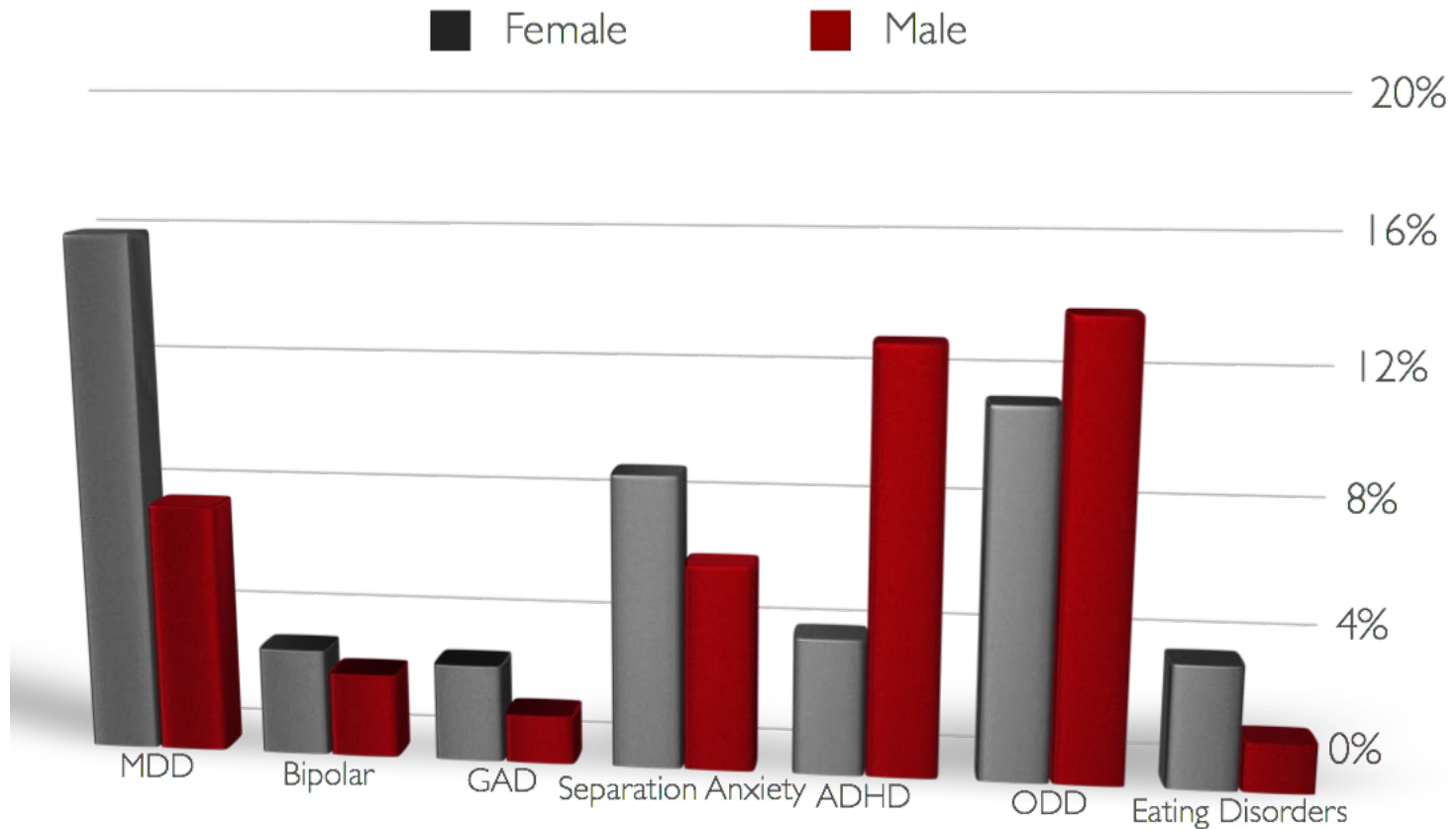
Prevalence of psychiatric disorders in childhood...



Based on data from: CDC, Vital and Health Statistics July 2008 and
CDC Surveillance Summaries March 30, 2012

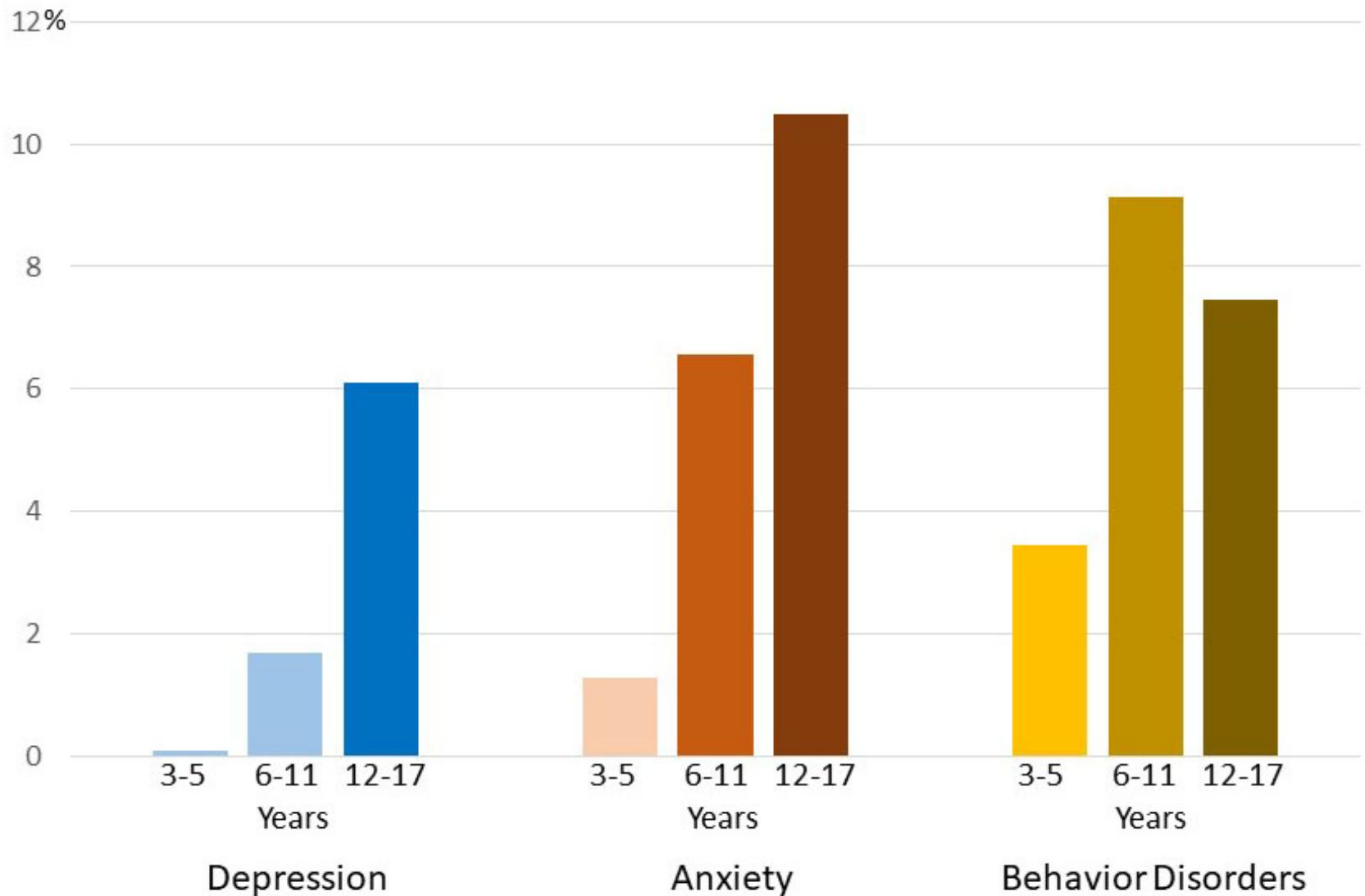
...And adolescence

Lifetime Prevalence of DSM-IV Disorders in the National Comorbidity Survey - Adolescent Supplement (NCS-A)



Based on data from: Merikangas K, et al. JAACAP 2010 49(10):980-989.

Depression, Anxiety, Behavior Disorders, by Age



Does X&Y variation posed increased risk?

Attention-Deficit Hyperactivity Disorder Symptoms in Children and Adolescents with Sex Chromosome Aneuploidy: XXY, XXX, XYY, and XXYY

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Table 2

Diagnoses Comorbid with Each Sex Chromosome Aneuploidy (Regardless of Attention-Deficit Hyperactivity Disorder Status)

Descriptive	47, XXY (n = 56), n (%)	47, XYY (n = 33), n (%)	47, XXX (n = 25), n (%)	48, XXYY (n = 53), n (%)	Significance Test
Intellectual disability	5 (9)	3 (9)	5 (20)	17 (32)	$\chi^2(3, n = 167) = 12.10^{**}$
Learning disability	35 (63)	23 (70)	14 (56)	51 (96)	$\chi^2(3, n = 167) = 21.79^{***}$
Mood or behavioral disorder	16 (29)	18 (54)	10 (40)	29 (55)	$\chi^2(3, n = 167) = 9.54^*$
Autism spectrum disorder	2 (4)	12 (36)	1 (4)	18 (34)	$\chi^2(3, n = 167) = 25.65^{***}$
Tics	6 (11)	13 (39)	5 (20)	13 (25)	$\chi^2(3, n = 167) = 10.18^*$
Seizures	3 (5)	4 (12)	6 (24)	7 (13)	$\chi^2(3, n = 167) = 5.83, ns$

ns, not significant.

* $p < .05$;

** $p < .01$;

*** $p < .001$.

Attention Deficit/Hyperactivity Disorder

Table 3

Proportion of Children Meeting DSM-IV Criteria for ADHD Subtypes Based on Parent Ratings and ADHD Symptom Counts Based on Parent and Teacher Ratings

	XXY (Parent: n = 56; Teacher: n = 27)	XYY (Parent: n = 33; Teacher: n = 12)	XXX (Parent: n = 25; Teacher: n = 10)	XXYY (Parent: n = 53; Teacher: n = 21)
Categorical data				
No ADHD diagnosis	36 (64%)	8 (24%)	12 (48%)	15 (28%)
Parent—Inattentive	19 (34%)	16 (49%)	11 (44%)	28 (53%)
Parent—Hyperactive	0	1 (3%)	0	0
Parent—Combined	1 (2%)	8 (24%)	2 (8%)	10 (19%)
Parent—any subtype	20 (36%)	25 (76%)	13 (52%)	38 (72%)

Social Cognition

[Res Dev Disabil.](#) Author manuscript; available in PMC 2013 Jul 1.

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PMCID: PMC3328784

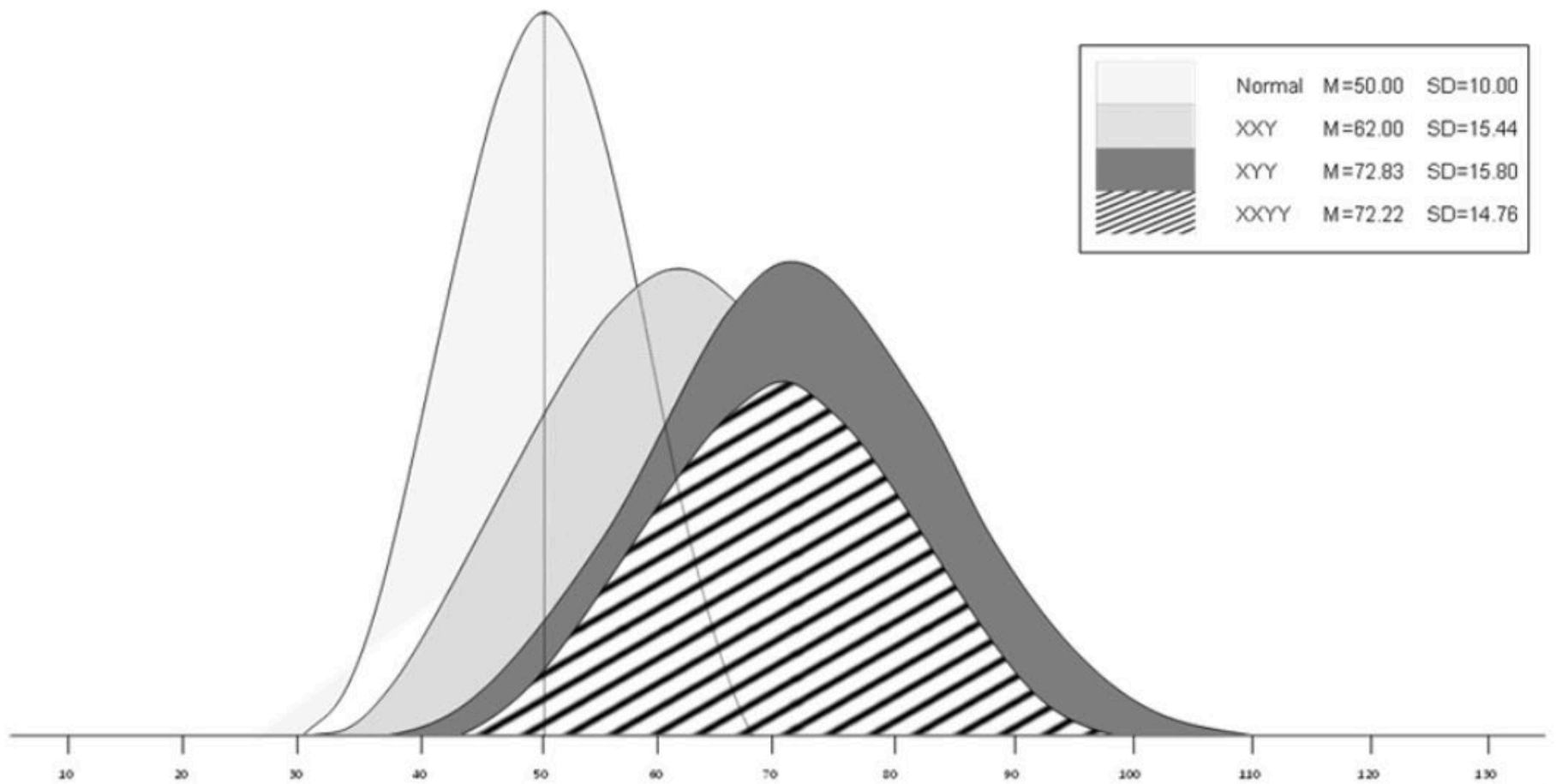
NIHMSID: NIHMS366259

Social Deficits in Male Children and Adolescents with Sex Chromosome Aneuploidy: A Comparison of XXY, XYY, and XXYY syndromes

[Lisa Cordeiro](#),^a [Nicole Tartaglia](#),^{a,b} [David Roeltgen](#),^c and [Judith Ross](#)^c

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Figure 1



Social responsiveness scale total t-score distributions in the normative sample, XXY, XYY and XXYY groups.

Clinical Phenotype

47 XXY

- **ADHD – rates of 35-55%** (Ross et al. 2012, Tartaglia 2010)
- **Dyslexia/Language-based disorders – 50-75%** (Rovet et al. 1996, Geschwind et al. 2000, Bender et al. 1986)
- **Schizophrenia – 4x increased in KS** (Cederlof et al. 2014, Bojesen et al. 2006)
- **Autism spectrum disorder – 6x risk** (Cederlof et al. 2014, Bruining et al. 2009)
- **Mood Disorders – up to 16-68% reporting depressive symptoms** (Close et al. 2015; Turiff et al. 2011)
- **Anxiety – higher proportion of elevated anxiety on parent rating scales** (van Rijn et al. 2015; Ross et al. 2012)

Clinical Diagnoses

- Are they just labels?
- What are they useful for?
- DSM-5
 - Focuses on the symptoms and not the 'cause'
- Starting point for a discussion to capture symptoms
 - Likely represent a specific slice of the overall clinical diagnostic group, but more likely reflects processes specific to sex chromosome aneuploidy
- Framework for making decisions about appropriate empirically-validated treatments



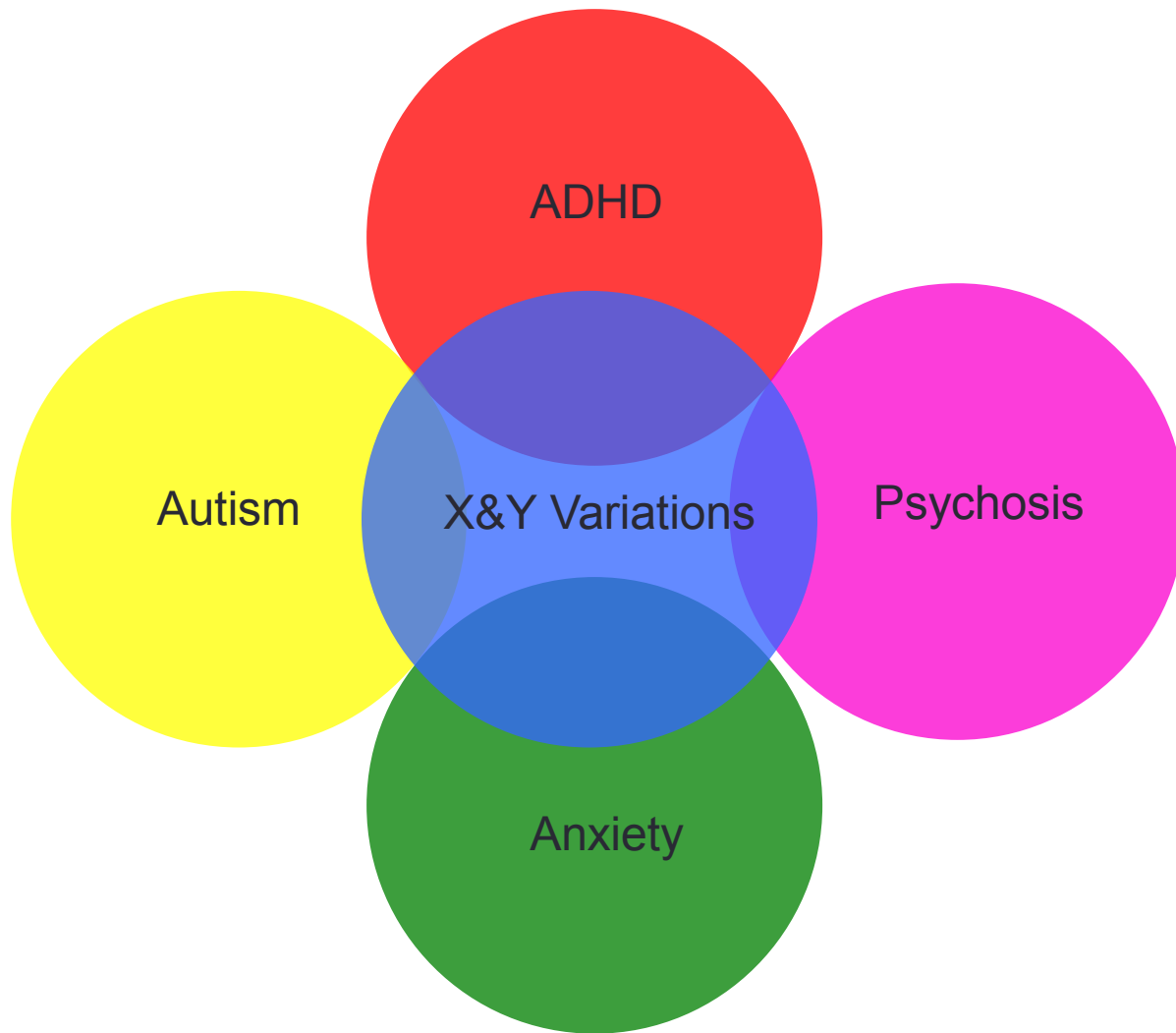
Autism

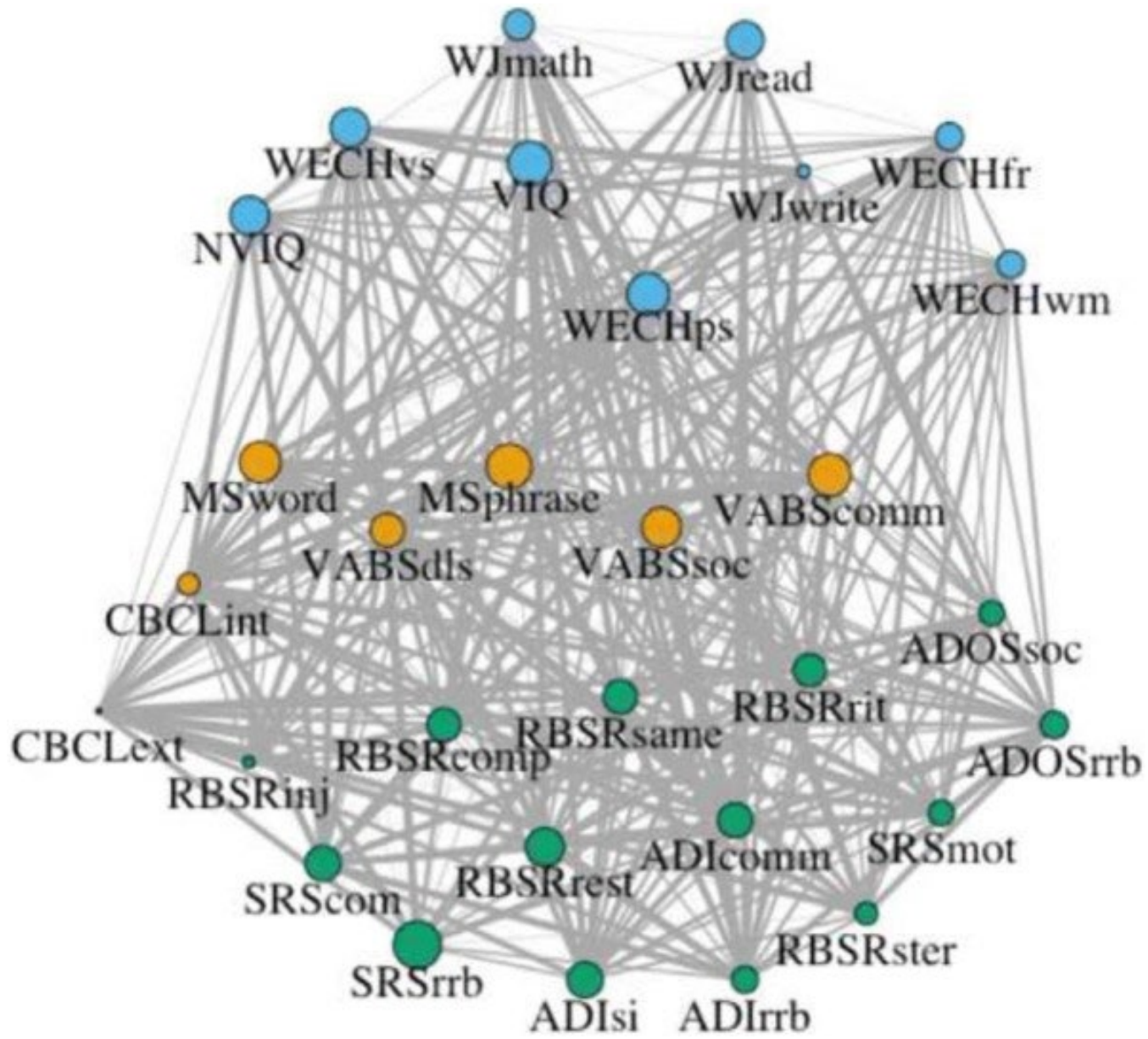
+

X&Y Variations

+

ADHD





What are some of these DSM-5 diagnoses?



Attention-Deficit/ Hyperactivity Disorder

- **Inattention:** At least 6
 - Fails to pay attention to details or makes careless mistakes.
 - Has trouble keeping attention on something.
 - Often does not seem to listen when spoken to directly.
 - Does not follow through on things and may be easily sidetracked.
 - Has trouble with organizing things or activities.
 - Dislikes or avoids tasks that take a lot of mental effort.
 - Often loses things.
 - Is often easily distracted.
 - Is often forgetful in daily activities.
- **Hyperactivity and impulsivity:** At least 6
 - Often fidgets with or taps hands or feet or squirms in seat.
 - Often gets up when staying seated is expected.
 - Often runs about or climbs in situations where it is inappropriate.
 - Often unable to play or engage in leisure activities quietly.
 - Is often “on the go,” acting as if “driven by a motor.”
 - Often talks excessively.
 - Often blurts out an answer before a question has been completed.
 - Often has difficulty waiting his or her turn.
 - Often interrupts or intrudes on others

Specific Learning Disorder

- Difficulties learning and using academic skills, for at least 6 months, despite the provision of interventions that target those difficulties:
- Relates to:
 - Word reading
 - Verbal comprehension
 - Spelling
 - Written expression
 - Calculation, number sense
- The learning difficulties begin during school-age years but may not become fully manifest until the demands for those affected academic skills exceed the individual's limited capacities (e.g., as in timed tests, reading or writing lengthy complex reports for a tight deadline, excessively heavy academic loads).
- Area where there is difficulty is should be determined. In individuals with KS, this is likely to be reading or writing

Autism Spectrum Disorder

- Problems with social communication and social interaction across multiple contexts, including:
 - difficulty with normal back-and-forth conversation, less sharing of interests and emotions than is typical, or not initiating or responding to social interactions.
 - nonverbal communicative behaviors used for social interaction, such as eye contact and body language.
 - building and maintaining typical social relationships.
- Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following:
 - Stereotyped or repetitive motor movements, use of objects, or speech
 - Inflexibility and insistence on things always being the same
 - Specific, narrow interests that are unusual or that are unusually strong
 - Over- or under-reactive to sensory input.

Social (Pragmatic) Communication Disorder

- Overall problems with the social use of verbal and nonverbal communication, including:
 - Problems communicating for social purposes, such as greeting people and sharing information, in an appropriate way for the situation.
 - Trouble changing speech based on setting or listener, such as talking differently in a classroom than on a playground or talking differently to a child than to an adult.
 - Trouble following rules for conversation and storytelling, such as taking turns or using and understanding nonverbal signals.
 - Problems inferring information that is not explicitly stated or understanding nonliteral or ambiguous meanings of language (ex., idioms, humor, metaphors).

Generalized Anxiety Disorder

- Characterized by frequent (more days than not) worrying about different things
- The individual with anxiety feels unable to control how much they worry
-
- Worrying causes an individual to experience one or more of the following:
 - Feeling on edge, restless, or worked up
 - Tiring easily
 - Trouble focusing
 - Feeling irritable
 - Muscle tension
 - Sleep problems

Social Anxiety Disorder

- Worry or anxiety about being in social situations (ex., having conversations, sharing meals, giving presentations)
 - In children, the worry must include worry about situations with peers, not just adults
- The individual fears that others will judge them, reject them, or be offended by them because of their actions or anxiety
- Social situations normally provoke anxiety and are either avoided or the anxiety and fear continues through the situation
 - Children may show their anxiety by crying, throwing tantrums, freezing, clinging, shrinking, or failing to speak in social situations.
- The fear or anxiety is much greater than would be expected for the situation and context

Psychotic Disorders

- *Delusions*: are fixed beliefs that can't be changed even when given evidence that they're wrong (e.g., persecutory, referential, somatic, religious, grandiose).
- *Hallucinations*: are experiences when someone perceives something that's not there. Can be any of the senses, but auditory are more common. Ones that happen while falling asleep/waking up aren't counted as psychotic symptoms.
- *Disorganized thinking (formal thought disorder)*: is normally determined by what the individual says, with limited coherence in thread of conversation
- *Grossly disorganized or abnormal motor behavior*: may show in many different ways, ranging from movements that seem silly to unpredictable agitation.
- *Negative symptoms* are uncommon outside of schizophrenia. They include decreased expression of emotion, decreased motivation, decreased speech, decreased happiness from positive experiences, and decreased social interest

Scenario #1

Carlos, a 19-year-old Hispanic college student, presented to a primary care clinic for help with academic difficulties. Since starting college 6 months earlier, he had done poorly on tests and been unable to manage his study schedule. His worries that he was going to flunk out of college were leading to insomnia, poor concentration, and a general sense of hopelessness. After a particularly tough week, he returned home unexpectedly, telling his family that he thought he should quit. His mother quickly brought him to the clinic that had previously helped both Carlos and his older brother. The mother specifically wondered whether Carlos's "ADHD" might be causing his problems, or whether he had outgrown it.

Carlos had been seen at the same clinic when he was age 9, at which time he had been diagnosed with attention-deficit/hyperactivity disorder (ADHD), predominantly combined type. Notes from that clinical evaluation indicated that Carlos had been in trouble at school for not following instructions, not completing homework, getting out of his seat, losing things, not waiting his turn, and not listening. He had trouble concentrating except in regard to video games, which he "could play for hours." Carlos had apparently been slow to talk, but his birth and developmental histories were otherwise normal.

Scenario #1 (cont.)

During the evaluation when Carlos was age 9, a psychoeducational assessment by a clinical psychologist confirmed reading problems (particularly problems in reading fluency and comprehension). Carlos did not, however, meet the school board criteria for learning disability, which required evidence of a 20-point discrepancy between IQ and achievement scores. Thus, he was not eligible for special education services. Carlos's primary care physician had recommended pharmacotherapy, but the mother did not want to pursue medication. Instead, she reported taking on an extra job to pay for tutors to help her son "with concentration and reading."

Carlos was referred to a psychologist for further testing. The psychoeducational reassessment confirmed that Carlos's reading and writing abilities were substantially and quantifiably below those expected for his age. That report also concluded that these learning difficulties were not attributable to intellectual disability, uncorrected visual or auditory acuity, psychosocial adversity, or lack of proficiency in the language of academic instruction. The report concluded that Carlos had specific difficulties with reading fluency and comprehension as well as spelling and written expression.

Now what?...Developmental assessment

- Routine screening
- Comprehensive evaluation of behaviors and skills
- Placed in a developmental context against expected skills for age
- Awareness of cognitive and behavioral profiles associated with X&Y chromosome variations
- Assessments should be multidisciplinary in nature

How to get an evaluation

- Many primary care doctors can help you start this process, including helping you determine the best mental health care provider to work with
- Ultimately, may need to see a mental health care provider
- Schools may be able to provide initial evaluations or referrals. This varies quite a bit between school districts, but the gold standard of assessment is through the IEP.

What to Expect: First Visit with a Mental Health Care Provider

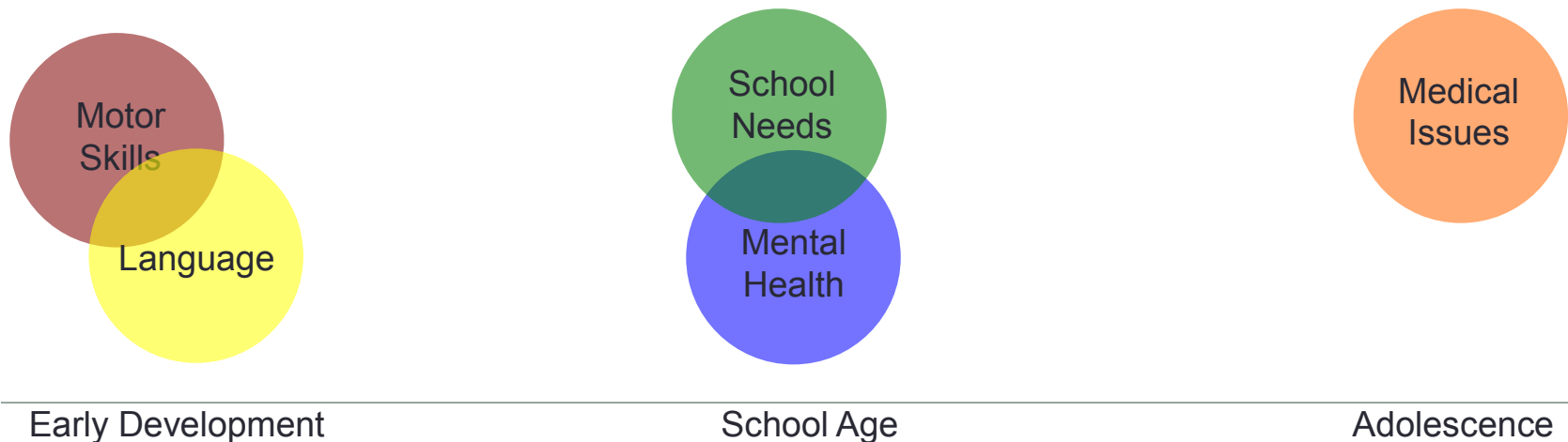
- A comprehensive clinical interview with the provider, including:
 - Questions about medical background
 - Questions about home, school, and other activities
 - Questions about family history
- Questionnaires, completed on paper or by computer
- Sometimes, formalized assessments may be done, including comprehensive neuropsychological testing
- Screening for comorbidities or underlying medical issues contributing to symptoms

Mental Health Providers 101

- MDs: If medication is needed, an MD typically needs to be involved in that decision: psychiatrists, developmental-behavioral pediatricians, pediatricians
- Psychologists: Typically cannot prescribe medications but can provide assessments, diagnosis, and therapeutic interventions.
- MFTs are trained to provide family therapy.
- LCSWs are trained to provide social work services to families.
- Other providers may be appropriate, such as psychiatric nurses and applied behavior analysts.

Multidisciplinary Treatment

- The most effective interventions often span a number of medical specialties...
- ...and non-medical specialties...
- ...and different life settings...
- ...with different needs at different points of development



Therapies

- A wide range of therapies exist and are based on different conceptualizations of mental health problems. Some examples include:
 - Behavioral, which tries to understand what causes behaviors to happen in order to change them by removing triggers and rewards.
 - Cognitive-Behavioral, which focuses on the interactions between thoughts, feeling, and actions
 - Social skills training, specific social program to develop social awareness, reciprocity
 - Psychosocial, which focuses on developmental stages
- Also:
 - Occupational and physical therapy
 - Speech Language Pathologists

Educational Interventions

- Individualized Education Plans
- Informal school accommodations
- Testing and achievement assessment
- Extracurricular assistance
- Organizational skills and executive function coaching

Medications

- May be appropriate when indicated and there are specific target symptoms to be addressed
- Limited empirical data specific to sex chromosome aneuploidies
- Follow treatment response and gauge targets and end goals
- Keep clinicians involved for long-term planning
- Treatment occurs in phases, it may be non-linear
- Be aware of alternative therapies

Treatment for ADHD

- Medications: MTA study indicates high rate of efficacy
 - First-line: Stimulants and Strattera
 - Alternate choices: Clonidine/Guanfacine
- Behavioral therapies: Parenting strategies, organizational and skills training
- School interventions
- Possible small benefit: Eliminating food dyes, omega-3 fatty acid supplementation
- Still being tested: Neurofeedback and cognitive training
- Specific to KS: Impact of testosterone replacement?
- Tartaglia et al. showed efficacy in X&Y variation: 78.6%

Treatment for Learning Disorders

- Primarily psychoeducational
 - Tutoring on learning strategies
 - Modification of learning environment
 - Accommodations around testing, assignments, seating preference
 - Assistance with scribes, tutors
 - Implementation with technology
- No indication that medications are useful
- Cognitive testing and neurofeedback also being tested

Treatment for Social Cognitive Deficits

- Behavioral therapies
 - Social skills training groups, such as SocialThinking
 - Applied Behavioral Analysis (ABA)
 - Psychosocial skills
 - Comprehensive therapy modules: Early Start Denver Model
 - Cognitive Behavioral Therapy
 - Sensory training
- Medications may be helpful for related symptoms such as:
 - Irritability
 - Self-injurious behavior
 - Rigidity
 - But do not change core symptoms – atypical antipsychotics, SSRIs
 - Some medications being trialed

Treatment for Anxiety Disorders

- Cognitive-behavioral therapy
 - First-line treatment for mild-to-moderate anxiety symptoms
 - Likely equally as effective as medications for this cohort
 - Focuses on triad of cognitions, behaviors and emotions
 - Incorporates exposure into treatment
- Medications
 - First-line treatment for severe anxiety symptoms in conjunction with CBT, i.e. CBT + meds > CBT or meds alone
 - Selective serotonin reuptake inhibitors (SSRIs), also SNRIs
 - Less common: benzodiazepines, buspirone, atypical antipsychotics, tricyclic antidepressants

Treatment for Psychosis

- Evaluation for other underlying etiologies
- Typically medications are first-line treatment
 - Atypical antipsychotics
- Therapies include: psychosocial rehabilitation, cognitive-behavioral therapy focused on reality testing

Advocacy and Case Management

- Often falls on the parent
- Need to coordinate across different systems of care
 - Clinical: psychiatry, psychology, neuropsychology, endocrinology, pediatrics
 - Schools: teachers, special educators, tutors, IEP plans
 - Ancillary services: State and federal organizations, early development programs
- Transition to adulthood and teach adolescents and young adults to manage and participate in their care

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Collaborators

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Psychiatry/Genetics

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- Tandy Aye, MD



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Scenario #2

Daphne, a 13-year-old in the ninth grade, was brought for a psychiatric evaluation because of academic and behavioral struggles. She had particular difficulty starting and completing schoolwork and following instructions, and she had received failing grades in math. When prompted to complete tasks, Daphne became argumentative and irritable. She had become increasingly resistant to attending school, asking to stay home with her mother.

Testing indicated that Daphne had above-average intelligence, age-appropriate achievement in all subjects except math, and some difficulties in spatial-visual skills. Several years earlier, her pediatrician had diagnosed attention-deficit/hyperactivity disorder (ADHD) and prescribed a stimulant. She took the medication for a week, but her parents stopped giving it to her because she seemed agitated.

At home, Daphne's parents' close supervision of her homework often led to arguments with crying and screaming. She had two long-standing friends but had made no new friends for several years. Generally, she preferred to play with girls younger than she. When her friends chose the activity or did not follow her rules, she tended to withdraw. She was generally quiet in groups and in school but bolder with family members.

Scenario #2 (cont.)

Beginning in early childhood, Daphne had had difficulty falling asleep, requiring a nightlight and parental reassurance. Recognizing that Daphne was easily upset by change, her parents rarely forced her into new activities. She did well during the summer, which she spent at a lake house with her grandparents. Her parents reported no particular traumas, stressors, or medical or developmental problems. Daphne had started her menses about 2 months prior to the evaluation. Her family history was pertinent for multiple first- and second-degree relatives with mood, anxiety, or learning disorders.

At first meeting, Daphne was shy and tense. Her eye contact was poor, and she had difficulty talking about anything other than her plastic horse collection. Within 15 minutes, she became more comfortable, revealing that she disliked school because the work was hard and the other children did not seem to care for her. She said that she was afraid of making mistakes and getting bad grades and of disappointing her teachers and parents. Preoccupation with earlier failures led to inattention and indecision. Daphne denied that she was good at anything and that any aspect of her life was going well. She wished she had more friends. As far as she could remember, she had always felt this way. These things made her sad, but she denied persistent depressive feelings or suicidal thoughts. She appeared anxious but brightened when discussing her horse figurine collection and her family.