Not Just a Checklist – Pediatric Diagnosis and Management of Autism Spectrum Disorder

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Disclosure

• Financial relationships with industry within the last 12 months:
  - None

• Off label uses:
  - Stimulant medication as a treatment for hyperactivity and disinhibition in children with autism spectrum disorder
In the DSM Era (since 1980), Rather Than a Medical Diagnosis Autism Has Become A Checklist
Diagnostic & Statistical Manual of Mental Disorders

• Published by the American Psychiatric Association
• Criteria for and inclusion of specific disorders change over time with each new publication of the DSM
• Autism did not appear in the DSM until the DSM-III in 1980
  - Criteria for autism have gotten easier to meet over time
  ➢ Prevalence of autism has increased over time
Changing DSM Criteria Over Time

• DSM-III:

“Pervasive lack of responsiveness to other people, gross deficits in language development, and bizarre responses to various aspects of the environment”
Changing DSM Criteria Over Time

• DSM-IV:

“Qualitative impairments in social interaction, qualitative impairments in communication (including delays in language development), and restricted, repetitive and stereotyped behaviors, interests, and activities”
Changing DSM Criteria Over Time

• DSM-5:

“Persistent deficits in social communication/social interaction and restricted, repetitive patterns of behavior, interests, or activities”
In the DSM Era, Rather Than a Medical Diagnosis Autism Has Become A Checklist

• DSM-IV: Pervasive Developmental Disorders (PDD)

• At least 6 of 12 items
  -2 from column A (impairment in social interaction)
  -1 from column B (impairment in communication)
  -1 from column C (repetitive/stereotypic behaviors)

• Diagnoses: Autistic Disorder, Asperger Disorder, PDD-NOS
To the DSM-5, Autism is Still a Checklist

• DSM-5:
  - 3/3 items for deficits in social communication and social interaction
  - 2/4 items for restricted, repetitive patterns of behavior, interests, or activities

• Diagnosis: Autism Spectrum Disorder
  - Specify:
    • With or without language disorder
    • With or without intellectual disability
    • Associated with known medical or genetic condition
    • Severity level: Requiring support; Requiring substantial support; Requiring very substantial support
DSM-IV: Pervasive Developmental Disorders

Developmental Language Disorder (Language-based)

Asperger Syndrome (Nonverbal-based)

SCD (Pragmatic Language Use)

Studential Language (Form and Content)

Autism

Ritualistic, Stereotypic, Repetitive Behavior

Stereotyped Behavior/Restricted Interests

DSM-5: Autism Spectrum Disorder

- **ASD & Lang D/O**
  - Structural Language (Form and Content)
  - Language Disorder
  - Social Communication (Pragmatic Language Use)
  - Social Communication Disorder

- **SCD & Lang D/O**
  - Ritualistic, Stereotypic, Repetitive Behavior
  - Stereotyped Behavior/Restricted Interests

Goal

• Understand autism as a medical diagnosis within the spectrum and continuum of pediatric developmental-behavioral disorders, NOT AS A CHECKLIST
Objectives

• Identify children with autism spectrum disorders based on their presenting developmental-behavioral profiles

• Identify evidence-based behavioral, educational, therapeutic, and medical interventions for children with autism spectrum disorders

• Describe the medical laboratory workup of children with autism spectrum disorders
AAP Developmental Screening Recommendations

• Standardized screening at well child visits at:
  - 9 months: Developmental Screening
  - 18 months: Developmental + Autism Screening (MCHAT)
  - 24 or 30 months: Developmental + Autism Screening (MCHAT)
Myth: Primary Pediatric Health Care Professionals Are Missing Most Children with Developmental Concerns

• Palfrey JS, et al (1987)*
  - Only 28.7% of children who required special educational services were identified before they reached school at 5 years of age.

  - Subsequently, perception developed that primary pediatric health care providers are to blame for missing the vast majority of children with developmental-behavioral disorders.**

  - This has led to mandated use of parent-completed developmental and behavioral screening questionnaires and an erosion of confidence in primary pediatric health care professionals’ clinical skills.**

Reality: Only Lower Prevalence, Higher Severity Developmental Disorders Can Be Reliably Identified Prior to School Age

<table>
<thead>
<tr>
<th>Developmental-Behavioral Disorder</th>
<th>Age/Grade of Reliable Identification</th>
<th>Prevalence</th>
<th>Reliably Identifiable Before School Age?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe ID (IQ &lt; 50) CP</td>
<td>1 year</td>
<td>0.4%</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4%</td>
<td></td>
</tr>
<tr>
<td>Mild ID (IQ &lt; 70) ASD</td>
<td>3 years</td>
<td>1.6-2.6%</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td>Slower Learning/Global Learning Disabilities (IQ 70-89)</td>
<td>Kindergarten to 1\textsuperscript{st} grade</td>
<td>23%</td>
<td>No</td>
</tr>
<tr>
<td>Specific Learning Disabilities/ADHD</td>
<td>1\textsuperscript{st} to 4\textsuperscript{th} grades</td>
<td>5-10%</td>
<td>No</td>
</tr>
</tbody>
</table>

• Thus, the vast majority of children with developmental concerns have milder severity conditions that **CANNOT BE RELIABLY IDENTIFIED BEFORE SCHOOL AGE!**
Is Pediatric Clinical Judgment So Bad??

• US Department of Education's goal:
  - Provide EI services to at least 2% of children < 3 years*

• In 2002: 2.2% of US children < 3 years receiving EI*

• In 2010: 2.8% of US children < 3 years receiving EI**

• In 2015: 2.95% of US children < 3 years receiving EI***
  - With 2.95% of children from 0-3 years of age being served by EI, it appears most likely that most children who can be reliably identified by 3 years of age are being identified!

AAP Algorithm for Autism Screening

- AAP recommends autism-specific screening at 18 months
  - Study of M-CHAT screening of 3793 children at 16-30 months –
    - **PPV only 0.11***
  - Study of M-CHAT screening of general population sample of 18 month olds –
    - **PPV only 0.015**

Meyer Center Faculty Developing New Autism Screener

Clinical Resource for Autism Prediction

C.R.A.P.®
## MCHAT vs CRAP®

<table>
<thead>
<tr>
<th></th>
<th>MCHAT</th>
<th>CRAP®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>Free</td>
<td>$0.25</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>0.11</td>
<td>0.015</td>
</tr>
</tbody>
</table>
Clinical Resource for Autism Prediction:

PPV = 0.015
“Evidence” for Autism Screening? (Don’t ask the USPSTF)

“The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for autism spectrum disorder (ASD) in young children for whom no concerns of ASD have been raised by their parents or a clinician.”
If Not Checklists, Then What???
Years of medical training/accumulated clinical experience & clinical judgment versus a checklist....
If Not Checklists, Then What?

• Medical Training:
  - History + Examination = Diagnosis

• Developmental-Behavioral Concerns:
  Developmental History + Neurodevelopmental Exam = Developmental Diagnosis
Medical Model of Developmental Diagnosis

• Chief complaint
  - Failed developmental screen

• Developmental history
  - Identify pattern of developmental delay (static, acute, progressive)
  - Identify delay, dissociation, deviation

• Neurodevelopmental exam
  - Confirm developmental history

• Make developmental diagnosis within the spectrum & continuum of developmental-behavioral disorders
Developmental History

• History of developmental milestone acquisition within each developmental stream

• Parents are best historians when developmental history focuses on milestones that are **memorable** and milestones that were **attained more recently**

**Functions of Developmental History:**

1. Identify pattern of developmental delay
   - Static, Acute, Progressive

2. Identify markers of atypical development
   - Delay, Dissociation, Deviation
Patterns of Developmental Delay

- Developmental Age (years)
- Chronological Age (years)
- Developmental History
- Developmental Exam

Patterns:
- Acute Encephalopathy
- Progressive Encephalopathy
- Static Encephalopathy

DQ = 100
DQ = 50

Texas Children's Hospital
Baylor College of Medicine
Developmental Delay

• Significant lag in one or more streams of development

• Most commonly represented by a more global delay affecting all streams of development
Developmental Dissociation

• Difference between developmental rates of two streams of development, with one stream significantly more delayed

• Dissociation is atypical compared to more global developmental delay
Developmental Deviation

• Deviation from the sequence of typical milestone acquisition within a stream of development

• Acquiring higher level developmental milestones before accomplishing lower level developmental milestones

• Development or behavior that is atypical at any age
Developmental Deviation

• 2 year old boy fails a developmental screen (“not talking”)

- **Gross Motor:** Walked at 1 year; ran at 18 months; just started to jump
- **Visual Perceptual/Fine Motor/Adaptive:** Intentionally released objects before 1 year and scribbled soon after 1 year. Copies strokes but not circle. Recognized all letters of the alphabet at 18 months
- **Speech/Language:** Began babbling at 1 year; currently has a 10 word vocabulary but does not use a specific “Mama” and “Dada”; Use multiword phrases by repeating phrases from videos; does not use gestured language; just started following gestured commands
Neurdevelopmental Exam

• Performed to confirm the developmental history
Developmental Diagnosis: Capute’s Triangle

Motor
- Gross Motor
- Fine Motor
- Oral Motor

Cognitive
- Language
- Nonverbal/Visual Problem Solving

Social

Adaptive

Neurobehavior
- Attention
- Activity
- All of Psychiatry

Capute’s Triangle
Key Neurodevelopmental Principles

• Spectrum of disability within each stream
  - Mild disabilities predominate over severe disabilities
  - The more severe the developmental-behavioral disability, the earlier it can be reliably identified

• Children with autism spectrum disorders are usually not noticed to behave appreciably differently from typically developing children until after 12 to 18 months of age

• Children with milder cases of autism spectrum disorders might not be reliably identified until older ages (when social demands exceed their social abilities)
Key Neurodevelopmental Principles

• **Continuum of disability across streams**
  
  • Presenting developmental complaint most often just the “tip of the iceberg”
  
  • Diffuse/global developmental-behavioral difficulties more common than dissociated/deviated development
  
  • Dissociation/deviation in one stream more commonly associated with dissociation/deviation in other streams
Key Neurodevelopmental Principles

- Delay, dissociation, and deviation reflect atypical CNS processing (connectivity)
  - The more delayed, dissociated, and deviated the development, the more atypical the development is
  - The more atypical the development is, the more atypical the behavior should be expected to be
  - The atypical neurobehavior observed in autism spectrum disorder is accompanied by atypical delayed, dissociated, and deviated cognitive development/central processing
SPECTRUM OF GLOBAL DEVELOPMENTAL DELAY

Mild Cognitive Delay/Slow Learning
DQ/IQ ≤ 89

- Behavior commensurate with cognitive abilities
- Motor skills commensurate with cognitive abilities

Increasing Delay

Global Cognitive Delay/Intellectual Disability
DQ/IQ < 70

- Behavior commensurate with cognitive abilities
- Motor skills commensurate with cognitive abilities

23% of the population

2-3% of the population
SPECTRUM OF COGNITIVE DISSOCIATION & DEVIATION

Age Appropriate Cognitive Development (Language, Social, Adaptive, Visual Problem Solving)

Dysphonic Dyslexia
VIQ = NV IQ (Difficulty with Reading Decoding)

Mixed Dyslexia

Dyslectic Dyslexia
VIQ = NV IQ (Difficulty with Reading Decoding)

Language LD
VIQ < NV IQ (Difficulty with Reading Comprehension, Math Word Problems, Written Expression, Oral Expression, Listening Comprehension)

Social Communication Disorder (& Language Disorder)

Mixed LD

Mixed Dyslexia

Dissociated Delays in Phonology

Language LD
VIQ < NV IQ (Difficulty with Reading Comprehension, Math Word Problems, Written Expression, Oral Expression, Listening Comprehension)

Dissociation in Verbal and Nonverbal Pragmatic Language + Deviation in Language & Reciprocal Social Interaction

Nonverbal LD
VIQ > NV IQ (Difficulty with Handwriting, Copying, Drawing, Right/Left Orientation, Telling Time, Written Math, Geography, Geometry)

Dissociation in Nonverbal Pragmatic Communication + Deviation in Nonverbal Skills & Reciprocal Social Interaction

Social Communication Disorder (with a language disorder)

Dysphonetic Dyslexia
VIQ = NV IQ (Difficulty with Reading Decoding)

1.7%

5-10%

Dissociated Delays in Orthography

Dissociated Delays in More Diffuse Aspects of Language (Phonology, Morphology, Syntax, and/or Semantics)

Dissociated Delays in More Diffuse Aspects of Nonverbal/Visual Problem Solving Development

Social Communication Disorder (without a language disorder)

Dyseidetic Dyslexia
VIQ = NV IQ (Difficulty with Reading Decoding)

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Dissociated Delays in More Diffuse Aspects of Nonverbal/Visual Problem Solving Development

Social Communication Disorder (without a language disorder)
SPECTRUM OF NEUROBEHAVIORAL DISSOCIATION & DEVIATION

Age Appropriate Neurobehavior

- Dissociation

Inattention

- Deviation

Excessive Motor Activity/Hyperactivity

- Dissociation

- Deviation

Atypical Attention:
- Lack of Sustained Eye Contact
- Perseveration/ Repetitive Play/Restricted Interests/Need for Routine
- Overfocus or Lack of Attention to Sensory Input (Sensory Hypo/Hyper responsiveness)

Atypical Excessive Motor Activity
- Stereotypic Motor Activity

1.7%

5-10%
CONTINUUM OF COGNITIVE & NEUROBEHAVIORAL DISSOCIATION AND DEVIATION

Age Appropriate Cognitive Development

Age Appropriate Neurobehavioral Development

Dissociation

Learning Disability

Inattention

Excessive Motor Activity (ADHD)

↑Dissociation & Deviation

“Minimal Brain Dysfunction”/“MBD”

Severe

Autism Spectrum Disorder/ASD

Social Communication Disorder

Atypical Attention:
- Lack of Sustained Eye Contact
- Perseveration/ Repetitive Play/Restricted Interests/Need for Routine
- Overfocus or Lack of Attention to Sensory Input (sensory hypo/hyper responsiveness)

Atypical Excessive Motor Activity:
- Stereotypic Motor Activity

Mild

“Minimal Brain Dysfunction”/“MBD”

Autism Spectrum Disorder/ASD
Early Intervention/Special Education


Early Intervention

• Refer to EI as soon as a diagnosis of autism is suspected

• Services should include intensive direct and consultative language, behavioral, and social skills interventions

• Provide a minimum of 25 hours per week
  - Individualized
  - Highly structured
  - Systematically planned
  - Developmentally appropriate
Early Intervention

• Priorities of focus:
  - Functional spontaneous communication
  - Social instruction delivered throughout the day in various settings (typical peers, home)
  - Cognitive development
  - Play skills
  - Proactive approaches to atypical and challenging behaviors.

• Generalization and maintenance of newly learned skills in natural environments as important as the acquisition of new skills.
Evidence-Based Intervention

• Applied Behavioral Analysis (ABA)
  - Strongest empirical support in the published, peer-reviewed research literature
  - Method to teach, reinforce, and maintain new skills and desirable behaviors
  - Method to extinguish problematic maladaptive behaviors (self-injury; aggression)
Other Educational/Therapeutic Interventions

• Developmental models
  - Focus on remediation of fundamental deficits in pivotal developmental skills
  - Early Start Denver Model: Developmental + ABA techniques

• Structured teaching (TEACCH)
  - Focus on improving skills and modifying environment to accommodate deficits
  - Emphasis on visual schedules, physical/task organization
Other Educational/Therapeutic Interventions

• Social Skills Instruction (e.g. “Social Stories”)
  - Address initiating social interactions, responding to social overtures, minimizing stereotyped behavior

• Speech and Language Therapy
  - Goal to promote verbal and nonverbal communication
  - Augmentative communication/PECS
Other Educational/Therapeutic Interventions

• Occupational Therapy
  - Address associated fine motor deficits and delays in activities of daily living
  - No evidence for “sensory integration therapy” (See AAP Policy Statement June 2012)

• Physical Therapy
  - Address associated gross motor deficits
Response to Intervention

• Outcomes extremely variable
  - Up to 25% may no longer meet criteria for ASD*
  - Others show very slow gains

• Possible predictors of improved outcomes
  - Higher IQ/Receptive language
  - Better imitation skills
  - Milder autism symptoms
  - Increased intensity of early behavioral interventions

Why Consider Laboratory Testing to Establish a Medical Diagnosis?

• Peace of mind for families in knowing cause of developmental difficulties

• Prevent other associated medical problems

• Provide specific genetic counseling for families

• Eliminate need for further unnecessary (standard and nonstandard) testing
Etiologic and Descriptive Diagnoses for Developmental-Behavioral Disorders

**Etiologic Diagnosis**

**NEUROBIOLOGIC FACTORS**
- Genetics/Epigenetics
- Prematurity
- Structural Brain Anomalies
- Metabolic
- Toxic
- Hypoxic-Ischemic
- Infectious/Inflammatory
- Traumatic Brain Injury

**ENVIRONMENTAL EXPERIENCES**
- Developmental Stimulation
- “Toxic Stress”
- Abuse/Neglect
- Caregiver Mental Illness
- Exposure to Violence
- Family Economic Hardship

**Developmental Brain Dysfunction**

**Descriptive Diagnosis**
- Spectrum/Continuum of Developmental-Behavioral Disorders
- Intellectual Disability
- Autism Spectrum Disorder
- Cerebral Palsy
- Learning Disability
- AD/HD
- Dysgraphia/Dyspraxia

**Capute’s Triangle**

- Motor Impairment
- Cognitive Impairment
- Neurobehavioral Impairment
Medical Workup

• Consider in all children with autism spectrum disorders
  - Audiology assessment
  - Fragile X DNA analysis
  - Chromosome microarray analysis
Medical Workup To Consider with Specific Indications

• Neurocutaneous findings: Tuberous Sclerosis, NF1 (MRI)
• Cleft palate, toe syndactyly: SLO (↑7-dehydrocholesterol)
• Marked macrocephaly, skin hamartomas: PTEN hamartoma syndromes
• Deceleration of head growth, hand wringing: Rett (MECP2)
• Progressive pattern of developmental delay, decompensation with mild illness, failure to thrive, hypotonia, hypertonia, ataxia, nystagmus, epilepsy, severe/profound intellectual disability, macrocephaly, coarse facial features, hepatosplenomegaly: Metabolic studies
• Isolated language regression; Concern about seizures (20-35%): EEG
• Mouthing non-food items/pica: Lead, iron, zinc
Medical Conditions That May Exacerbate Maladaptive Behaviors*

- GI: constipation, esophagitis
- Sleep disorders
- Anxiety/depression
- Malnutrition/side effects of dietary supplements
- Allergies: atopic dermatitis, conjunctivitis
- Headaches
- Corneal abrasion
- Dental: abscess, caries, impaction, trauma
- ID: OM, otitis externa, pharyngitis
- Sprains, occult fractures

Psychopharmacology

• Risperidone /Aripiprazole
  - Only meds with FDA-approved labeling specific to autism (Risperidone > 5 yr and Aripiprazole > 6 years)
  - For treatment of irritability, including aggressive behavior, deliberate self injury, and temper tantrums

• Hyperactivity/impulsivity*
  - Methylphenidate

Psychopharmacology

• Psychotropic meds for children with ASD typically not as effective compared to treating same target behaviors in children without ASD
  
  - Fewer with positive response
  
  - Decreased magnitude of positive response
  
  - More side effects

• “Start low, go slow”
Unproven Therapies

- Dietary/vitamin supplements
- Restrictive diets
- Chelating agents
- Facilitated Communication
- Auditory Integration Therapy
- Music Therapy
- Sensory Integration Therapy
- Swimming with dolphins
- Antifungals, antivirals, antibiotics
- IVIG
- Craniosacral therapy
- Hyperbaric oxygen
- Interactive metronome
- Transcranial magnetic stimulation
- Secretin
Unproven Therapies

• Take advantage of:
  - Lack of evidence-based biomedical treatments for neurodevelopmental disabilities
  - Desire to “do something”
  - Natural course of neurodevelopmental disabilities
  - Waxing & waning course of behavioral problems
  - Cognitive Dissonance
  - Placebo Effect

• Need for randomized, double-blind, placebo-controlled trials, just like for any other medical treatment
“Keeping an open mind is a virtue – but not so open that your brains fall out”

Potential Harm of Nonstandard Therapies

• Side effects
  - Including death (chelation)

• Financial Cost
  - Not covered by insurance

• Time Cost
  - Lost family time
  - Time away from evidence-based interventions

• Emotional Cost
  - False Hope
  - Parental Guilt
Conclusions

• Autism spectrum disorder is a developmental diagnosis within the spectrum of developmental disabilities, not a simple checklist

• Children with autism spectrum disorder most commonly present with an atypical developmental profile (dissociated delays and deviation)

  • Atypical development (dissociation/deviation) is usually accompanied by atypical behavior
Conclusions

• Early intervention should begin as soon as autism is even suspected

• Medical Workup: Audiology evaluation, DNA for Fragile X, CMA should be considered in all children with ASD

• ABA has most evidence in treatment of ASD

• Beware of non-evidence based interventions that may take advantage of desperate parents who would try anything to help their children