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Autism: Beyond Behavior

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Pervasive Developmental Disorder (PDD; as defined by DSM-IV)

- Autism
- Asperger's Syndrome
- Rett Syndrome
- Childhood Disintegrative Disorder
- PDD - not otherwise specified (PDD-NOS)

AUTISM

Definition (DSM-IV):

- Impaired social interaction
- Delayed and disordered language
- Markedly restricted repertoire of activities and interests

Features in young children:

- Lack of joint attention
- Lack of pointing response
- Impaired imaginary/symbolic play

Preliminary Infant Observations

- The socially serious baby
- Reduced social reciprocity
- Limited babbling/vocalizations
- Atypical motor patterns
- Abnormal response to maternal "still face"
- "Is this baby like the last one?"
- Head lag

Autism (Inconsistent Features)

- Atypical prosody (intonation, rate, rhythm, stress)
- Echolalia; scripted phrases; pronoun reversals
- Repetitive & stereotypic behaviors
- Insistence on sameness
- Odd responses to sensory stimuli

Autism (Statistical Data)

- Onset of symptoms before 36 months of age
- Males > females by 4-5:1
- Prevalence: literature suggests rates of 2-5/10,000
- New data suggests rates of 13/10,000 (Bryson et al., 1988)
- Seizures may develop in 25-33% of affected ind.
- 70-75% are said to function in the mentally retarded range
- High incidence of non-right handers

POSSIBLE CAUSES OF AUTISM

- Multifactorial
- Genetic
- Viral
- Environmental factors

What is the definition of “Behavior”?

- The manner in which an organism behaves in response to social stimuli or inner need.
- Observable activity in response to an external or internal stimulus
- Anything that the organism does that involves action or reaction to stimulation.

What do we know?

- Research indicates that typically developing children often show elevated rates of problem behavior in association with physical illness.
- Physical illnesses are common in persons with developmental disabilities.
- Studies have documented significantly higher rates of acute and chronic medical conditions in developmentally disabled persons than in the general population.

What medical conditions have been documented?

- Problem behaviors have been linked to conditions such as constipation, allergies, premenstrual syndrome, ear infections, urinary tract infections.
- Plausible explanation relates to the degree of discomfort or pain that the individual experiences at the time rather than to the physical illness per se.

Monitoring pain & Discomfort in the DD population is a complex process.

- DD persons often lack the communication and cognitive skills to allow for direct assessment of pain using a patient scale, checklist and/or interview strategies.
- Recent data suggests that those with the most severe cognitive impairment and fewest communication skills are likely to experience the most pain over time (Breau et al., 2003).

Neurological Assessments of the Child with Autism

1. Obtain a medical and developmental history
2. Neurological examination and behavioral observation
3. Consider need for additional studies:
 - a. Chromosomal/DNA analysis
 - b. Electroencephalogram (EEG)
 - c. Imaging studies (MRI, CT)
 - d. Metabolic (blood/urine) studies

What have we been missing?

- ASD is more than a disorder of information processing, language and behavior.
- ASD children, adolescents and adults can and often do have medical issues that have largely gone unrecognized and unaddressed.

Why have these been overlooked?

- 1) Longstanding, deep-seeded assumptions about what autism is and who ASD persons are.
- 2) ASD individuals do not present with the same symptoms or “red flags” as their “neurotypical” peers.
- 3) Many ASD persons cannot tell us if they hurt/are uncomfortable nor accurately localize the discomfort.

Associated Medical Concerns?

Seizures
Sleep disturbances -
Allergies
Gastrointestinal disorders
Genitourinary
Hormonal imbalance/endocrine dysfunction
Metabolic Disorders

Associated Medical Conditions (cont)

- Endocrine dysfunction (diabetes)
- Immune system (PANDAS)
- Infections (Lyme Disease)
- Headaches (Migraine)
- Osteoporosis
- Dental Disorders
- Psychiatric disorders (anxiety, depression)

Seizures - are they real?

- Often hard to tell - presentation may be atypical
- Routine EEG may not be helpful
- More prolonged EEG by high quality lab may help - the study is only as good as the person who interprets it.
- Use of video monitoring
- Use of video taping

Epilepsy in Autism

- Cumulative incidence: 25-33%
- Olsson, Steffenburg, & Gilberg: 20% (n=52)
- Volkmar & Nelson: 21% (n=196)
- Tuchman, Rapin & Shinner: 14% (43/302)
- Wong: 7.6% infantile autism; 5% ASD (n=246)
- Rossi et al: 23.6% (n=106)
- Aman et al: 19.2% (n=1595)
- Tuchman & Rapin: 11% (n=585)

Seizure Types in Autism

- Complex Partial Seizures (10/14 Olsson et al)
- Generalized tonic/clonic seizures
- Febrile seizures
- Infantile spasms
- Tonic seizures
- Myoclonic seizures

Autism: Seizures in Adolescence

- Volkmar & Nelson: Two peaks - the highest incidence of onset was in infancy, with a second peak in adolescence
- Rossi et al: 66.7% had seizure onset after the age of 12 years.

EEG abnormalities in Autism

- Minshew review: 32-45% incidence
- White, De Meyer and De Meyer: EEG abnormalities in 58%, epilepsy in 19%
- Small (1975): EEG abnormalities in 65%; related to number of EEGs done: one EEG-40%, two EEGs -60%; three EEGs - 80%
- Rossi et al: 18.9%

Seizures: Persistent Recurring Stereotyped Episodes

- 30% ASD will have seizures by age 20 years
- Predisposition for those with low IQ, dysmorphic features, motor impairment
- Long list of syndromes associated with MR, seizures and autism
- Co-occurrence of autism and seizures - probably reflects a shared biology

Syndromes: Epilepsy & Autism

- Chromosomal disorders
- Encephalitis
- Tumors
- Hydrocephalus
- Tuberous sclerosis
- Lennox-Gastaut Syndrome
- Landau Kleffner Syndrome
- Rett syndrome

Risk Factors for Seizures in ASD and seizure rate

- No risk except ASD - 6%
- Severe MR, some motor deficit - 25%
- Severe MR and severe motor deficits - 42%
- Verbal auditory agnosia without MR - 41%

Seizures or Not?

- Abnormal EEGs exceed seizure occurrence
- Medication trials should only come after clinical conviction.
- Many psychotropic medications can make seizures worse.
- Video tapes, reports of teachers and therapists can be helpful.

Sleep Disorders

- Problems with sleep onset or staying asleep
- Is this coming from the brain (centers of arousal)?
- Is this due to GI disorder? Acid reflux?
- Is this a respiratory problem? Does the child mouth breath suggesting big tonsils/adenoids?
- Sensory integration issues - needs deep pressure?
- Allergies?

Sleep Disordered Breathing in Non-ASD Preschoolers

- Neurobehavioral issues:
 - Hyperactive/inattentive
 - Daytime tiredness/sleepiness
 - Emotional/social problems
 - Behavioral issues significantly associated with snoring
 - Significant improvement with cessation of snoring

» Urschultz et al, Ped. 2004; 114:1041-48

Sleep Disordered Breathing in Typical Preschoolers

- Snoring/difficulty breathing - 5-12%
- Waking during the night - 16-25%
- Difficulty getting to sleep - about 9%
- Seems tired in the morning - about 1%

Sleep Disordered Breathing (SDB) in Non-ASD School Age (8-11 yrs)

- Obstructive sleep apnea - 5%
- Primary snoring - 15%
- Neither - 80%
- SDB associated with significant increase in hyperactivity, emotional lability, oppositional behavior, aggression, somatic complaints, antisocial behaviors. (Rosen et al. Ped. 2004; 114:1640-48.

Polysomnography in ASD Ages 3- 9 years

Disorders of REM sleep

- Obstructive sleep apnea
- Periodic limb movements of sleep (restless leg syndrome)
- Seizures
- Bruxism

– Thirumalai et al. J Child Neurol. 2002; 17:173-178.

Gastrointestinal Disorders signs and symptoms

- Chronic diarrhea or constipation
- Feeding/eating disorder/GE reflux
- Change in sleep patterns
- Concerns about food allergies, special diet
- Possible abdominal pain/discomfort
- Behavioral changes or increased severity.
- Difficulty with toilet training

Behavioral Signs of GI Issues

- Increase in any negative behavior
- Increased anxiety
- Increased aggression
- Presence of or increase in self-injurious behavior
- Pressing on abdomen, or pressing abdomen against anything firm
- Sleep disturbances.

Causes of Gastrointestinal Disorders

- Lactose intolerance - maybe familial, follow flu or antibiotic use
- Gastric/esophageal ulcers, reflux irritation
- Colitis
- Celiac Disease
- Crohn's Disease
- Poor diet/ limited nutritional intake.
- Food sensitivities, allergies
- Side effects of some medications - including OTCs (Mg, CoQ)

Other Mechanisms of GI Disorders

- Genes that code for brain development may also code for GI function and maintenance (MET gene)
- Every neurotransmitter in the brain is also found in the gut: GABA, dopamine, acetylcholine, serotonin. All affect GI motility and sensitivity. All involved in autism
- Psychotropic medication may affect neurotransmitter levels.
- Unknown.

Endocrine/Hormonal Disorders

- ASD girls whose behavior worsens with onset or during adolescence.
- Small subset with Congenital Adrenal Hyperplasia
- Should we also be looking at teenage ASD boys?

ASD/Puberty Related Issues

- Males:
 - Increased testosterone production
 - Secondary sex characteristics
 - Physical growth
 - Possibility of increased aggression
 - Brain growth

ASD Females

- Worsening of behavior during puberty
- Increased behaviors associated with menstrual cycle. Appear to be associated with dysregulation of estrogen and progesterone levels (Herzog)
- Behaviors may be related to PMS and menstrual discomfort.
- Small subset found to have congenital adrenal hyperplasia

Reason for GU referral

- Previously continent child becomes incontinent
- Usually a preteen
- May be a “spastic bladder”
- Treatment with Ditropan may be helpful

Bladder Control

Consider urinary tract infection
Consider structural urinary tract abnormality
Possible renal disorder/dysfunction

Allergies and ASD

Allergies occur in about 20% pediatric population
– Do ASD children have more allergies than NTs?

Allergic rhinitis, asthma, atopic skin disease/eczema
Food and environmental allergies
Need to be diagnosed and treated vigorously
Referral Pediatric allergist may be indicated.

Infection and ASD

- Always keep high index of suspicion
 - Consider untreated URI - may be acute or chronic
 - Otitis media
 - Sinusitis
 - Untreated Group A Streptococcal tonsillitis
- UTI
Aggressively diagnose and treat
Problem: underserved population

Group A-Beta Hemolytic Strep (GABHS) Tonsillopharyngitis (TP)

- School-aged children
- Sore throat, fever, headache, abdominal pain - all hard to diagnosis in ASD
- Winter and spring months
- Diagnosis confirmed by throat culture
- Treatment: antibiotics
- Course: ST illness self-limited, resolved in about 5 days

GABHS

- Diagnosis: serum antibodies, ASO titer, Anti-DNase B
 - In some cases, AB production leads to end-organ damage. AB cross-react with:
 - Kidney - glomerulonephritis (10 days)
 - Heart - rheumatic fever (18 days)
 - Brain - Sydenham's Chorea (months later)
- Diagnosis dependent on elevated titers of Strep antibody
Only one required.

Pediatric Autoimmune Neuropsychiatric Disorder with GABHS (PANDAS)

- Pediatric onset
- Neuropsychiatric disorder (OCD) +/- Tic disorder
- Abrupt onset, relapsing/remitting course.
- Association with GABHS and symptoms
- Associated with motoric hyperactivity, adventitious movements, tics, clumsiness, choreiform movements
- Controversial Pediatric Concept.

PANDAS: Proposed Etiology

- Post-GABHS autoimmunity (i.e. Sydenham's)
- GABHS infection in susceptible host incites AB to GABHS. AB cross reacts with cellular components of basal ganglia (bg), interacts with bg neurons, results in neuropsych symptoms.
- Controversial hypothesis but positive MRI - inflammation of thalami and bg.
- Anti-bg antibodies found in some acute cases.

How to diagnose PANDAS

- History
- Physical Exam
- Evidence of GABHS infections
 - Throat swab for rapid antigen-detection assay
 - Throat culture
 - GABHS antibody titers - ASO, Anti-Dnase B, Anti-neuronal antibodies

– Swedo et al, Am J. Psychiatry 1998; 155:264-271

Lyme Disease - hard to recognize in ASD

- Caused by tick-borne spirochete *Borrelia burgdorferi*
- Can induce cognitive deficits when CNS involved.
- Involve memory, verbal fluency and psychomotor performance.
- Treatment - 4 weeks of ceftriaxone.
- Use of longer term antibiotic controversial.

Genetic “Red Flags”

- Multiple minor/major physical anomalies
- Unusual skin findings, suggesting chromosomal or genetic disorder
- Failure to thrive
- Multiplex family (2 or more affected members)

- Refer to Geneticist. Obtain genetic studies.

“Red Flags” for Metabolic Work-up

- Poor physical endurance
- Late walking (i.e. 24 months)
- Repeated regressions after age 2 1/2 years
- Dysmorphic features
- Making poor progress despite excellent services
- Qualitatively “different”
- Involvement of multiple organ systems

Metabolic “red flags” (cont)

- Unusual odor
- Spells of vomiting
- Lethargy
- Organomegaly
- Coarse facial features, joint contractures
- Progressive hearing loss
- Deteriorating neurologic/developmental status

Bullets

- Children, adolescents and adults with autism need and deserve appropriate medical care.
- ASD individuals may not present with typical symptoms.
- Unexplained changes in behavior or prolonged episodes of behavioral abnormalities merit a closer medical look.
- Many of these disorders are treatable.

The Autism Treatment Network (ATN)

- Began in the fall of 2003. Modeled after LADDERS program in Boston.
- Originally consisted of five academic sites
 - U. Wash (Seattle), Baylor, Columbia, OHSU, MGH
- Involves multidisciplinary medical teams
- Involves the use of common protocols.
- Commitment to data sharing across/between sites.

Why a consortium?

- Evaluate potential “red flags” in differing populations - are they valid?
- Are there other “red flags” as yet to be identified?
- What proportion of the ASD population affected?
- Accurate identification of medical disorders.
- What interventions are most effective?
- Establish scientifically sound and meaningful standards of care.

Why is this Initiative Important?

- Improve quality of life.
- If ASD persons feel better, they can take better advantage of the services/therapies provided.
- Subsets of ASD persons may be more specifically identified - genetically and metabolically
- Understanding associated medical conditions could enhance our understanding of the neurobiology of ASD.

Where are we now?

- There is a growing consensus that ASD is a multi-system disorder.
- In January 2007, Autism Speaks initiated a Request for Proposals - to expand the ATN
- As a result, there are now 15 multidisciplinary medical ATN sites associated with academic centers in the USA and Canada. Centers met in LA in January 2008.
- Sites will provide high quality medical evaluation and care for ASD persons, share protocols and submit data into a common database.

Other interventions - who else should be involved?

- Parents
- Teachers
- Therapists
- Schools
- Psychopharmacologists
- Other medical specialities as needed
- Technology

Programmatic Models

- Behavioral Models - (Applied Behavioral Analysis) - ABA, Pivotal Response Training, Lovaas, Discrete Trial Training
- Developmental Models - (TEACCH; Floor Time/DIR, Social Stories, Sensory Integration)
- Eclectic Models - "Work Bench", "Tool Belt"

Models for Intervention

- Early childhood:
 - Home based program and/or center based program
 - Behavioral and language based curriculum
- Elementary school years:
 - Inclusion/integration
 - Self-contained class in public school
 - Private day or residential school
 - Need for home based component
 - Social skills program/curriculum

Models for Intervention

- Adolescent and adulthood:
 - Life skills
 - Academic curriculum - with modification
 - Vocational training
 - Future planning - group home, supervised apartment, independent living
 - Financial planning for the future

Intervention Strategies

- Educational Programs
- Occupational Therapy
- Speech and Language Therapy
- Counseling (individual and/or Group)
- Social Skills training
- Behavior Therapy
- Psychopharmacology
- Parental/Family Counseling
- Genetic Counseling

Alternative Means of Communication

- PECS
- Sign language
- Assistive technology
 - Autistic individuals tend to be strong visual learners
 - Many devices available for communication
 - Use of computers for educational purposes - touch screens

Universal Best Practice Features

- Earliest diagnosis & implementation of effective intervention
- Program to child's specific needs
- Highly structured skilled teaching and treatment programs
- Frequent reassessment and systematic data-based tracking of skill growth, and related plan review
- Individual motivational strategies & systems

Best Practices (continued)

- Teaching sites are structured, organized and distraction-free
- Intensive 1:1 and small group sessions
- Time spent waiting is minimal
- Consistency of methodology across sites to promote generalization
- Well-trained, experienced personnel. Ongoing staff training and skill evaluation

Best Practices (continued)

- Comprehensive home-programming and parent training within a team approach
- Five day, full day, full year services beginning in preschool years through adulthood if/as needed.

Pharmacological Intervention

- Approach to the question of medication management:
 - Identify target symptoms/behaviors of concern
 - Consider the risk and benefits of choosing medications

Psychopharmacology

- Adjunct to other interventions
- Evidence of depression, anxiety, distractibility, OCD
- Out of control behaviors - assuming medical causes have been ruled out.

Pharmacological Intervention

- Choosing a medication:
 - Choice of provider may influence which medication is chosen
 - Insurance coverage may influence choice
 - Consider medical risks, cost to patient, target symptoms, need for invasive procedures (blood work), method of administration, tolerance of side effects.
- Crucial that family finds a psychopharmacologist with whom they are comfortable

Controversial Therapeutic Approaches

- | | |
|---------------------------------|-------------------------------------|
| • Allergies and yeast | •Gluten and casein free diet |
| • Applied behavior analysis | •Immune therapy |
| • Auditory integration training | •Secretin |
| • Facilitated communication | •Sensory integration therapy |
| • Fast ForWord | •Vitamin/dietary supplement therapy |
| • Floor therapy (Greenspan) | |
| • Chelation | |
| • Hyperbaric oxygen | |