Neurological Evaluation of Autism

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Regular Questions About Autism

- What regular screening tests should doctors do?
- If Autism is suspected, what other tests should be done?
- If Autism is suspected or diagnosed, what can be done to help your child?
- What does Autism mean for your child's future?

Objectives

1. Identify different types of Neurological studies.
2. Understand different causes of Autism.
3. Understand what benefits a child with Autism may have from certain types of Neurologic studies.

Neurological Studies

- What are all of the Neurodiagnostic studies that can be done in a child with diagnosed or suspected Autism?
- What is the standard evaluation a child with Autism should have?
- When are other test indicated?

My Approach

- Common things are common.
- What are disorders that can be identified.
  - Example: Down's Syndrome
- What are disorders that can treat be treated.
  - Example: Biotinidase Deficiency
- What disorders may progressively get worse.
  - Example: Lead
- What are the guidelines, standards of practice.
  - Child Neurology Society.
- What are common comorbid (associated) conditions.

Neurologic Studies

- EEG
- EMG
- BAERS
- Sleep Study
- Neuroimaging
- Laboratory Studies
- Psychological / Psychometric Testing
- Other
  - PET, SPECT, MEG

Concept

To understand what the Neurologic evaluation of Autism entails, I need to provide insight into:

1. Causes of Autism.
2. Disorders that may mimic Autism.
3. Comorbid (Associated) Neurologic conditions seen with Autism.

Neurodevelopmental Disability

- How is Autism different then Developmental Delay?
- Children develop skills in five main areas of development:
  1. Cognitive
  2. Social and emotional
  3. Speech and language
  4. Fine motor
  5. Gross motor
- Developmental delay occurs when children have not reached developmental milestones by the expected time period.

- Autism is a disability that affects the skills needed to socialize, communicate, and cooperate with other people.

Differential Diagnosis of Autism

- Acanthocytosis
- Angelman syndrome
- Anxiety Disorder: Obsessive-Compulsive Disorder
- Anxiety Disorder: Trichotillomania
- Attachment disorder
- Biotin Deficiency
- Child Abuse & Neglect
- Childhood disintegrative disorder
- Cornelia De Lange Syndrome
- Cri-du-chat Syndrome
- Cognitive Deficits
- CMV virus
- Deletion 1p35
- Developmental language disorder
- Duplication of bands 15q11-13
- Down Syndrome
- Eating Disorder: Pica
- Extra bisatellite marker chromosome
- Fragile X Syndrome
- Gaucher Disease
- Global delay/intellectual disability (mental retardation)
- Habit disorder
- Hearing Impairment
- Human Immunodeficiency Virus Infection
- Hypomelanosis of Ito
- Hydrocephalus, infantile
- Interstitial deletion of (17)(p11.2)
- Inv Dup (15)(pter->q13)
- Language disorder: mixed, phonology, receptive, stuttering
- Landau-Kleffner
- Learning Disorder: Reading
- Long Y chromosome
- Minamata disease
- Moebius syndrome
- Nonketotic hyperglycinemia (NKH)
- Obsessive compulsive disorder
- Partial 6p trisomy
- Rett disorder
- Seizures
- Seizures, frontal lobe
- Spasms, infantile
- Tourette disorder
- Toxicity, Lead
- Tuberous Sclerosis
- Trisomy 22
- 44,XXX karyotype
- 47 chromosomes
- (7;20) balanced chromosomal translocation

Concept

- 10% of Autism Spectrum Disorder can be traced back to an identifiable medical reason.
  - 90% of the cases we don't have the technology available or developed.
- When considering a diagnostic test, consider testing that can help lead down the path of a diagnosis (or treatment).
  - What are you treating?
  - What is your diagnosis?

Where To Start?

Number one is identification.

- Screening Tools
- Diagnostic Tools
- Tools for associated conditions

Screening Tools

- Screening tools are tests that have been tested on large groups of children.
- Child Neurology Society recognizes Checklist for Autism in Toddlers and the Autism Screening Questionnaire as useful screens for Autism.
- There Child Neurology Society also recognizes there are several tools to screen for Autism.

Practice Parameter: Screening and Diagnosis of Autism

Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society

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Methods of evidence review:

- Evidence was identified through literature searches using MEDLINE and PsychINFO.
- 2,750 studies met the following inclusion criteria
- Experts in the surveillance/screening and diagnosis of Autism
  - Reviewed and evaluated the quality of the evidence from the published literature,
  - Developed a consensus of evidence-based management recommendations,
  - Published a comprehensive background paper on the surveillance, screening, and diagnosis of autism.

Clinically identifying children with Autism

- Identification requires two levels of investigation.
- Each level addresses a distinct component of patient management.
- For these two areas of investigation,
  - Specific clinical questions were defined,
  - Clinical evidence was summarized,
  - Diagnostic recommendations were developed.

Clinically identifying children with Autism

- Level one: *Routine Developmental Surveillance and Screening Specifically for Autism*
  - Should be performed on all children.
  - Involves first identifying those at risk for any type of atypical development, followed by identifying those specifically at risk for autism.
  - Mental retardation or other medical or neurodevelopmental conditions require separate evaluations.

Clinically identifying children with Autism

- Level Two: *Diagnosis and Evaluation of Autism*
  - Involves a more in-depth investigation of already identified children and differentiates autism from other developmental disorders.
  - In-depth diagnosis and evaluation are important in determining optimal interventional strategies based on the child's profile of strengths and weaknesses.

Developmental Delay

- Global developmental delay means a child is delayed in 2 or more areas of development.
  - Motor skills
    - Rolling over, walking, picking up objects
  - Speech and language
    - Identifying a sound, babbling, speech
  - Social and personal skills
    - Exploring, interacting with others
  - Daily activities
    - Eating or dressing
  - Ability to learn new things and to reason

How are conventional developmental milestones defined?

- Conventional language milestones are based on normative data from standardized language instruments for infants. Failure to meet these milestones is associated with a high probability of a developmental disability.
- Lack of acquisition of the following milestones within known accepted and established ranges is considered abnormal:
  - no babbling by 12 months
  - no gesturing (e.g., pointing, waving bye-bye) by 12 months
  - no single words by 16 months
  - no 2-word spontaneous (not just echolalic) phrases by 24 months
  - any loss of any language or social skills at any age

Can autism be reliably diagnosed before 36 months of age?

- There are no biological markers for autism, so screening must focus on behavior.
- Studies comparing autistic and typically developing children show problems with eye contact, orienting to one's name, joint attention, pretend play, imitation, nonverbal communication, and language development are measurable by 18 months of age.
- Current screening methods may not identify children with milder variants of autism, those without mental retardation or language delay, such as verbal individuals with high-functioning autism and Asperger's disorder, or older children, adolescents, and young adults.

Screening Tools

- Children under 3 years of age
  - CHAT (Checklist for Autism in Toddlers) – 18 months to 24 years
  - MCHAT (Modified CHAT) – 16 to 30 months of age
  - PDD Screening Test-II – Beginning at 18 months
  - Screening Tool for Autism in Two Year Olds
  - Infant Toddler Checklist – 6 to 24 months
- Preschool and School Age Children
  - Social Communication Questionnaire
  - Developmental Behavior Checklist for Pediatrics
- Asperger Disorder and High Functioning Autism
  - Childhood Autism Syndrome Test
  - Australian Scale for Asperger Disorder
  - Autism Spectrum Screening Questionnaire
  - Autism-Spectrum Quotient

Diagnosis of Autism

DSM-IV

A. A total of six or more items from 1., 2., and 3., with at least two from 1., and one each from 2. and 3.:1.
   1. Qualitative impairment in social interaction
   2. Qualitative impairments in communication
   3. Restricted repetitive and stereotyped patterns of behavior, interests, and activities

B. Delays or abnormal functioning in at least one of the following areas, with onset prior to age three years:
   1. social interaction
   2. language as used in social communication
   3. symbolic or imaginative play

C. The disturbance is not better accounted for by Rett disorder or (CDD) childhood disintegrative disorder

DSM-IV

1. Qualitative impairment in social interaction, as manifested by at least two of the following:
   - a. Marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction
   - b. Failure to develop peer relationships appropriate to developmental level
   - c. A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (eg, by a lack of showing, bringing, or pointing out objects of interest)
   - d. Lack of social or emotional reciprocity

DSM-IV

2. Qualitative impairments in communication as manifested by at least one of the following:
   - a. Delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime)
   - b. In individuals with adequate speech, marked impairment in the ability to initiate or sustain conversation with others
   - c. Stereotyped and repetitive use of language or idiosyncratic language
   - d. Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level

DSM-IV

3. Restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following:
   - a. Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that are abnormal either in intensity or focus
   - b. Apparently inflexible adherence to specific, nonfunctional routines or rituals
   - c. Stereotyped and repetitive motor mannerisms (eg, hand or finger flapping or twisting, or complex whole-body movements)
   - d. Persistent preoccupation with parts of objects

Caution with DSM-IV

- DSM-IV-TR(TM) and the ICD-9-CM are poor textbooks of child development and child psychopathology.
- They do not fully describe the concepts incorporated in the criteria for autism and related conditions.
- Therefore, an inexperienced clinician is likely to incorrectly apply the criteria for autism and related conditions in the DSM-IV-TR(TM).

Diagnostic Tools for Autism

- DSM-IV criteria
- Autism Behavior Checklist (ABC)
- Gilliam Autism Rating Scale (GARS)
- Childhood Autism Rating Scale (CARS)
- Autism Diagnostic Interview-Revised (ADI-R)
- Social Responsive Scale (SRS)
- Autism Direct Observation Schedule (ADOS)
  - Gold standard for diagnosis of autism in children >30 months of age in research studies.

Mimickers of Autism

May Appear Like Autism Early.

- Developmental Language Disorder (DLD)
  - In contrast to children with ASD, children with DLD have normal reciprocal social interactions, normal desire and intent to communicate, and appropriate imaginative play.
- Language-Based Learning Disorder
- Hearing Impairment
- Landau-Kleffner Syndrome
- Attachment Disorder
- Anxiety Disorder
- ADHD
- Obsessive Compulsive Disorder

Other Psychological Screening Tools and Rating Scales

- Anxiety Symptoms
  - Spence Children's Anxiety Scale (SCAS)
  - Revised Children's Manifest Anxiety Scale (RCMAS-2)
  - Depression and Anxiety in Youth Scale (DAYS)
  - Beck Anxiety Inventory for Youth (BYI)
  - Self-Report for Childhood Anxiety Related Emotional Disorders (SCARED)
  - Multidimensional Anxiety Scale for Children (MASC)
  - State-Trait Anxiety Inventory for Children (STAIC)
  - Endler Multidimensional Anxiety Scales (EMAS)
  - Anxiety Disorders in Children: A Test for Parents
  - Anxiety Disorders in Adolescents: A Self-Test
- Social Anxiety Symptoms
  - Liebowitz Social Anxiety Scale-Child Adolescent version (LSAS-CA)
  - Social Phobia and Anxiety Inventory for Children (SPAI-C)
- Obsessive Compulsive Symptoms
  - Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)
  - Yale-Brown Obsessive Compulsive Scale (YBOCS)

Other Psychological Screening Tools and Rating Scales

- Depression Symptoms
  - Weinberg Depression Scale for Children and Adolescents (WDSCA)
  - Children's Depression Rating Scale-Revised (CDRS-R)
  - Center for Epidemiological Studies Depression Scale Modified for Children (CES-DC)
  - Kiddie Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS)
  - Children's Depression Scale (CDS)-3rd Ed.
  - Child Depression Inventory (CDI)
  - Beck Depression Inventory-II (BDI-II)
  - Reynolds Child/Adolescent Depression Scales-RCDS (Child) & RADS-2 (Adolescent)
  - Multiscore Depression Inventory for Adolescents and Adults (MDI)
  - Multiscore Depression Inventory for Children (MDI-C)
  - Mood and Feelings Questionnaire (MFQ)

Other Psychological Screening Tools and Rating Scales

- Bipolar Disorder / Mania Symptoms
  - Young Mania Rating Scale (YMRS)
  - Parent Version of the Young Mania Rating Scale (P-YMRS)
  - General Behavior Inventory (GBI)
  - Parent Version, General Behavior Inventory (P-GBI)
  - Kiddie Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS)
  - Weinberg Screening Affective Scale (WSAS)
  - Mood Disorder Questionnaire (MDQ)
- Suicide Risk Symptoms
  - Suicidal Ideation Questionnaire (SIQ)

Other Psychological Screening Tools and Rating Scales

- Attention Deficit / Hyperactivity Symptoms
  - Attention Deficit Disorders Evaluation Scale (ADDES-3)
  - ADHD Rating Scale-IV (ADHD-IV)
  - ADHD Rating Scale
  - Vanderbilt ADHD Diagnostic Parent Rating Scale
  - Vanderbilt ADHD Diagnostic Teacher Rating Scale
  - SSNAP-IV Rating Scale - Revised (SNAP-IV-R)
  - ADD-H: Comprehensive Teacher's Rating Scale: Parent Form (ACTeRS)
  - ADHD Comprehensive Teacher Rating Scale (ACTeRS)
- Nonverbal Learning Disability Symptoms
  - Children's Nonverbal Learning Disabilities Scale (C-NLD)
- Disruptive Behavior Symptoms
  - Conduct Disorder Scale (CDS)
  - Adjustment Scales for Children and Adolescents (ASCA)
  - Social Skills Rating System (SSRS)
  - Reynolds Adolescent Adjustment Screening Inventory (RAASI)

Lead

- Lead is the most common toxic substances in the environment that can harm the nervous system.
- The National Center for Environmental Health of the Centers for Disease Control and Prevention recommends that children with developmental delays, even without frank pica, should be screened for lead poisoning.

Genetic Testing in Autism

- There is increasing evidence for the role of genetic factors in etiology of Autism.
- Unequal sex distribution, with 4:1 male predominance
- Increased prevalence in siblings

Standard Genetic Testing

- Standard genetic testing is Chromosome testing.
- Can provide information about some inherited problems and genetic disorders.
- A chromosomal abnormality reported in possibly more than 1% of autistic individuals involves the proximal long arm of chromosome 15 (15q11-q13), which is a greater frequency than other currently identifiable chromosomal disorders.

Other Genetic Testing

- Fragile X is the most common inherited disorder causing developmental delay.
  - Clinical studies report that 3% to 25% of patients with Fragile X have Autism.
- Rett Syndrome is a leading diagnosable cause of developmental delay in girls.
  - Girls with Rett syndrome appear to develop normally until 6 to 18 months of age, then can lose developmental milestones and abilities.

Genetic Testing

- Routine karyotype analysis is available from most genetic laboratories.
  - Other more specific genetic tests may be available on a clinical basis from only a limited number of laboratories.
  - Subtelomeric chromosomal rearrangements and submicroscopic deletions can be detected by fluorescence *in situ* hybridization (FISH)
- Fragile X syndrome is associated with large expansions of the number of CGG triplet repeats within the FMR-1 gene on the X chromosome.
- Rett Syndrome Testing evaluates for mutations in the MECP2 gene on chromosome Xq28.
- Prader-Willi syndrome (PWS) Testing evaluates for is the absence of the paternally derived portions of chromosome 15q11-q13.
- Angelman syndrome (AS) Testing is similar to that of PWS, evaluating for the loss of the maternal contribution of chromosome 15q11-q13.
- An excellent source of information regarding common genetic syndromes, genetic test availability, and individual laboratory sample requirements, testing procedures, and contact information is available via the internet at the publicly funded website:
  - www.genetests.org
    - PRACTICE PARAMETER: EVALUATION OF THE CHILD WITH GLOBAL DEVELOPMENTAL DELAY (Published in NEUROLOGY, Feb 12, 2003)

Genetic Testing

- What is a gene?
  - A unit of DNA sequence that encodes specific function.
- What are Chromosomes?
  - A chromosome is an organized structure of DNA and protein that is found in cells.
  - In humans, each cell normally contains 23 pairs of chromosomes, for a total of 46.
    - Twenty-two of these pairs look the same in both males and females.
    - The 23rd pair, the sex chromosomes, differ between males and females.
    - Females have two copies of the X chromosome, while males have one X and one Y chromosome.
- English: Chromosomes are our genetic road map.
- What does the lab test Chromosomes identify:
  - Mutation, an altered version of a gene.
- Example of what a Chromosome Test can identify:
  - Down Syndrome

Down Syndrome

- Down syndrome (DS) is the most common chromosome abnormality among live born infants.
- Trisomy 21 (47,+21): An extra chromosome 21 is present.
- It is the most frequent (identifiable) form of Neurodevelopmental disability caused by a microscopically demonstrable chromosomal aberration.
- Has characteristic facial and anatomical features.
- Most are mildly to moderately intellectually disabled, with IQ in the 50 to 70 or 35 to 50 range, respectively, although some are severely impaired with IQ 20 to 35.
- Hypotonia is frequently present.
- Developmental impairment becomes apparent in the first year of life.
- In general, the average age of sitting (11 months), creeping (17 months), and walking (26 months) is twice the typical age.
- Autism is a common comorbidity of DS, affecting as many as 7 percent of DS children.

Down Syndrome

- Can also affect multiple body systems that can affect other disorders.
  - Seizures, Heart defects, GI problems, Short stature, Obesity, Hematologic/Cancer disorders, Eye problems, Hearing loss, Immune deficiency, Thyroid disorders, Diabetes, Urologic abnormalities, Arthritis, Obstructive sleep apnea, Skin disorders, Behavior disorders
- In this circumstance the test of Chromosomes can give
  1. An identifiable cause for Autism.
  2. Identifies a disorder that has other organ system implications.

Chromosomal Microarray

- How is a Chromosomal Microarray Different?
  - Array comparative genomic hybridization is a technique to detect genomic copy number variations at a higher resolution level than chromosome-based comparative genomic hybridization (CGH).
  - Also called: CMA, Chromosomal Microarray Analysis, Microarray-based comparative genomic hybridization, array CGH, a-CGH, aCGH, Virtual Karyotype.

- Google Maps vs. Google Earth Comparison.
  - Chromosomes – Map of the continents
  - Microarray – North America
  - Other Specific Testing – FGCU Campus

Chromosomal MicroArray

- Abnormalities in Chromosome 15 have been associated with Autism
- A "chromosome 15 phenotype" has begun to emerge that is characterized by hypotonia, joint laxity, global (especially motor) developmental delays, seizures, speech delay, social deficits, stereotypies, and a variable pattern of mild facial dysmorphisms.
- Other potential loci are close to known locations of a gene for tuberous sclerosis (chromosome 16p) or neurofibromatosis type 1 (chromosome 17)

Angelman syndrome (AS)

- Angelman syndrome (AS) has features of characteristic facial dysmorphisms, developmental delay, speech impairment, ataxia or tremor, and frequent laughter or smiling.
- Other frequently associated findings are acquired microcephaly and seizures.
- The genetic basis for AS is similar to that of PWS, involving the loss of the maternal contribution of chromosome 15q11-q13.

Prader-Willi syndrome (PWS)

- Prader-Willi syndrome (PWS) is associated with characteristic facial dysmorphisms, hypogonadism, developmental delay, feeding problems and hypotonia in infancy followed by hyperphagia and obesity in childhood.
- The genetic basis is the absence of the paternally derived portions of chromosome 15q11-q13.

Metabolic Testing

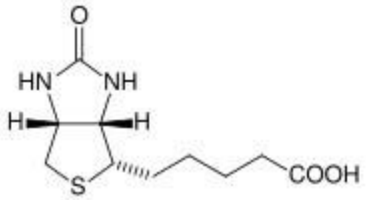
- Metabolic tests are blood and urine tests that can spot disorders of the body's chemistry.
- Inborn errors in amino acid, carbohydrate, purine, peptide, and mitochondrial metabolism, as well as toxicologic studies have been studied, but the percentage of children with autism who have a metabolic disorder is probably less than 5%.

Metabolic Testing

- Selective metabolic testing should be initiated by the presence of suggestive clinical and physical findings such as the following:
  - Lethargy
  - Cyclic vomiting
  - Early seizures
  - Dysmorphic or coarse features
  - Evidence of mental retardation
    - or if mental retardation cannot be ruled out
  - If occurrence or adequacy of newborn screening for a birth is questionable.
- Doctor should order metabolic tests if:
  - Child is delayed and did not have these tests at birth.
  - If there is a family history of developmental delay.

Metabolic Testing

- While no standard has been set for what constitutes routine testing for an inborn error of metabolism, the studies most commonly performed on a screening basis include measures of serum glucose, bicarbonate, lactate, pyruvate, ammonia, creatine kinase, and amino acids and of urine pH, ketones, and organic acids.
- Measures of serum long chain fatty acids, carnitines, and acylcarnitines, of urine mucopolysaccharides, and of cerebrospinal fluid lactate and amino acids are more often considered to be part of a second tier of tests, performed when initial screening tests are positive or when there are specific clinical suspicions. The tests that are frequently available only on a send-out basis are further described.
  - PRACTICE PARAMETER: EVALUATION OF THE CHILD WITH GLOBAL DEVELOPMENTAL DELAY (Published in NEUROLOGY, Feb 12, 2003)



Example of a Metabolic Test

Biotinidase Deficiency

- Metabolic disorder in which biotin is not released from proteins in the diet during digestion or from normal protein turnover in the cell.
- Biotin deficiency can result in behavioral disorders, lack of coordination, learning disabilities and seizure.
- Has been reported that biotin deficiency in brain and cerebrospinal fluids may produce neurological problems, such as stereotyped and autistic behaviors.
- Biotin supplementation can alleviate and sometimes totally arrest such symptoms.
  - However, if identified late the effects may be irreversible in spite of biotin supplementation.

EEG

What is an EEG?

- Electroencephalography is the recording of electrical activity along the scalp produced by the firing of neurons in the brain.
- Records the brain's spontaneous electrical activity.
- Parallel Example:
  - Just as an EKG gives information about the heart rhythm and can give information about heart rhythm problems, an EEG gives information about the brain activity and can give information about potential brain activity problems.
- Such brain activity problems may include seizure disorders, brain maturity, or general dysfunction (term called encephalopathy).

EEG

- An EEG records the electrical activity of the brain.
  - Can help to determine if a child has epilepsy.
  - Can give insight into brain maturity.
  - Can identify potential dysfunction.

- However, An EEG does not determine the cause of developmental delays.

Seizures and Autism

- The prevalence of epilepsy in autistic children has been estimated at 7% to 14%.
- If a child with Autism has had a seizure, an EEG may help in showing the pattern of a particular seizure disorder.
- A higher incidence of epileptiform EEG abnormalities in Autistic children with a history of regression has been reported when compared to autistic children with clinical epilepsy.

Absence Seizures

- Absence seizure are one of several kinds of seizures.
- Frequently referred to as petit mal seizures.
  - French term for “little illness”.
- Person may appear to be staring into space.
- May last less then a second or range to several seconds.
- There may be twitching of eye muscles or other body muscles.
- May occur up to hundreds of times per day.
- May be confused with attention problems.

Atonic Seizures

- Atonic seizures consist of brief lapse in muscle tone caused by alterations in brain function.
- Also called Drop Seizures, Akinetic Seizures, or Drop Attacks.
- Commonly seen in Lennox-Gastaut Syndrome.
- Can cause head drops and sometimes body damage due to fall.

Landau-Kleffner Syndrome

- LKS is characterized by the development of aphasia (inability to understand or express language) and an abnormal EEG.
- Also called Acquired Aphasia or Epileptic Aphasia
- Many children may have other types of seizures, some only have EEG seizures including ESES (Electrical Status Epilepticus of Sleep)
- May be misdiagnosed as Autism, hearing impairment, learning disability, childhood schizophrenia, or ADHD.

Movement Abnormalities

- Movement abnormalities are a prominent feature in a subset of individuals with Autism.
  - Motion anomalies often stand out as odd in crowds because of the motions.

Stimming

- Example of a motion typical in autism occurs when the child places a hand with fingers outstretched before the eyes and rapidly moves the hand back and forth.
- This action is described as self-stimulation because it produces a visual sensation of movement.

Stereotypy

- Some movements observed in individuals with autistic disorder may include purposeless, repetitive, patterned motions, postures, and sounds).
- Stereotypies are divided into the following 3 topological classes:
  - Oro-facial (eg, tongue, mouth, and facial movements; smelling; sniffing; sounds)
  - Extremity (eg, hand, finger, toe, leg)
  - Head and trunk (eg, rolling, tilting, or banging of the head; rocking the body

- EEG may be helpful in separating seizures from other known movement abnormalities.

Types of EEG

- Routine EEG
  - Usually 20-30 minutes.
- Sleep Deprived EEG
  - Sleep deprivation provokes seizure activity.
  - Also sleep shows potential epileptiform activity that is not seen during awake.
- Video EEG
  - The video allows correlation between certain movements or question and EEG findings.
- Prolonged EEG
  - 1 to 4 hour study
  - Good for if Neurologist needs to see some degree of sleep or if events of question are very frequent such as multiple time an hour.
- Long Term Video EEG monitoring
  - Usually 24 hours or longer.
  - Allows for better assessment of sleep activity as well as higher yield of capturing certain events.

Types of EEG

- Ambulatory EEG
  - Usually 24 hour study that is taken home.
  - Advantage is that patient is in natural environment setting, more convenient for family.
  - Disadvantage is that without video it may be difficult to tell what is seizure and what is artifact (chewing, scratching).
  - Also does not give clear correlation of subtle movements and seizure.
- EMU
  - Epilepsy Monitoring Unit allows a facility with 24 hours or even up to a week of monitoring for seizures.
  - Gold standard of diagnosing seizures is to capture the seizure with EEG and with video.

Guideline – EEG

- There is inadequate evidence at the present time to recommend an EEG study in all individuals with autism.
- Indications for an adequate sleep-deprived EEG with appropriate sampling of slow wave sleep include:
  - Clinical seizures,
  - Suspicion of subclinical seizures,
  - History of regression (clinically significant loss of social and communicative function) at any age.
    - Especially in toddlers and preschoolers.

Neuroimaging

- Neuroimaging tests help doctors see if there is any damage to tissues of the brain.
- Recommended as part of the evaluation of some children with developmental delays.

Neuroimaging

- What is an MRI
- What is a CT scan
- Advantages, Disadvantages, and Risks

Magnetic Resonance Imaging

- MRI is an imaging technique used to visualize detailed internal structures using a magnetic field that allows information to be gathered from tissues that contain various amount of water.
- MRI is used to visualize soft tissues such as brain, muscle, organs, and cancers.

CT Scan

- X-ray computed tomography.
- CT is medical imaging method created by computer processing of X-ray images around a circular axis of rotation.

MRI vs. CT

- Advantages of MRI
  - It is better for soft tissue visualization, such as brain.
  - There is no radiation.
- Advantages of CT
  - Quick procedure, approximately 5 minutes.
  - Better for visualizing bones and blood.
- Disadvantage of MRI
  - Long procedure may produce risks associated with anesthesia.
  - Cost is more expensive then CT.
- Disadvantage of CT
  - Radiation exposure.
  - May miss soft tissue abnormalities that a detailed MRI could see.
  - Example: CT does not visualize the white matter well.

Examples of Potential Neuroimaging Findings

- Tuberous Sclerosis Complex
  - 17 to over 60% of individuals with TS are also autistic.
  - These patients commonly have epilepsy.
  - May also involve multiple organ systems.

- Agenesis of the corpus callosum
  - Occurs when the corpus callosum, the band of white matter connecting the two hemispheres of the brain, fails to develop normally.
  - Common characteristics include vision impairments, low muscle tone, cognitive impairment, poor motor coordination, delays in motor milestones.
  - Social difficulties (missing subtle social cues) has been seen, even when their Intelligence Quotient is normal.
    - May be a result of impaired face processing.
    - May be mistaken for Asperger syndrome or other autism spectrum disorders.

Guideline – Neuroimaging

- There is no clinical evidence to support the role of routine clinical neuroimaging in the diagnostic evaluation of Autism, even in the presence of megalencephaly.
- Neuroimaging is recommended as a part of the diagnostic evaluation of the child with global developmental delay.
- Physicians can more readily consider Neuroimaging in the presence of physical findings.
  - Microcephaly, Focal motor findings
- MRI should be obtained in preference to CT.

Hearing Assessment

- All children with developmental delays, particularly those with delays in social and language development, should have a formal audiologic hearing evaluation (American Speech–Language–Hearing Association).
- Children with global delay may undergo appropriate audiometric assessment at the time of their diagnosis (Child Neurology Society).
  - Can include behavioral Audiometry or Brainstem Auditory Evoked Response testing when feasible.

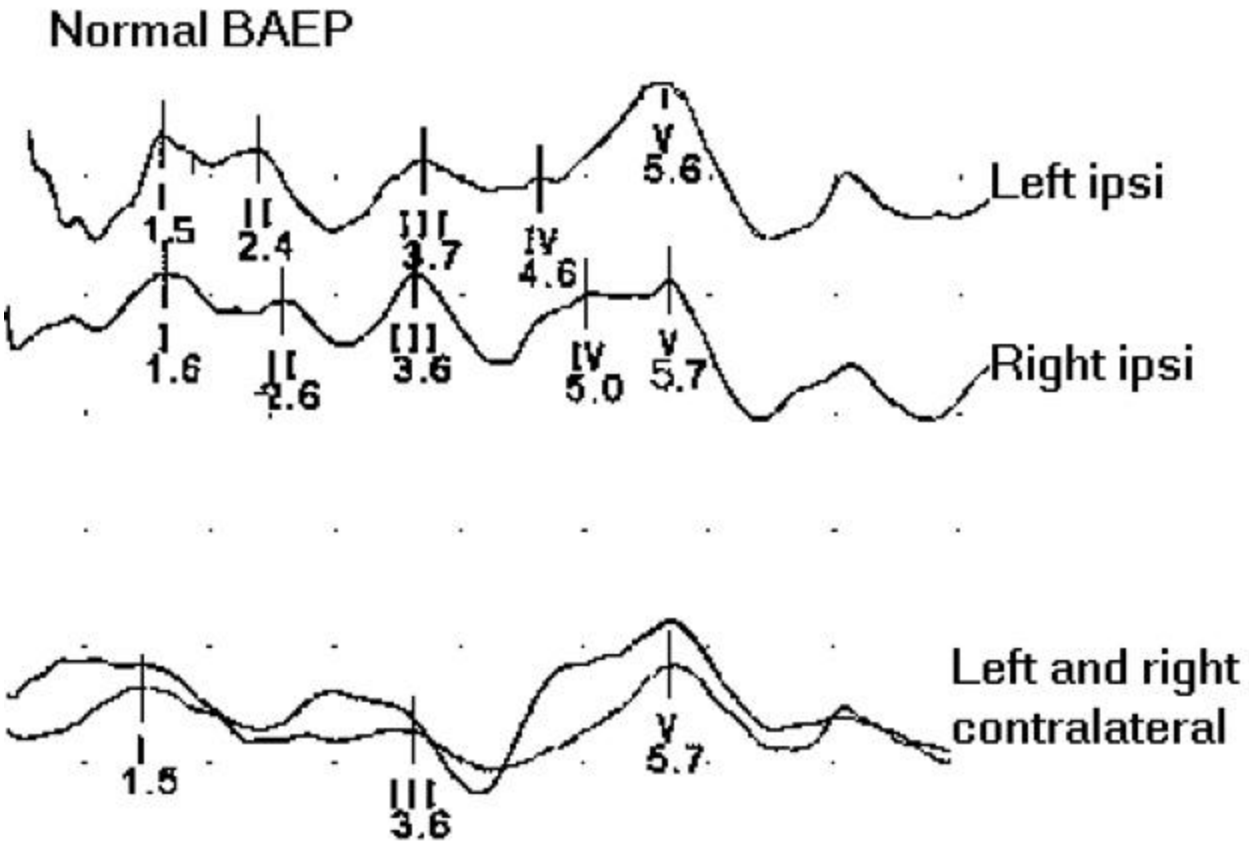
Audiometry

- Audiometry is the testing of hearing ability.
- Audiometric tests
  - Determine a subject's hearing levels with the help of an audiometer,
  - May also measure ability to discriminate between different sound intensities, recognize pitch, or distinguished speech from background noise.

BAER

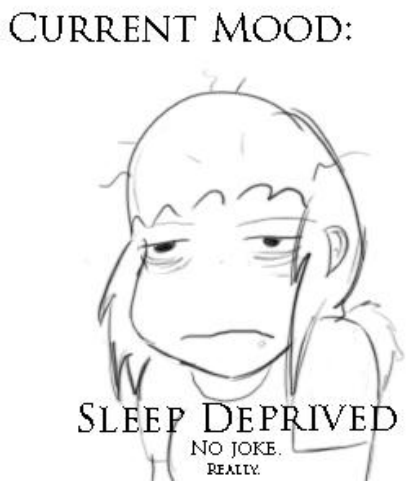
- Brainstem Auditory Evoked Response (or Potential)
- BAER measures the function of the auditory nerve and auditory pathways in the brain stem.
- Useful in estimating or aiding in the assessment of hearing loss
- Can be used to screen those who might benefit from auditory amplification in order to achieve more normal speech and language development.

Brainstem Auditory Evoked Response



Sleep Studies

- Parental reports of sleep concerns in Autism range from 44%-83%.
- Complaints include Insomnia, Daytime Sleepiness, Sleep Disorder Breathing, and Parasomnias.

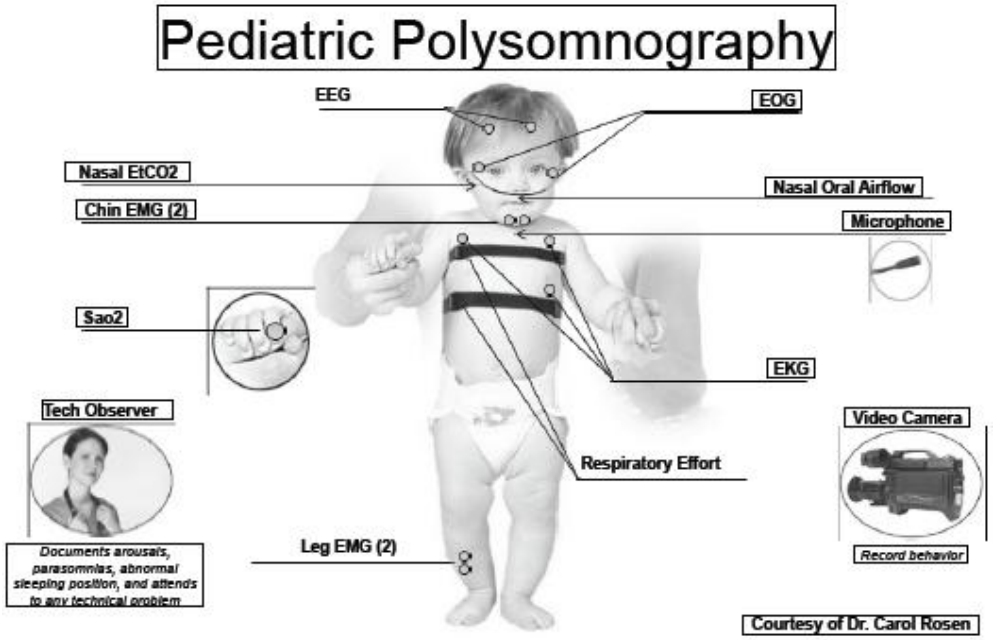


Polysomnography

- Polysomnography is a multi-parametric test that records the biophysiological changes that occur during sleep.
  - Electroencephalogram (EEG) along with electro-oculogram (EOG) provides the basis for differentiating the stages of sleep.
    - Some extended EEG montages may also provide insight to potential seizure activity.
  - Electromyogram (EMG) can assess skeletal muscle from the chin and extremities that help in sleep staging as well as provide objective information on motor behavior exhibited during sleep and wake.
  - Electrocardiogram (ECG or EKG) activity monitors rate and rhythm of cardiac activity.
  - Respiratory activity is monitored through airflow, respiratory effort, and oxygen saturation.
  - Nasal or oral airflow can be monitored with combinations of nasal pressure transduction, thermistor, and continuous capnography.
  - Respiratory effort is evaluated by measuring chest and abdominal effort with inductive plethysmography or piezo crystal belts.
  - Hemoglobin-Oxygen saturation is monitored by continuous pulse oximetry.
  - Audio-Video (AV) monitoring allows the multiple channels of information obtained to be correlated with a particular physical event of question.

Pediatric Polysomnography

- Children may remove sensors during the night, reducing the amount of available data, making the presence of the sleep technician more important.



Sleep And Autism

- Blood and urinary melatonin levels are low in Autism
- Parental reports of sleep problems in Autism range from 11% to 37%.
- PSG identified sleep disturbances in Autism ranges from 44% to 83%.
- Sleep Problems in Autism
  - Insomnia
  - Coexisting Epilepsy
  - GER
  - Anxiety
  - Mood disorder
  - OSA – general population

OSA

- 3% of Pediatric population may have Obstructive Sleep Apnea (OSA), whereas up 10% of the Pediatric population may have BPS (Benign Primary Snoring). Clinical practice guidelines by the American Academy of Pediatrics recommends Polysomnography as the diagnostic test of choice in evaluating children with suspected sleep disorder breathing. The American Thoracic Society states that an attended overnight Polysomnography in a designated pediatric sleep laboratory is the gold standard for the diagnosis of sleep disorder breathing in children. (American Thoracic Society; *American Journal of Respiratory Critical care medicine*. 153:866-878 / American Academy of Pediatrics; *Pediatrics* 109:704-712)

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Sleep Med Clin 3 (2008) 479–488

Sleep Disturbances and Autism

Beth A. Malow, MD, MS[a,*], Susan G. McGrew, MD[b]

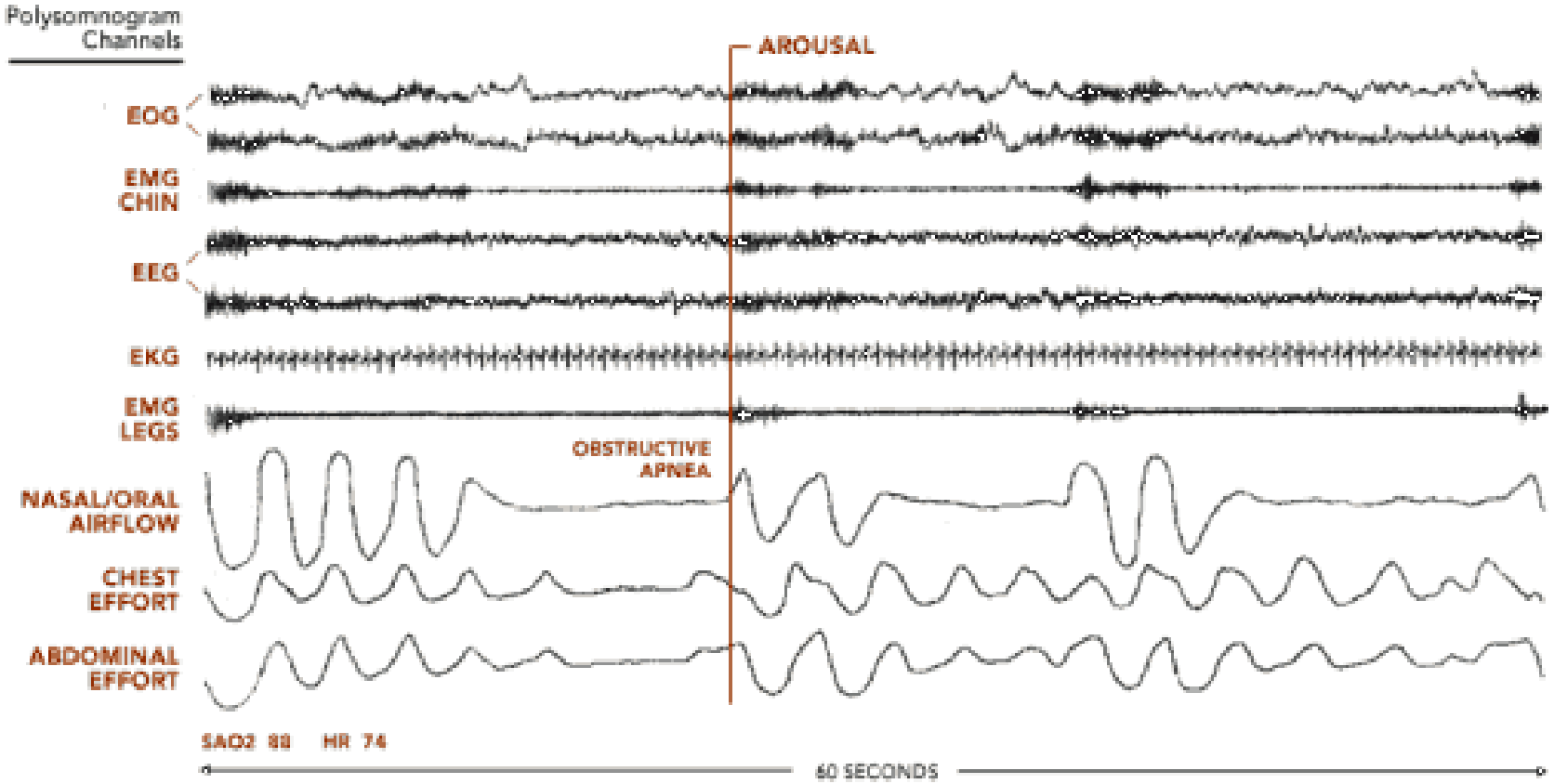
Neurocognitive Effects Of Sleep Disorders

- "Sleep deprivation can cause daytime hyperactivity and decrease in focused attention. This can be mistaken for ADHD or other behavior disorders."
  - National Institutes of Health
- Inadequate sleep causes decrease in:
  - Performance, Concentration, Reaction times, Consolidation of information
- Inadequate sleep causes increases in:
  - Memory lapses, Accidents and injuries, Behavior problems, Mood problems and irritability

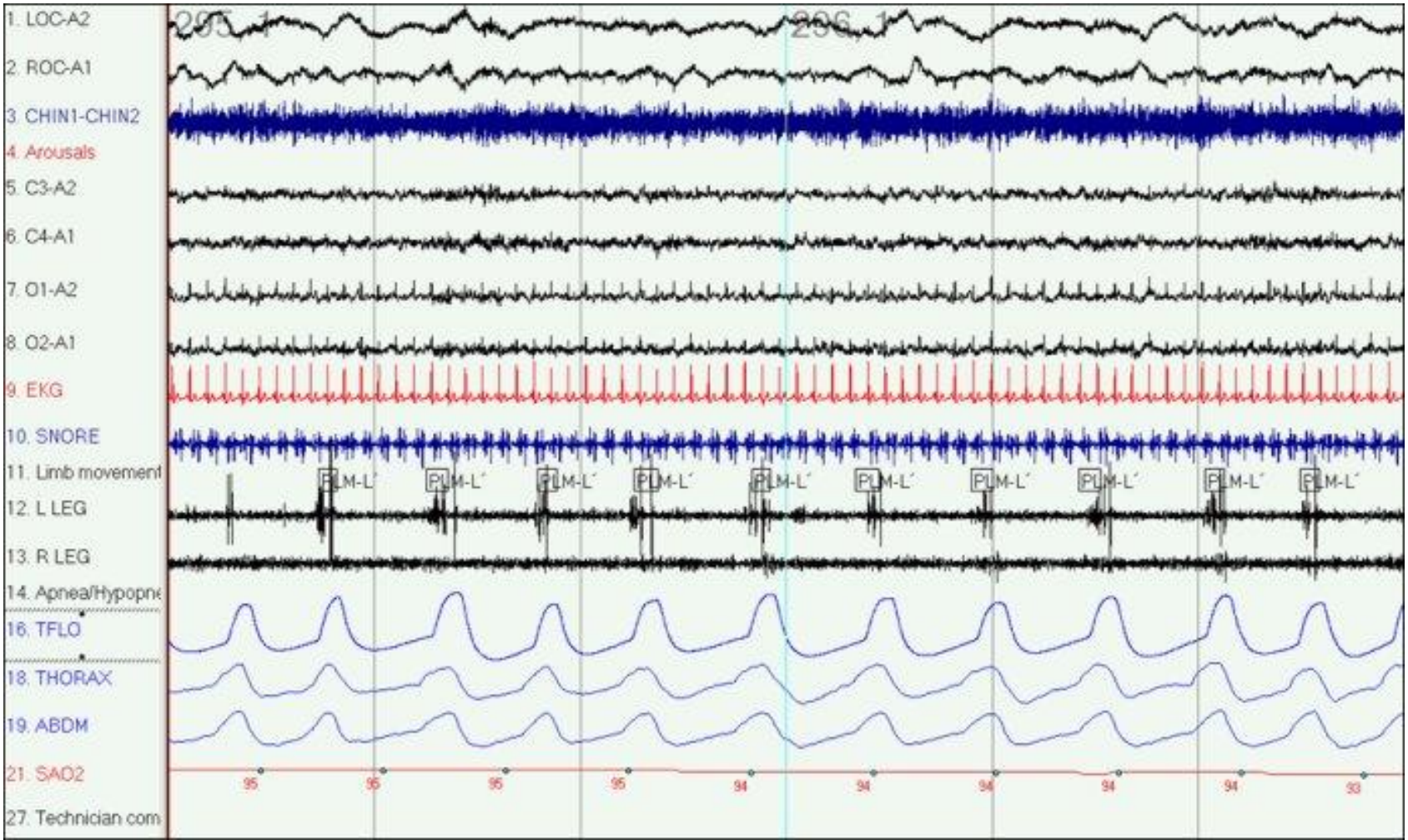
Reported Sequela of Poor Sleep

- Mood and Behavior
  - Impulsivity
  - Inattention
  - Hyperactivity
  - Restlessness
  - Aggression
  - Defiance
  - Lack of impulse control
  - Excessive daytime sleepiness (EDS)
- Cognition
  - Learning problems
  - Reading, math, or writing delays
  - Memory deficits
  - Intelligence scores
  - Verbal fluency
  - Executive functioning

Polysomnogram in OSA



Polysomnogram in PLMD



Treatment of Sleep and Autism

- Improvement of quality of life.
- Improvement in daytime neuropsychiatric symptoms.
- Relationship between sleep problems and stereotypic behaviors.
- Improvement in affective problems.

Why Get a Sleep Evaluation?

- What are you treating?
- Appropriate therapy is dependent on:
  - Condition
  - Severity
- Failure to treat leads to:
  - Increased morbidity and mortality
  - Motor vehicle crashes
  - Daytime cognitive dysfunction
  - Confounding symptoms of other Psychiatric disorders
- Signs and symptoms poorly predict disease severity
- Other causes of daytime sleepiness

Regression Subtype

- Thirteen to forty-eight percent of people with autism had apparently normal development until 15-30 months of age when loss of communication skills by verbal and nonverbal means occurs.
- This can occur due to genetic reasons or metabolic reasons such as inborn errors of metabolism.

Summary of CNS Guidelines of Autism Evaluation

1. Genetic testing in children with autism, specifically high resolution chromosome studies (karyotype) and DNA analysis for FraX, should be performed in the presence of mental retardation (or if mental retardation cannot be excluded), if there is a family history of FraX or undiagnosed mental retardation, or if dysmorphic features are present (**Standard**). However, there is little likelihood of positive karyotype or FraX testing in the presence of high-functioning autism.
2. Selective metabolic testing (**Standard**) should be initiated by the presence of suggestive clinical and physical findings such as the following: if lethargy, cyclic vomiting, or early seizures are evident; the presence of dysmorphic or coarse features; evidence of mental retardation or if mental retardation cannot be ruled out; or if occurrence or adequacy of newborn screening for a birth is questionable.

Summary of CNS Guidelines of Autism Evaluation

3. There is inadequate evidence at the present time to recommend an EEG study in all individuals with autism. Indications for an adequate sleep-deprived EEG with appropriate sampling of slow wave sleep include (**Guideline**) clinical seizures or suspicion of subclinical seizures, and a history of regression (clinically significant loss of social and communicative function) at any age, but especially in toddlers and preschoolers.
4. Recording of event-related potentials and magnetoencephalography are research tools at the present time, without evidence of routine clinical utility (**Guideline**).
5. There is no clinical evidence to support the role of routine clinical neuroimaging in the diagnostic evaluation of autism, even in the presence of megalencephaly (**Guideline**).

Summary of CNS Guidelines of Autism Evaluation

6. There is inadequate supporting evidence for hair analysis, celiac antibodies, allergy testing (particularly food allergies for gluten, casein, candida, and other molds), immunologic or neurochemical abnormalities, micronutrients such as vitamin levels, intestinal permeability studies, stool analysis, urinary peptides, mitochondrial disorders (including lactate and pyruvate), thyroid function tests, or erythrocyte glutathione peroxidase studies (**Guideline**).

Summary of CNS Guidelines of Autism Evaluation

- Requires a comprehensive multidisciplinary approach, and can include one or more of the following professionals: psychologists, neurologists, speech–language pathologists and audiologists, pediatricians, child psychiatrists, occupational therapists, and physical therapists, as well as educators and special educators.
- Reevaluation within 1 year of initial diagnosis and continued monitoring is an expected aspect of clinical practice because relatively small changes in the developmental level affect the impact of autism in the preschool years.

Summary of CNS Guidelines of Autism Evaluation

- A comprehensive speech–language–communication evaluation should be performed on all children who fail language developmental screening procedures by a speech–language pathologist with training and expertise in evaluating children with developmental disabilities.
- Comprehensive assessments of both preverbal and verbal individuals should account for age, cognitive level, and socioemotional abilities, and should include assessment of receptive language and communication, expressive language and communication, voice and speech production, and in verbal individuals, a collection and analysis of spontaneous language samples to supplement scores on formal language tests.

Summary of CNS Guidelines of Autism Evaluation

- Cognitive evaluations should be performed in all children with autism by a psychologist or other trained professional.
- Cognitive instruments should be appropriate for the mental and chronologic age, provide a full range (in the lower direction) of standard scores and current norms independent of social ability, include independent measures of verbal and nonverbal abilities, and provide an overall index of ability.

Summary of CNS Guidelines of Autism Evaluation

- Evaluation of sensorimotor skills by a qualified experienced professional (occupational therapist or physical therapist) should be considered, including assessment of gross and fine motor skills, praxis, sensory processing abilities, unusual or stereotyped mannerisms, and the impact of these components on the autistic person's life.
- An occupational therapy evaluation is indicated when deficits exist in functional skills or occupational performance in the areas of play or leisure, self-maintenance through activities of daily living, or productive school and work tasks.