Neuropsychological Profile of the 22q11.2 Deletion Syndrome

Edward M. Moss, Ph.D.
Behavior & Learning in Students With 22q11.2 Deletion Syndrome

October 1-2, 2011

Goals for this Presentation

- Introduction to the NLD Syndrome
- Neuroanatomy Data
- Genetic Models
- Interventions

Human Fetal Brain Development

- Lateral view: human brain at several stages of fetal development.
- Gradual emergence of gyri and sulci.

MRI contrast changes over time

White Matter Development

What happens when things go *slightly* wrong with this highly complex process?

- LD, NLD
- ADHD, CAPD
- Autism, Asperger’s Syndrome
- etc.
**Neuroanatomy of 22qDS**

**Volumetric MRI (Eliez, 2000)**
- Overall 11% ↓ brain volume (gray and white matter)
- Relative preservation of the frontal lobe
- ↓ left parietal volume
- ↓ right cerebellar volume

**All Learning Disorders**

**Neuropsychological Evaluation**
- Intelligence (Verbal, Nonverbal)
- Academic Abilities (Reading, Math, Writing)
- Mood & Behavior (Parents, Teachers, Self)
- Abstract Reasoning (Verbal, Nonverbal)
- Attention & Concentration (Visual, Auditory)
- Executive Functions / Working Memory
- Memory (Verbal, Nonverbal)
- Expressive & Receptive Language
- Visual Perception & Visual-Motor Integration
- Fine Motor Speed & Dexterity / Sensory-perceptual

**Hemispheric Specialization**

**Left Hemisphere**
- Language functions
- SPEECH
- READING
- WRITING
- Semantic tasks
- Verbal memory

**Right Hemisphere**
- Visual imagery
- Object recognition
- Visual-spatial perception/judgment
- Face recognition
- Visual memory

**When to test:**
- Key TRANSITION points!
  - Preschool / Kindergarten: prepare for Academics
  - Before 3rd grade: "read to learn" / independence
  - Before Middle School: ↑ transitions
  - Before High School: ↑ multi-tasking
  - Before College: Placement & Accommodations

*Pennington, 1990*
**Epidemiology**

Prevalence estimates among US school-age children

**Verbal LD**
- 10 - 12%
  - Population-based

**Nonverbal LD**
- .01 - 1.0%
  - Clinic-based

**Nonverbal (Right Hemisphere) LD Syndrome**

Myklebust, 1971, 1975, Rourke, 1989; 1995

**Hallmarks**
- VIQ > PIQ (at least 10 points)
- Reading > Math
- Fine motor delays

**Basic NLD Assets & Deficits**

**Assets**
- Verbal IQ
- Rote Verbal Learning
- Word Reading, Phonics
- Immediate Auditory Attention
- Simple Focused Attention

**Deficits**
- Visual Perception
- Vis.-Motor Integration
- Mathematics
- Complex Verbal Memory (Stories)
- Fine & Gross Motor
- Visual Memory

**Mathematics LD (Dyscalculia)**

**Integrate Automated Skills**
- Visual Information Processing
- Symbolic Interpretation
- Mental Manipulation
- Logical reasoning

**NLD typically detected later than LD**

- Strong verbal skills
- Strong rote learning skills
- Early readers
- Good phonemic awareness
Brain Disorders Increase NLD Risk

NLD Reported Among
Developmental disorders
- Neurofibromatosis (NF-1)
- Turner’s Syndrome (females)
- ADHD (specifically ADD-I)

Acquired disorders
- Traumatic Brain Injury (TBI)

Emotional & Behavioral Problems Associated with NLD

- ADHD
- Poor Social Skills
- Poor Adaptability
- Internalizing Disorders:
  - Depression & Anxiety
  - Increased Suicide Risk

Nonverbal LD Syndrome
Rourke; 1989, 1995

Socialization Problems
Nonverbal Aspects of Communication
- Language subtleties
- Facial expressions
- ‘Body Language’
- Turn-taking / Reciprocity

Social Skills Disorders

- Understand another point of view
- Understand humor, sarcasm, subtlety
- Abnormal paralinguistic skills

Genetic Contributions to LD & NLD

- 40,000 Genes in Average Human
- 12,000 (30%) Specific to the Brain
  - very complex organ
  - also consumes 20% of body’s oxygen

Behavioral Phenotyping
Turk & Hill, 1995

Introduced the concept that many genetic disorders
“...seem to have a constellation of behaviors or cognitive anomalies which are characteristic”
Behavioral Phenotyping

Some genetic syndromes with a characteristic Behavioral Phenotype:

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down syndrome</td>
<td>Trisomy 21</td>
</tr>
<tr>
<td>Williams syndrome</td>
<td>7q microdeletion</td>
</tr>
<tr>
<td>Klinefelter syndrome</td>
<td>XXY</td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td>15q11-13 microdeletion</td>
</tr>
</tbody>
</table>

Genetic Contributions to LD

Not a new concept (Thomas, 1905)
- 2 affected brothers
- Boy with affected sister & mother

Evidence
- Family History
- Heritability: MZ / DZ Twin Studies
- Persistence into adulthood, despite intervention

Genetic Contributions to LD

Familial Contributions
- General population risk: 5-10%
- First Degree relative risk: 35-40%

Critical data
Screen high risk children

Chromosome 22 Deletion
Subject Demographics

N = 260 (Consecutively Referred)
- Sex: 51% Male 49% Female
- Mean Age: 10.6 ± 3.7 years
- Age Range: 4.8 – 20.8 years
- Handedness: 87.3% Right

Wechsler Intelligence Scales

Mean FSIQ = 76
- Verbal IQ > Performance IQ 70.9% of subjects
- Verbal IQ < Performance IQ 27.9% of subjects

Wilcoxon signed ranks: z = -5.06, p < .0001

Full Scale IQ scores are misleading

VIQ / PIQ Discrepancy
6-8 points is normal

PIQ Higher
Mean = 4.8
PIQ HI 1-13 points

VIQ Higher
Mean = 12.9
VIQ HI 1-46 points
Case Example

VIQ = 111 (Above Average)
PIQ = 65 (Mild MR)
VIQ/PIQ SPLIT = 46
FSIQ = 87 (Low Average) INVALID

Memory & Learning

Rote Verbal Learning is Normal
Stronger than:
- Verbal IQ
- Story Memory
- Visual Learning

Academic Skills (WIAT)

All Reading Skills are stronger than all Math Skills:
- Word Attack
- Sight Words
- Spelling
- Comprehension (weaker)

Psychiatric Findings

Schizophrenia
Shprintzen et al (1992)
12 / 120 pts. (10%)
Chow et al (1994)
2 Adults / 100 pts.

Bipolar Disorder
16 / 25 pts. (64%)
ADD = 20% (N=5)
ADHD = 16% (N=4)
Schizophrenia = 0

20-25% of children with 22qDS will eventually develop a major psychiatric disturbance

22qDS Conclusions

Children with Chromosome 22q11.2 microdeletions:
1. Are not accurately represented by Full Scale IQ scores.
2. Display an NLD profile
3. Usually have normal rote memory skills.
4. Are at greatly increased risk for developing psychopathology.

A genetic etiology for NLD must map within the 22q11.2 microdeletion.

Why is this important?

- Provides support for a biological basis for NLD
- Helps predict strengths & weaknesses of children with 22qDS
- Provides insights into Normal reading and memory skills
Parent Resources for the NLD student

- Sue Thompson, *The Source for Nonverbal Learning Disability* (LinguiSystems)
- Peg Dawson & Richard Guare, *Executive Skills in Children and Adolescents: A practical guide to assessment and intervention* (Guilford Press)

NLD on the Web: www.nldontheweb.org
NLDline: www.nldline.com
LD Online (section on NLD): www.ldonline.org

---

Education Modifications for the NLD student

**Individualized Education Program (IEP)**

**Classification:**
- Other Health Impaired (OHI): medical problems
- Specific Learning Disability (SLD): if applicable
- LD, NOS: fine motor problems, inattention, etc.

**Section 504 Plan (IEP Lite?)**
- Civil Rights Law
- Case law supports 504 Plans for ADHD accommodations

---

Classroom Modifications for the NLD student

- Well-planned classroom schedule
- Consistent classroom rules & routines
- Clear presentation of assignments
- Elimination of distractions
- Special work station: desk placement near teacher
- Explicit identification of assignment goals and subgoals
- Frequent monitoring of student work pace and product
- Immediate feedback on performance

---

NLD Classroom Interventions

**Encourage / Train student to Self-Advocate**
- Feel comfortable asking clarifying questions
- Feel comfortable asking teacher to slow down
- Train them to recognize when they are inattentive
- Catch them being good: support pro-learning behavior
- Integrate home-based reward system for good classroom behavior (standard ADHD intervention)
- Involve / collaborate with parents

---

Adjunctive Software

**Earobics**
- *Step 1* (Ages 4 – 7) Six interactive games that focus on auditory skills.
- *Step 2* (Ages 7 – 10) Earobics for adolescents and adults (ages 10+)

**SoundBending**
- Inexpensive, multi-dimensional. Multiple ages.
Cogmed
- Working Memory training
- Auditory & Visual Skills
- Evidence-based ADHD intervention
- Web-based; can be done at home or school
- Weekly professional coaching calls
- 25 sessions / 40 minutes / 5X per week
- Multiple programs for different ages

Cogmed Working Memory Training: preliminary data