From ABC to ADHD

Eric Tridas, MD

April 3 & 4, 2009
The Hawai‘i Branch of the
International Dyslexia Association
The Developmental Web

Developmental Profile

Behavioral Profile

Health

Environment

Academic–Occupational
Behavioral–Emotional
Social Interaction
Health

Educational & Developmental

Behavioral & Cognitive

Medical

Environmental
Developmental Web

Contributing Factors to Clinical Presentation
Visual Perceptual Problems

- IMAGINE HOW CONFUSING IT WOULD BE IF EVERYTHING YOU READ LOOKED LIKE THIS!
- ORI FTH EWOR DSBE GINA NDEN DI NPLAC ESTH ATDON’NTM AKES ENSET OY OU?
- TAHW FI EHT SRETTEL EREW DESREVER, or OUT FO ODRER
- re o n al pa
  T oset aelv e g e.
  e ds m c er h
  h d t
Language Processing

- Phonology
- Semantics
- Morphology
- Syntax
- Discourse
- Metalinguistics
- Pragmatics
Tactile-kinesthetic Processing

• Impacts Fine Motor Function
  – Progresses in a proximal-distal fashion
  – Affected by:
    • Sense of body position or movement
    • Visual spatial processing
    • Verbal-motor integration
    • Motor planning
    • Motor sequential memory
    • Monitoring
    • Tone
    • Coordination
Memory

- Short Term
- Active working
- Long Term
Short Term Memory

- Holds information for a few seconds
- Limited storage capacity
- Depends on:
  - Volume
  - Modality
    - Visual, Auditory, Tactile - Kinesthetic
  - Attention
Working Memory

- Intermediate duration
- Holding an idea in mind while developing, elaborating, clarifying, using it
  - Recalling answers while thinking of the question
  - Complex math problems
  - Reading (summarizing/comparing while decoding
  - Selecting color while remembering what you are drawing
Working Memory

• Factors affecting it:
  – Attention
  – Rate
  – Volume
  – Automaticity of skill
Long Term Memory

• Unlimited storage capacity
• Long duration
• Retrieval affected by:
  – Relevancy of stimulus
  – Frequency of use
  – Strategy for memorization (consolidation)
Output

• Oral
  – Casual
  – Benefits from tone, gestures, etc.

• Written
  – Very formal
  – Depends on fine motor / graphomotor function
    • Motor sequences, pencil grip, spatial organization
Fine Motor Function

- Progresses in a proximal-distal fashion
- Affected by:
  - Sense of body position or movement
  - Visual spatial processing
  - Verbal-motor integration
  - Motor planning
  - Motor sequential memory
  - Monitoring
  - Tone
  - Coordination
Behavioral Profile

DEPRESSION
ANXIETY
OPPOSITIONAL-DEFIANT
CONDUCT
AUTISM
SCHIZOPHRENIA

INTERNALIZING
EXTERNALIZING
ATTENTION
ATYPICAL
Medical Factors

- Chronic Health Problems
- Associated Health Problems
- Iatrogenic Health Problems
Environmental Factors

- Temperament
- Parenting
- Stressors
- Parents
- Peers
- Temperament
- Physical Facility
- Curriculum Demands
- Teachers
Developmental Web

Management
Educational Management

Educational Therapy
Speech & Language Therapy
Occupational Therapy

REMEDIATION

Weakness

CIRCUMVENTION

Strengths

Volume
Rate
Technology
Complexity
Psychological Management

ADULT FOCUSED → Behavioral Therapy

CHILD FOCUSED → Cognitive Therapy
Medical Management

- MEDICATION
  - SURGERY
Environmental Management

HOME

SCHOOL
Dyslexia

Etiology
Phonological Processing
Phonology

- **Phoneme:**
  - Building block of words
  - Smallest unit of speech
  - There are 40 - 52 phonemes in the English language
  - Are put together to form words

- Words can be broken down into their elemental sounds allowing us to decipher words

- *Deficits in phonology strongly correlate with reading problems*
Phonologic System

- Processing and production of speech sounds
- Earliest language system to develop
- It is natural – does not have to be taught
- It is the foundation of language
Phonological Processing Deficits

Phonological Awareness → Rapid Naming → Phonological Memory → Phonological Awareness
Fluency

• The ability to read text
  – Quickly
  – Accurately
  – With good understanding
• The hallmark of a good reader
• Is the bridge between decoding and comprehension
• It is acquired word-by-word
Dyslexia Etiology

• Language problem specific to the *Phonologic Module*
  – Functional part of the brain where
    • Sounds of language (phonemes) are put together to form words
    • Words are broken down into their elemental sounds (phonemes)
    • Discriminates words from noise
  – Learning to read is not a natural biological process
Dyslexia: Neurobiology

Phoneme Processing
Speech
Visual Word - Fluency

Typical Readers
Dyslexic Readers
Typical Readers: Elision versus Repetition

Eden et al., 2004
Dyslexia: Neurobiology

Reading: Neurobiology
Phonological processing

Phoneme Processing

cat

k  æ  t

[Diagram showing brain activity and phoneme processing]
Reading: Neurobiology
Visual - Fluency

Visual Word - Fluency

cat
Reading Disability

\[(D \times F) + C = \text{Reading}\]

\[D = \text{Decoding}\]
\[F = \text{Fluency}\]
\[C = \text{Comprehension}\]

M. Joshi; IDA National Conference November 2004
Reading Disability

Text → Decoding Fluency → General Intelligence, Vocabulary, Word Identification, Reasoning, Concept Formation → Meaning
Early Identification

What to look for
Early Signs of Dyslexia

• By age of onset:
  – Delay in speaking
  – Difficulty in pronunciation
  – Insensitivity to rhyme
  – Poor word retrieval or word finding
  – Naming the letters and their sounds
Early Signs of Dyslexia

• Infants and toddlers
  – Delay in speaking
    • First word by 1 year
    • Phrases by 18 - 24 months
    • Parents may ascribe it to family history
      – Speech delay and dyslexia are familial
Early Signs of Dyslexia

• Preschool years
  – Difficulty in pronunciation
    • No “baby talk” by 5 or 6 years of age
    • Typical problems:
      – What to listen for
        » Omission of initial sounds: *lephant for elephant, chi-en for chicken*
        » Inverting sounds: *aminal for animal*
Early Signs of Dyslexia

• Preschool years
  – Insensitivity to rhyme
    • Unable to recite nursery rhymes
      – *Children that remember nursery rhymes tend to be good readers*
    • Unable to differentiate between similar and different words
      – Can not focus on parts of the words
        » What rhymes with: *food, talk*
Early Signs of Dyslexia

• Poor word retrieval or word finding
  – *Talking around a word (circumlocution)*
  – *Uses words like “stuff” or “things”*
Early Signs of Dyslexia

• Naming the letters and their sounds
  – Before entering Kindergarten
    • Knows the names of upper and lower case letters
  – Before entering 1st grade
    • Knows the names and sounds of letters
    • Alphabetic principle
      – Sequence of letters = number and sequence of sounds
    • Matches beginning sounds of words
    • Pronounces beginning sounds of words
    • Counts phonemes in small words
Early Signs of Dyslexia

• Typical development
  – 4 – 6 y/o aware that words come apart
  – 6 y/o 70% can count phonemes in small words

• Early signs of dyslexia
  – After 1 year of reading instruction (end of 1st grade) can’t separate sounds of spoken word
Common Signs of Dyslexia

• Problems with:
  – Phoneme segmentation
  – Phoneme deletion
  – Specific word retrieval (i.e. tornado for volcano, prostitute for prosecute)
  – Rapid word retrieval
History Screening: Infancy

- Single words by 1 yr
- Phrases by 2 yrs
- Family history of language or reading problems
# History Screening: Preschool

<table>
<thead>
<tr>
<th>End of K – 4</th>
<th>Y</th>
<th>N</th>
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</thead>
<tbody>
<tr>
<td>• Omission of sounds</td>
<td>□</td>
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<tr>
<td>– Eliminates initial sounds</td>
<td>(i.e., lephant for elephant)</td>
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<td></td>
</tr>
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<td>□</td>
<td>□</td>
</tr>
<tr>
<td>– Can’t memorize nursery rhymes</td>
<td></td>
<td></td>
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<tr>
<td>– Can’t tell if words rhyme</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Does not know lower case alphabet</td>
<td>□</td>
<td>□</td>
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</tbody>
</table>
History Screening: Kindergarten

By the end of year **CAN NOT:**

- Name upper and lower case alphabet
- Name most letter sounds
- Match beginning sounds to words
- Pronounce beginning sounds of words

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<thead>
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</table>
History Screening: 1st Grade

By the end of year **CAN NOT:**

- Can separate and / or count sounds in a word
- Find the right words
### Screening Test: End of 1st Grade

- **Alphabetic principle**
  - Names beginning letters of words
  - Names beginning sounds of words
  - Names ending letters of words
  - Names ending sounds of words
  - Can tell # of sounds in a word
### Screening Test: K.5 and 1\textsuperscript{st} Grade

<table>
<thead>
<tr>
<th>Rhyming</th>
<th>P</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Say a word that rhymes with</td>
<td></td>
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<tr>
<td>- Food</td>
<td></td>
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<tr>
<td>- Walk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can recite a rhyme</td>
<td></td>
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History Screening: Infancy

- Single words by 1 yr
- Phrases by 2 yrs
- Family history of language or reading problems
History Screening: Preschool

**End of K – 4**

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History Screening: Kindergarten

By the end of year **CANNOT:**

- Name upper and lower case alphabet
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# History Screening: 1st Grade

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<td><strong>•</strong> Can separate and / or count sounds in a word</td>
<td></td>
<td>■ ■</td>
</tr>
<tr>
<td><strong>•</strong> Find the right words</td>
<td>■</td>
<td>■</td>
</tr>
</tbody>
</table>
Screening Test: End of 1st Grade

- Alphabetic principle
  - Reads the words accurately
  - Names beginning letters of words
  - Names beginning sounds of words
  - Names ending letters of words
  - Names ending sounds of words
  - Can tell # of sounds in a word
Screening Test: K.5 and 1st Grade

• Rhyming
  – Say a word that rhymes with
    • Food
    • Walk
Intervention

What to do about it.
Research Based Reading Instruction

- Essential Components
  - *Phonemic awareness*
    - Recognize, remember and manipulate individual sounds
  - *Phonics and word recognition*
    - Sound – symbol relationship, word meaning
  - *Reading Fluency*
    - Read with sufficient speed an accuracy to support comprehension
  - *Vocabulary development*
    - Individual word meanings
  - *Reading comprehension*
    - Verbal reasoning, background knowledge, comprehension strategies
Reading Instruction

• Other components
  – *Basic writing skills*
    • Compose English with accuracy, fluency and clarity of expression
  – *Comprehending and using language*
    • The ability to listen and understand the meaning of what someone is saying
Effective Reading Instruction

• Explicit
  – Clearly and directly explained not left to discovery
• Systematic
  – The speech sounds, spelling patterns, sentence structures, text genre and language conventions
• Cumulative
  – Continual review one skill builds on another
• Multisensory
• Sequential and Incremental
  – Manageable steps
• Data driven
  – Emphasis, speed of instruction and support are determined by student's progress
Dyslexia: Management

• Critical to start before 3rd grade
• It is almost impossible to remediate after 4th grade
Early Intervention IS Urgent

- **10TH %ile 5th Grade reader**
  - 50,000 words/year
- **50TH %ile 5th grade reader**
  - 600,000 words/year
- **Average students receive approximately 10 TIMES as much practice in a year**

<table>
<thead>
<tr>
<th>Percentile Rank</th>
<th>Minutes Per Day</th>
<th>Books</th>
<th>Text</th>
<th>Words Read Per Year</th>
<th>Books</th>
<th>Text</th>
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<tr>
<td>98</td>
<td>65.0</td>
<td>4,358,000</td>
<td>4,733,000</td>
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<tr>
<td>90</td>
<td>21.2</td>
<td>1,823,000</td>
<td>2,357,000</td>
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<tr>
<td>80</td>
<td>14.2</td>
<td>1,146,000</td>
<td>1,697,000</td>
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<tr>
<td>70</td>
<td>9.6</td>
<td>622,000</td>
<td>1,168,000</td>
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<tr>
<td>60</td>
<td>6.5</td>
<td>432,000</td>
<td>722,000</td>
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<tr>
<td><strong>50</strong></td>
<td><strong>4.6</strong></td>
<td><strong>282,000</strong></td>
<td><strong>601,000</strong></td>
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<td></td>
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<tr>
<td>40</td>
<td>3.2</td>
<td>200,000</td>
<td>421,000</td>
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<td>30</td>
<td>1.8</td>
<td>106,000</td>
<td>251,000</td>
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<td>20</td>
<td>0.7</td>
<td>21,000</td>
<td>134,000</td>
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<td><strong>10</strong></td>
<td><strong>0.1</strong></td>
<td><strong>9,000</strong></td>
<td><strong>51,000</strong></td>
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<td></td>
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<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>8,000</td>
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</tbody>
</table>

Dyslexia: Management

Dyslexia-specific brain activation profile becomes normal following successful remedial training

Simos, Fletcher, et al. Neurology, 2002
What About Attention?

ADHD:
What it is and what is not!
ADHD: Historical Timeline

Hyperkinetic Reaction of Childhood (DSM-II)

Minimal Brain Damage

Attention Deficit Hyperactivity Disorder (DSM-III-R)


Minimal Brain Dysfunction

ADHD-like syndrome first described

Attention Deficit Disorder + or - Hyperactivity (DSM-III)

Attention Deficit/Hyperactivity Disorder (DSM-IV)
Diagnostic Criteria for ADHD: 

*DSM-IV*

- Persistent symptoms of inattention and/or impulsivity and hyperactivity
- Onset of symptoms before age 7
- Impairment in 2 or more settings (eg, school, work, home)
- Evidence of clinically significant impairment in social, academic, or occupational functioning
- Symptoms not a result of other disorders

DSM-IV Diagnostic Criteria

Symptoms for ADHD

- Inattention (≥6)
  - Is careless
  - Has difficulty sustaining attention in activity
  - Does not listen
  - Does not follow through with tasks

- Is disorganized
  - Avoids/dislikes tasks requiring sustained mental effort
  - Loses important items
  - Is easily distracted
  - Is forgetful in daily activities

DSM-IV Diagnostic Criteria
Symptoms for ADHD (cont’d)

- Hyperactivity (≥6)
  - Squirms and fidgets
  - Cannot stay seated
  - Runs/climbs excessively
  - Cannot play/work quietly
  - Is on the go/driven by a motor
  - Talks excessively

- Impulsivity
  - Blurts out answers
  - Cannot wait turn
  - Intrudes/interrupts others

ADHD: *DSM-IV* Subtypes

- **ADHD Combined Type**
  - Criteria are met for both inattention and impulsivity/hyperactivity ($\geq 6$ of each)

- **ADHD Inattentive Type**
  - Criteria met for inattention but not for impulsivity/hyperactivity ($\geq 6$)

- **ADHD Hyperactive-Impulsive Type**
  - Criteria met for impulsivity/hyperactivity but not for inattention ($\geq 6$)
ADHD: Comorbid Conditions

Comorbidity is common with ADHD.

- Oppositional Disorder (40-50%)
- Anxiety Disorder (35%)
- Conduct Disorder (10%)
- Mood Disorder (5-25%)

ADHD Only (50%)
Etiology
A Variety of Functional & Structural Differences Appear in the ADHD Brain

Twin Studies Show ADHD
Is a Genetic Disorder

Average genetic contribution of ADHD based on twin studies

- Hudziak, 2000
- Nadder, 1998
- Levy, 1997
- Sherman, 1997
- Silberg, 1996
- Gjone, 1996
- Thapar, 1995
- Schmitz, 1995
- Edelbrock, 1992
- Gillis, 1992
- Goodman, 1989
- Willerman, 1973

Impairment Caused by ADHD

How does it present?
Impact on quality of life
Impairment

Academic
Behavioral/Emotional
Socialization
Medical
Impairment

- ADHD is a disorder of performance, not skill
- ADHD disrupts executive function
- ADHD creates problems with self-regulation
- ADHD increases health risks
Impairment

- ACADEMIC
  - Production vs. Knowledge
- BEHAVIOR - EMOTIONAL
  - Spacey/Over-Reactive vs. Defiant
- SOCIALIZATION
  - Insatiable vs. Malicious
- MEDICAL
  - Cigarette smoking, Car accidents, SUD
ADHD: Impairment over time
ADHD: Impact on Family

Parents of children with ADHD experience higher levels of:

- Stress
- Self-blame
- Social isolation
- Depression
- Marital discord

ADHD: Adults
Performance Limitations

- Despite similar educational levels and IQ scores, non-medicated adults with ADHD display:
  - Significantly more academic difficulty in school (25% repeat a grade)
  - Lower levels of occupational advancement

ADHD Affects Socialization

• Children are stigmatized by their behavior
  – Disruptive behavior
    • Troublemakers
    • Bad sportsmanship
    • Excessive talking
    • Cannot sit still
    • Unfocused, not responsive to others
    • Impulsive aggression
  – Immaturity and impulsiveness
    • Center of attention
    • Breaks the rules
    • Blurting out answers
    • Peer rejection

• Adolescents continue to demonstrate social problems
  • Poor participation in group activities
  • Few friends
  • Vulnerable to antisocial groups, drug abuse
Increased Traffic Violations and Motor Vehicle Accidents in Adolescents and Adults with ADHD

Increased Smoking with ADHD

Adult patients with ADHD

- Current smokers
  - ADHD: 40.8%
  - General population: 25.8%

- Quit ratio
  - ADHD: 29%
  - General population: 48.5%

*Smokers Quit ratio

*P<0.01

Earlier Initiation of Smoking with ADHD

6- to 17-year-old boys

P<0.003

Untreated ADHD Is Associated With Higher Risk of Substance Abuse

Adolescent & Adult Outcome

- Symptoms Persist in 50-65%
- Associated Problems
  - Conduct
  - Emotional
  - Socialization
  - Education
  - Employment
- Satisfactory Outcome in 60-70%
Management of ADHD
Good Management of ADHD Involves Multimodal Therapy

Multimodal Therapy

Medication
- Stimulants
- Antidepressants
- SNRI’s

Psychosocial Therapy
- Parent Training
- Child-Focused Treatment
- School-Based Intervention

Normalization in Many Areas
MTA Study Objective and Design

Objective:
• To compare the long-term efficacy of pharmacotherapy, behavioral therapy, and combination therapy in the treatment of ADHD

Protocol:
• Population: 579 children with ADHD combined type, aged 7-9.9 years
• In a 4-group parallel design, children randomly assigned to:
  – Medication alone (primarily methylphenidate)
  – Behavioral therapy alone
  – Combination of medication and behavioral treatment
  – Routine community care (medication and behavioral treatment)
• Duration of study treatment: 14 months

The MTA Cooperative Group. *Arch Gen Psychiatry*. 1999;56:1073-1086.
Long-term Outcomes of Therapies for ADHD in the MTA Study

Hyperactive Impulsive Symptoms (Teacher Reports)

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Improvement at 14 months (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication management</td>
<td>56%</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>60%</td>
</tr>
<tr>
<td>Behavioral treatment</td>
<td>45%</td>
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<tr>
<td>Community-based treatment</td>
<td>36%</td>
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</tbody>
</table>
The Developmental Web

- Developmental Profile
- Behavioral Profile
- Health
- Environment

Academic – Occupational
Behavioral – Emotional
Social Interaction
Health

- Educational & Developmental
- Behavioral & Cognitive
- Medical
- Environmental
American Academy of Pediatrics: Guidelines for the Treatment of ADHD

- Establish a treatment program that recognizes ADHD as a chronic condition
- Specify appropriate target outcomes to guide management
- Prescribe stimulant medication and/or behavior therapy to improve target outcomes in children with ADHD
- **If the treatment program has not met target outcomes, evaluate:**
  - Original diagnosis
  - Use of all appropriate treatments
  - Adherence to the treatment plan
  - Presence of coexisting conditions
- Using information from parents, teachers, and the child, follow-up to evaluate target outcomes and adverse effects

Types of Medications Used In Managing ADHD

**STIMULANTS**
- methylphenidate
  - Immediate Release
  - d-methylphenidate
- Amphetamines
  - Immediate Release Pulse
  - Immediate Release Pulse
  - lisdexamfetamine
- Mixed Amphetamines

**SNRI’s**
- Atomoxetine

**ADHD**
Dopamine
Norepinephrine
Rt k
Reuptake pumps
Medication
Receptors
Dopamine
Norepinephrine
Reuptake pumps
Medication
Receptors
Proposed Effect of Stimulants

Increase Dopamine Production

Atomoxetine

Amphetamines
Methylphenidate

Decreases Dopamine Reuptake
Medications: Clinical Impact

- Increase control of attention
- Increase impulse control
- Decrease activity
- Decrease disruptive behavior
- Improve handwriting (in 50%)
Medications: Clinical Impact

- Academic
- Behavior
- Socialization

- Increase Production
- Increase Compliance
- Decrease Disruption
- Increase Awareness
Stimulant Medications

• Side Effects
  – Insomnia (50-60%)
  – Anorexia (50-60%)
  – Irritability (30%)
  – Headache
  – Stomachache
  – Nausea
  – Tics
Atomoxetine: Side Effects

- Anorexia
- Dizziness - Sleepiness
- Dyspepsia
- Dermatitis
- Constipation
- Mood Swings
- Transient elevation of liver enzymes
- Increased suicidality
Medications: Duration of Action

- Short Acting: 4 hours
- Intermediate Acting: 6 – 8 hours
- Long Acting: 8 – 12 hours, 24 hours
# Medications

- **Short-Acting**
  - Ritalin, Dexedrine, DextroStat, Focalin Methylin (Tablet, Chewable & Liquid)

- **Intermediate-Acting**
  - Ritalin SR, Metadate ER, Adderall, Ritalin LA, Metadate-CD, Methylxir, Focalin XR

- **Long-Acting**
  - Dexedrine Spansules, Cylert, Adderall-XR, Concerta, Daytrana, Vyvanse

- **24 hours**
  - Strattera
MPH OROS (Concerta®)

![Graph showing concentration over time for MPH 10 mg tid (n=15) and CONCERTA® 36 mg qd (n=15).](image)

- **IR MPH 10 mg tid (n=15)**
- **CONCERTA® 36 mg qd (n=15)**

Outer Coat of Medicine
MPH SODAS™ (Ritalin® LA) Pulse Release

Each Ritalin® LA capsule contains 50% immediate-release beads and 50% extended-release beads.

How the extended-release beads work:
1. Over 4 hours, fluid creates small pores through polymer coating
2. Fluid enters and dissolves the Ritalin® layer
3. This provides a second release of Ritalin® equivalent to the immediate release

SODAS™ is a trademark of Elan Corporation, Plc
Pulse Delivery System (SODAS, Difucaps)
Mixed Amphetamine Salts (Adderall XR®) Formulation Study

Bioequivalence of Adderall XR® 20 mg QD to Adderall® 10 mg BID

Daytrana DOT Matrix™
Transdermal Technology

- Methylphenidate is mixed with adhesive

DOT Matrix is a trademark of Noven Pharmaceuticals, Inc.
Pharmacokinetics with Daytrana

Lower limit of quantification 0.25 ng/mL.

Application and Removal/Disposal

- Holding the patch down, the rest of the liner should be removed slowly and the exposed half should be pressed against the skin.
- The patch should be pressed down with the palm of the hand for 30 seconds.
- Upon removal, the patch should be folded in half, with sticky sides together, and discarded immediately in toilet or lidded container.
**Vyvanse™**

- Is a pro-drug
  - Inactive until the body breaks it down
- Combines an amphetamine and an amino acid
  - Dextroamphetamine and lysine
- It lasts 12+ hrs
- Not affected by GI transit time or pH
Atomoxetine (Strattera<sup>™</sup>) Efficacy

Long-Term Efficacy (76 Weeks) (cont.)

*<sup>p</sup><.01 for Strattera vs placebo.
*p<.001 for Strattera within-group change.
Behavioral Management

What to do at Home
Core Principles for Behavior Management

- Immediacy of Consequences
- Frequency of Consequences
- Saliency of Consequences
- Frequent Changes in Rewards
- Act, Don’t Yack
- Positives Before Negatives
- Anticipate Problems
- Pick Your Fights - Prioritize
- Expect Variability
- Practice Forgiveness
It is not your fault…

But it is your problem