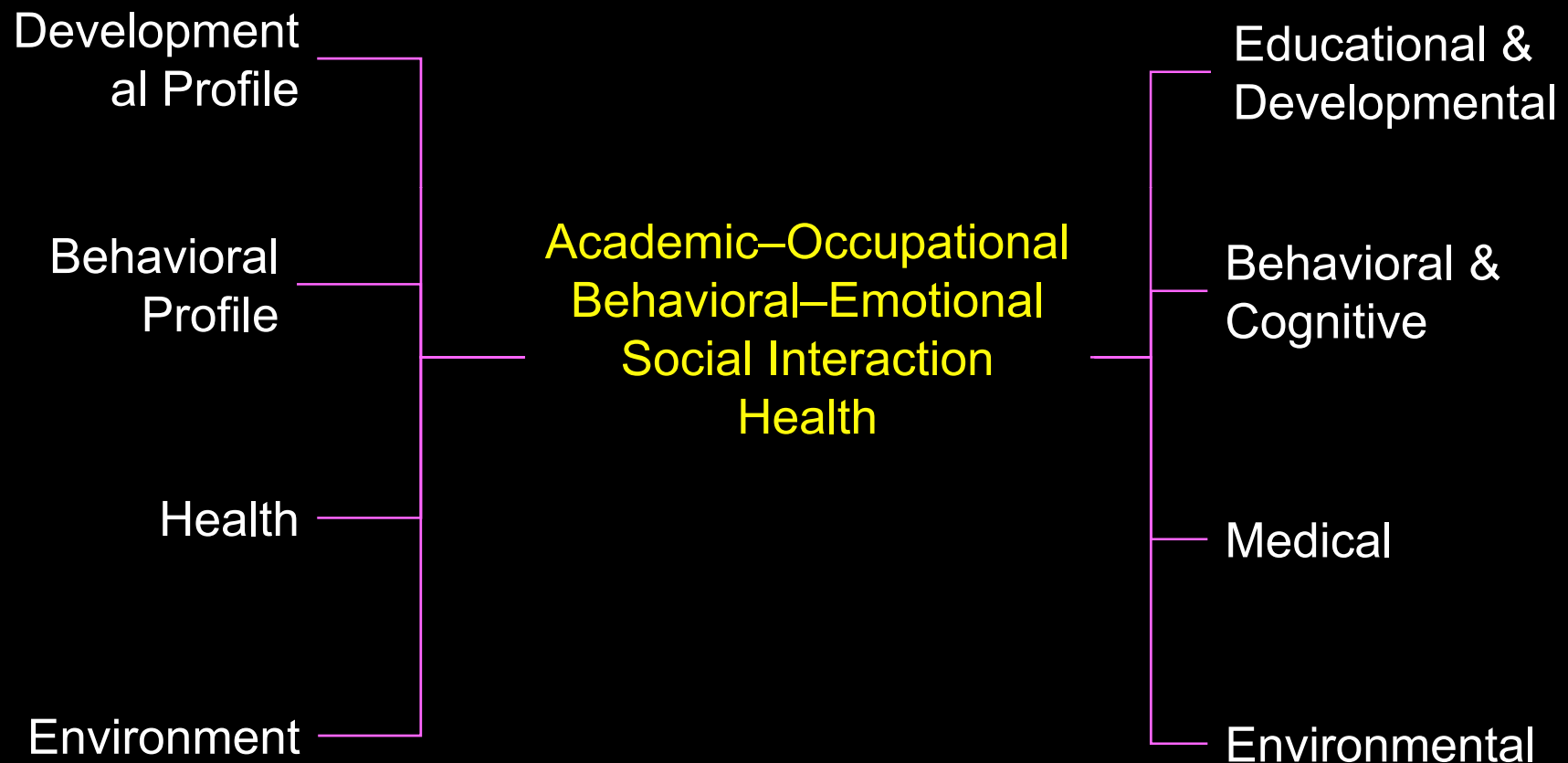


From ABC to ADHD

Eric Tridas, MD

*April 3 & 4, 2009
The Hawai'i Branch of the
International Dyslexia Association*

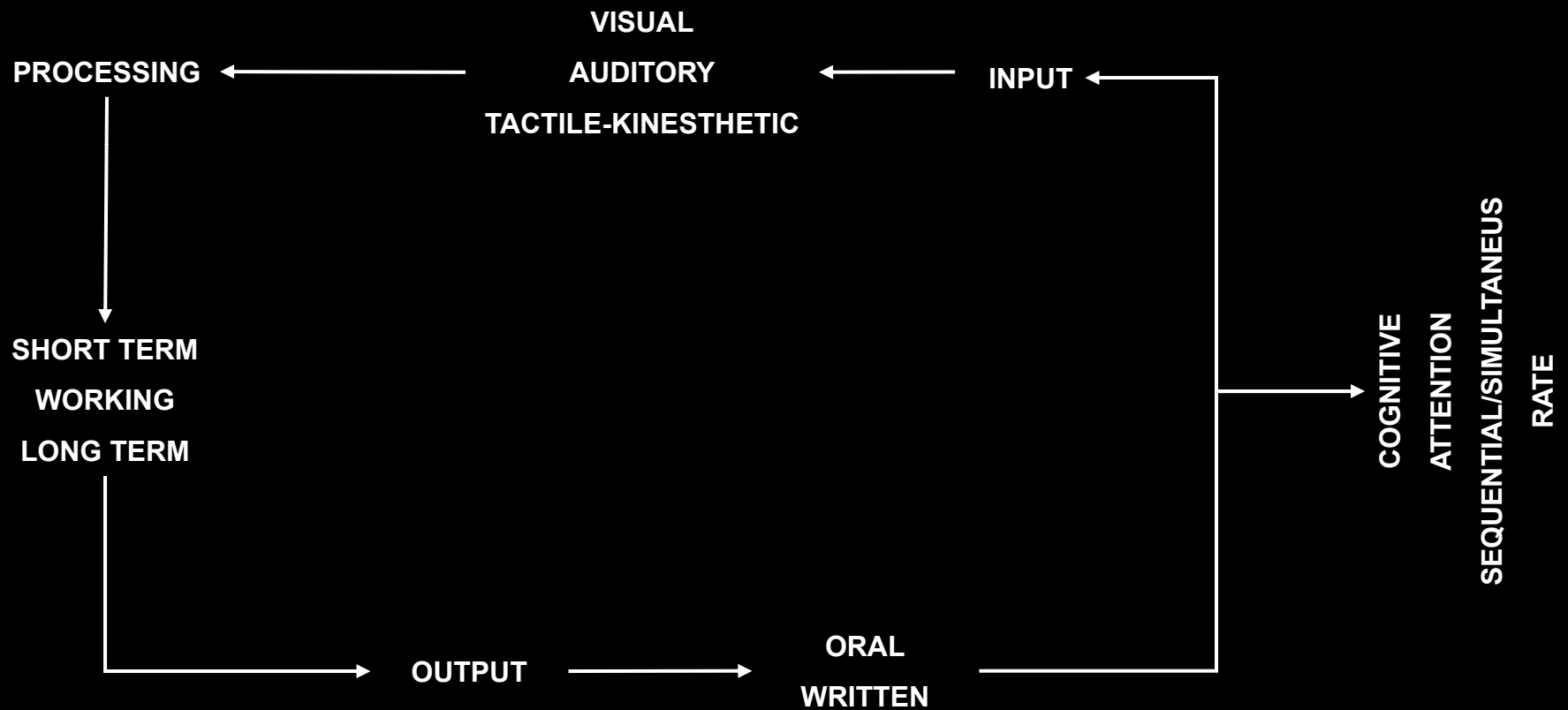
The Developmental Web



Developmental Web

Contributing Factors
to Clinical Presentation

Developmental Profile



Visual Perceptual Problems

- IMAGINEHOWCONFUSINGITWOULDBEIFEVERYTHINGYOUREADLOOKEDLIKETHIS!
- ORIFTHEWORDSBEGINDENONPLACESTHATDON'TMAKESENSETOYOU?
- TALKFIRETHESRETTLEWEREDESREVER, or
OUT OF ORDER
- w r e o n a l p a
T o s e t a e l v e g e .
e d s m c e r 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)

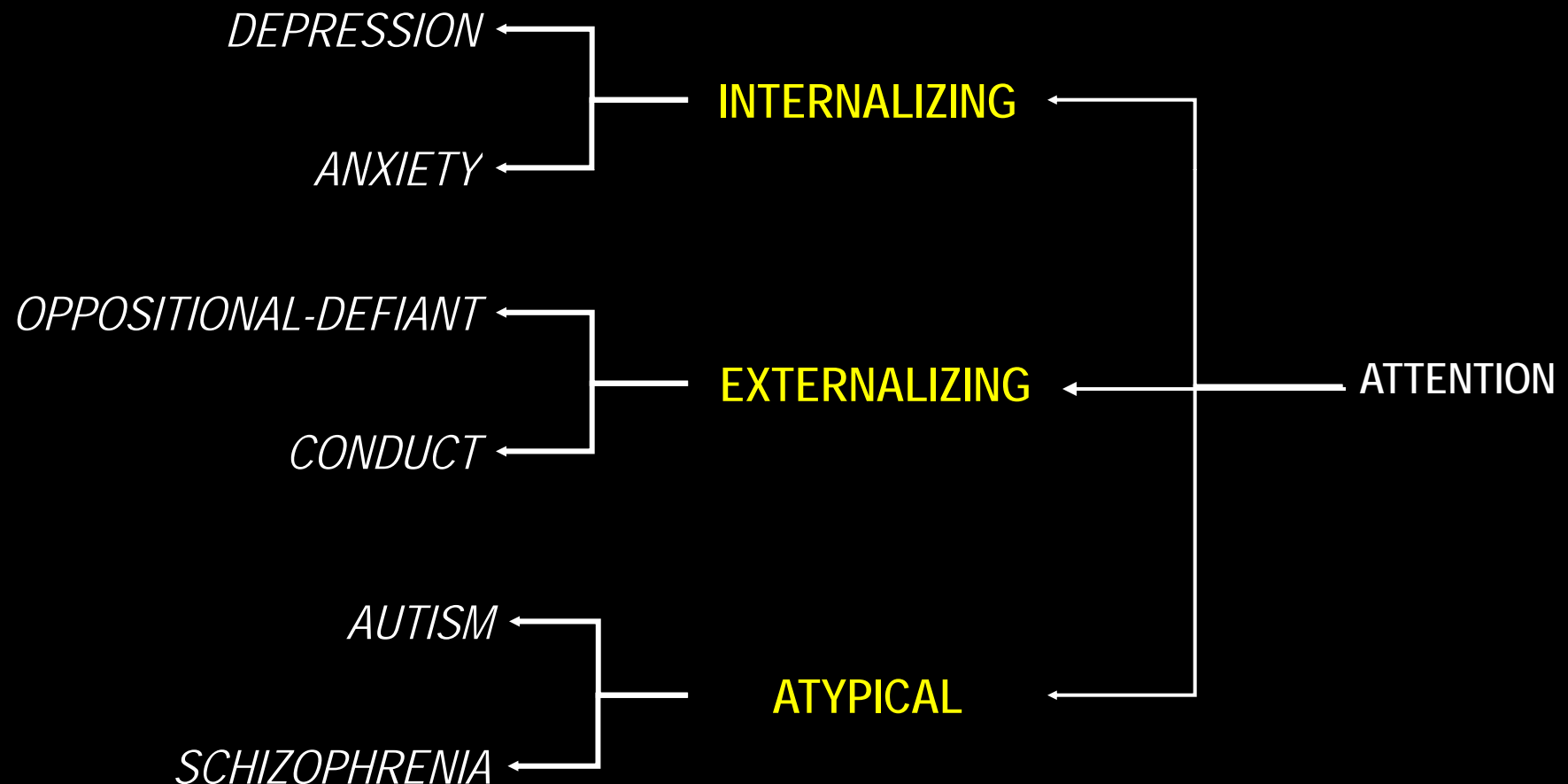
Output

- Oral
 - Casual
 - Benefits from tone, gestures, etc.
- Written
 - Very formal
 - Depends on fine motor / graphomotor function
 - Motor sequences, pencil grip, spatial organization

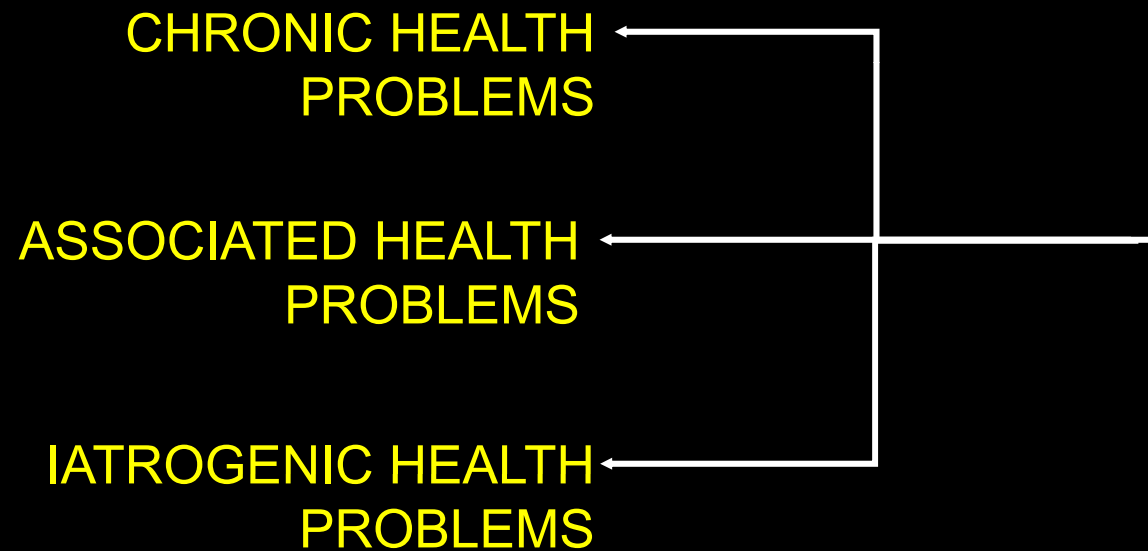
Fine Motor Function

- 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

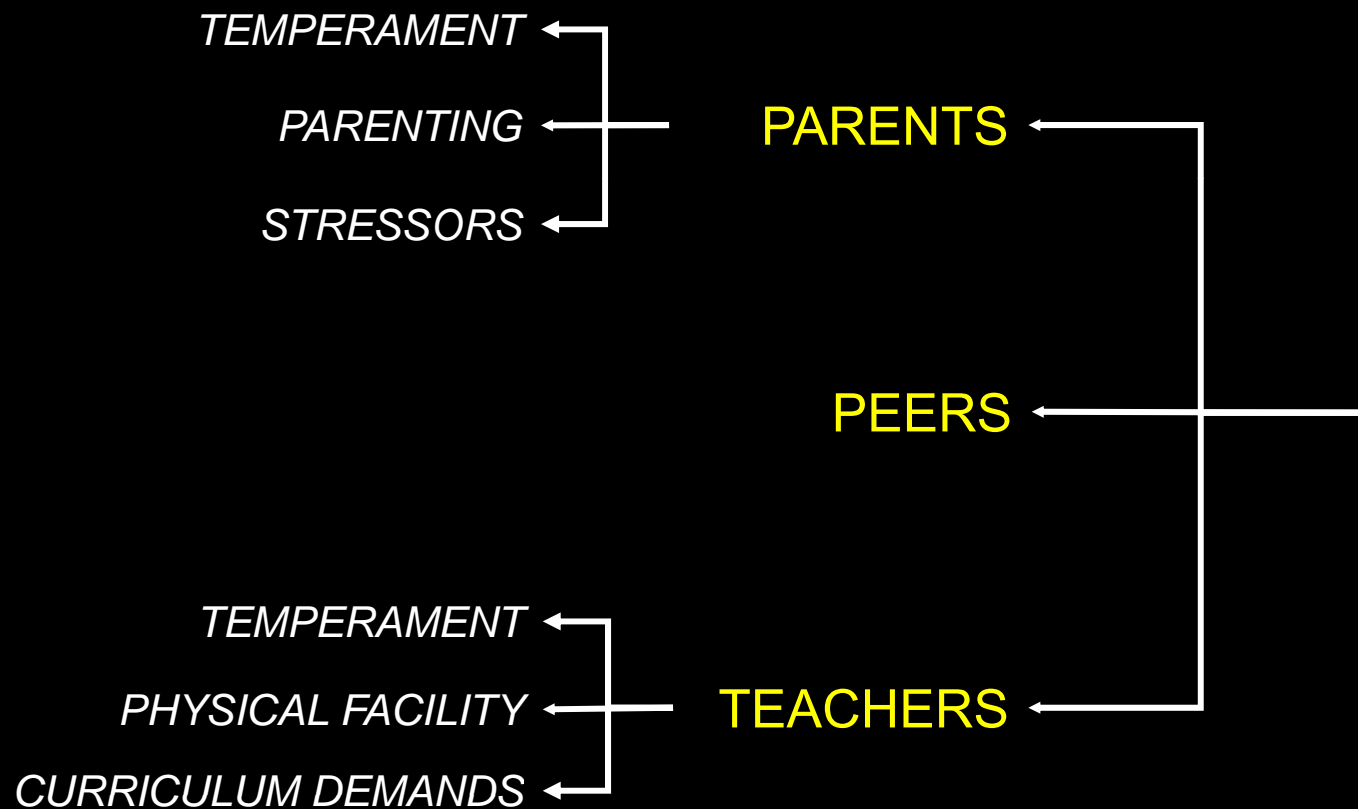
Behavioral Profile



Medical Factors



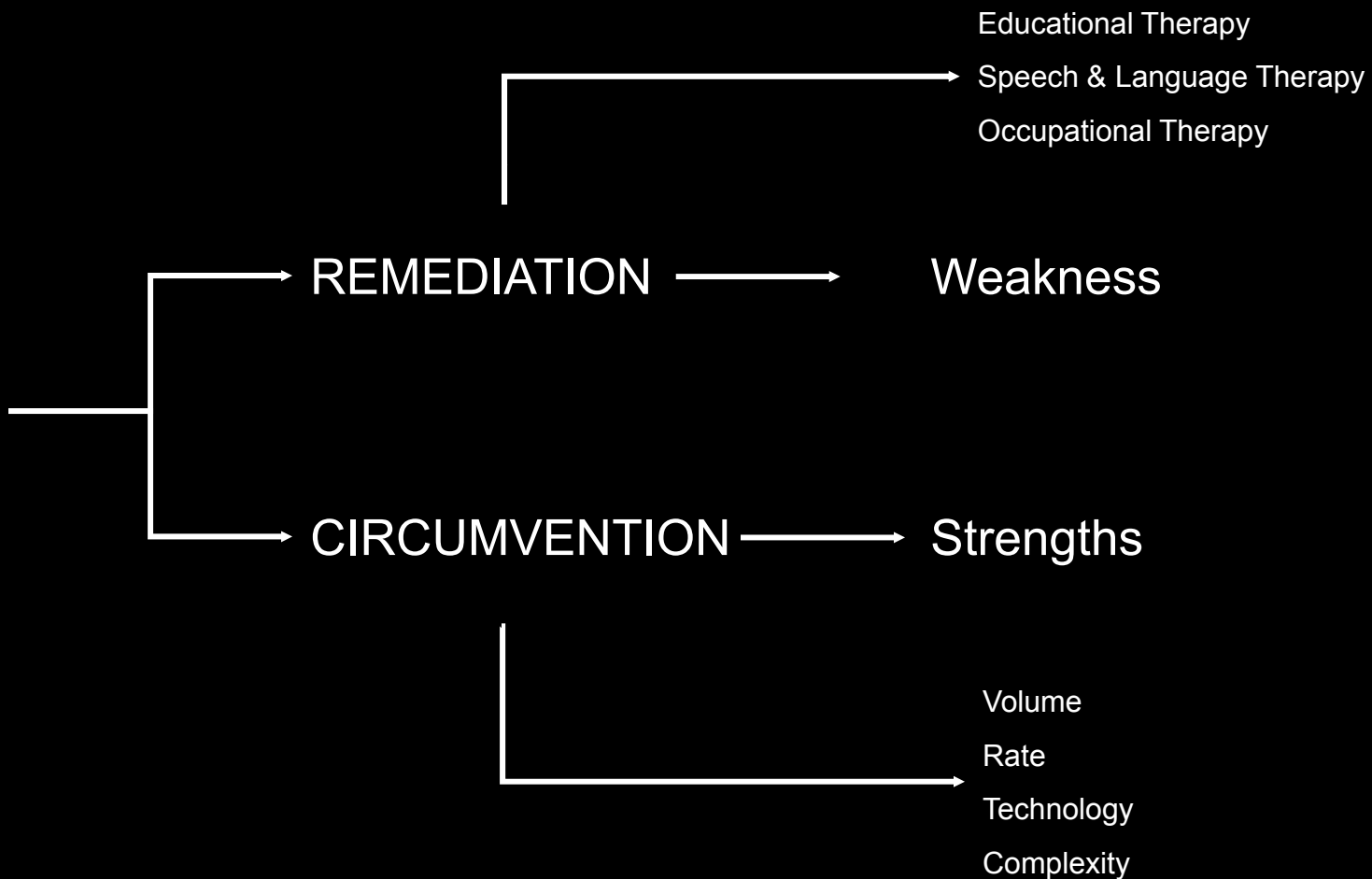
Environmental Factors



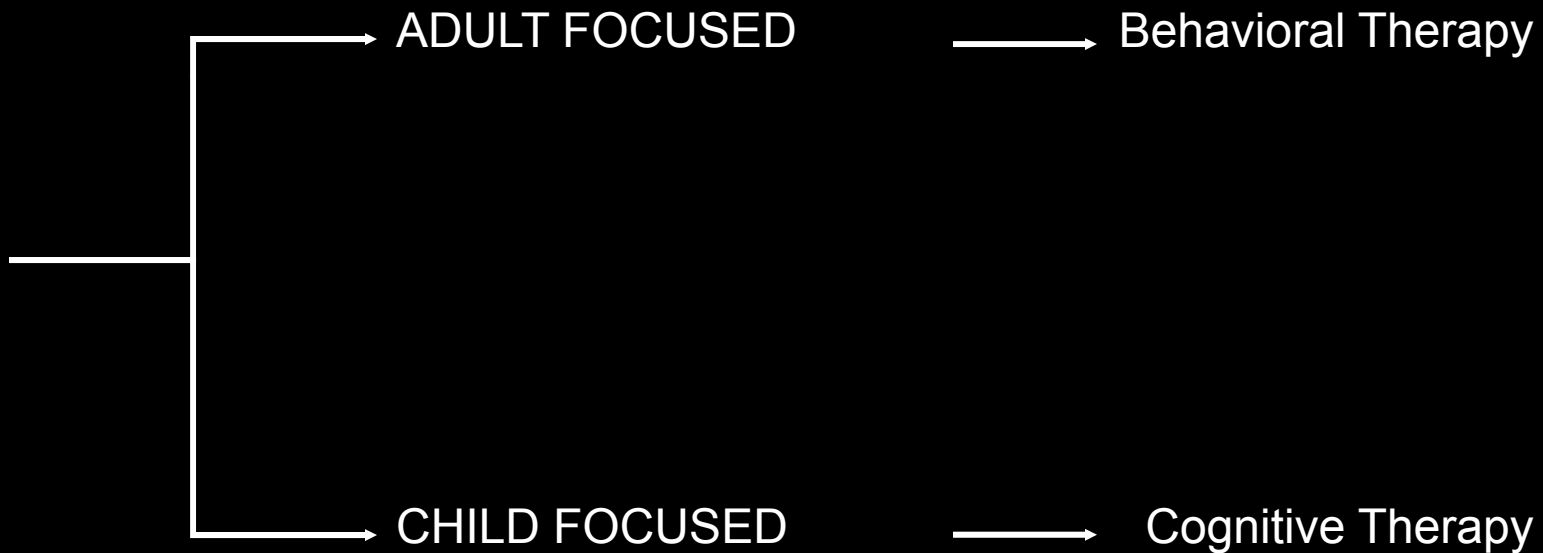
Developmental Web

Management

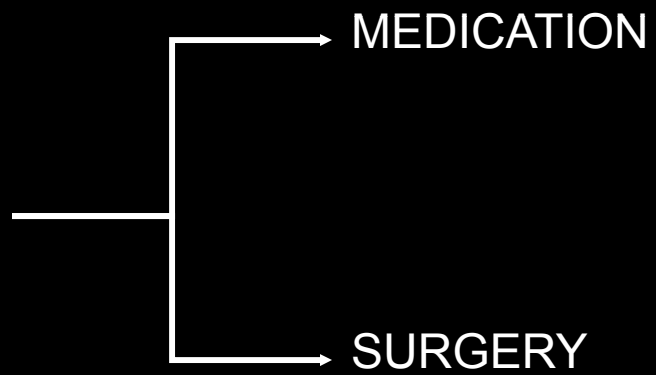
Educational Management



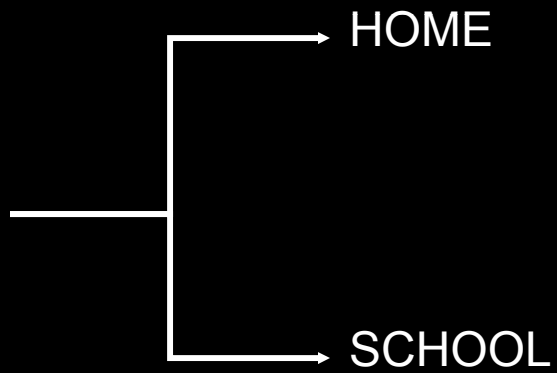
Psychological Management



Medical Management



Environmental Management



Dyslexia

Etiology

Phonological Processing

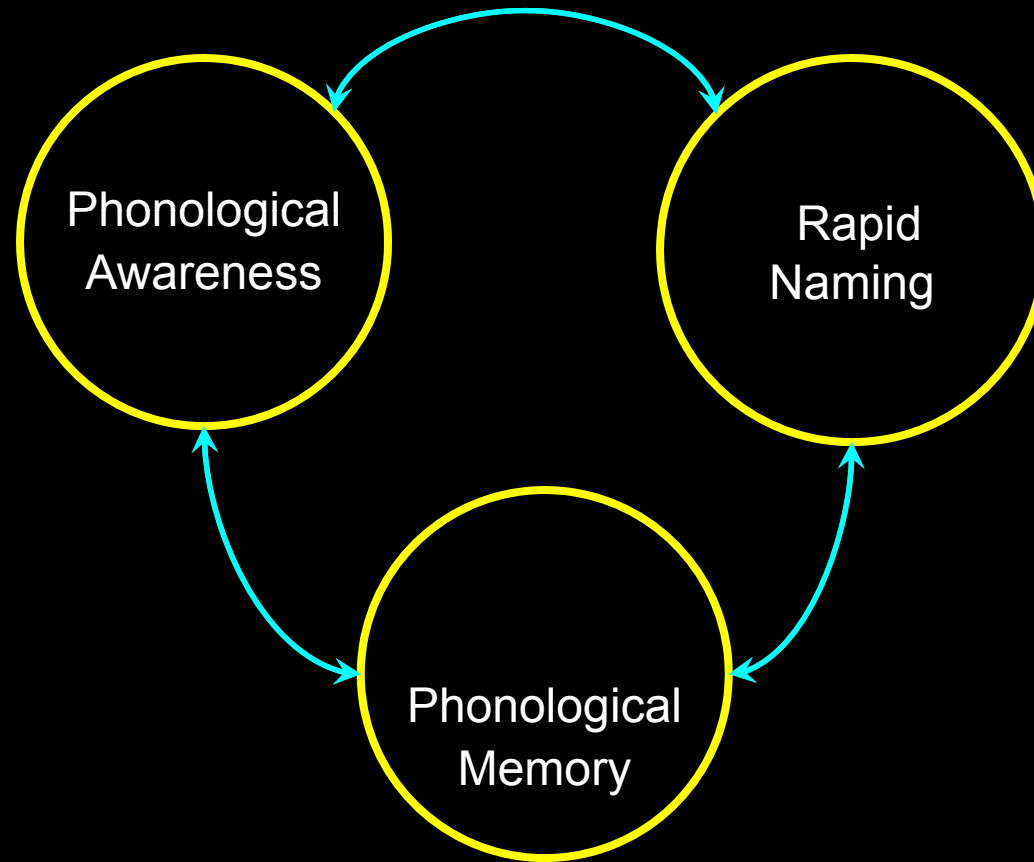
Phonology

- 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



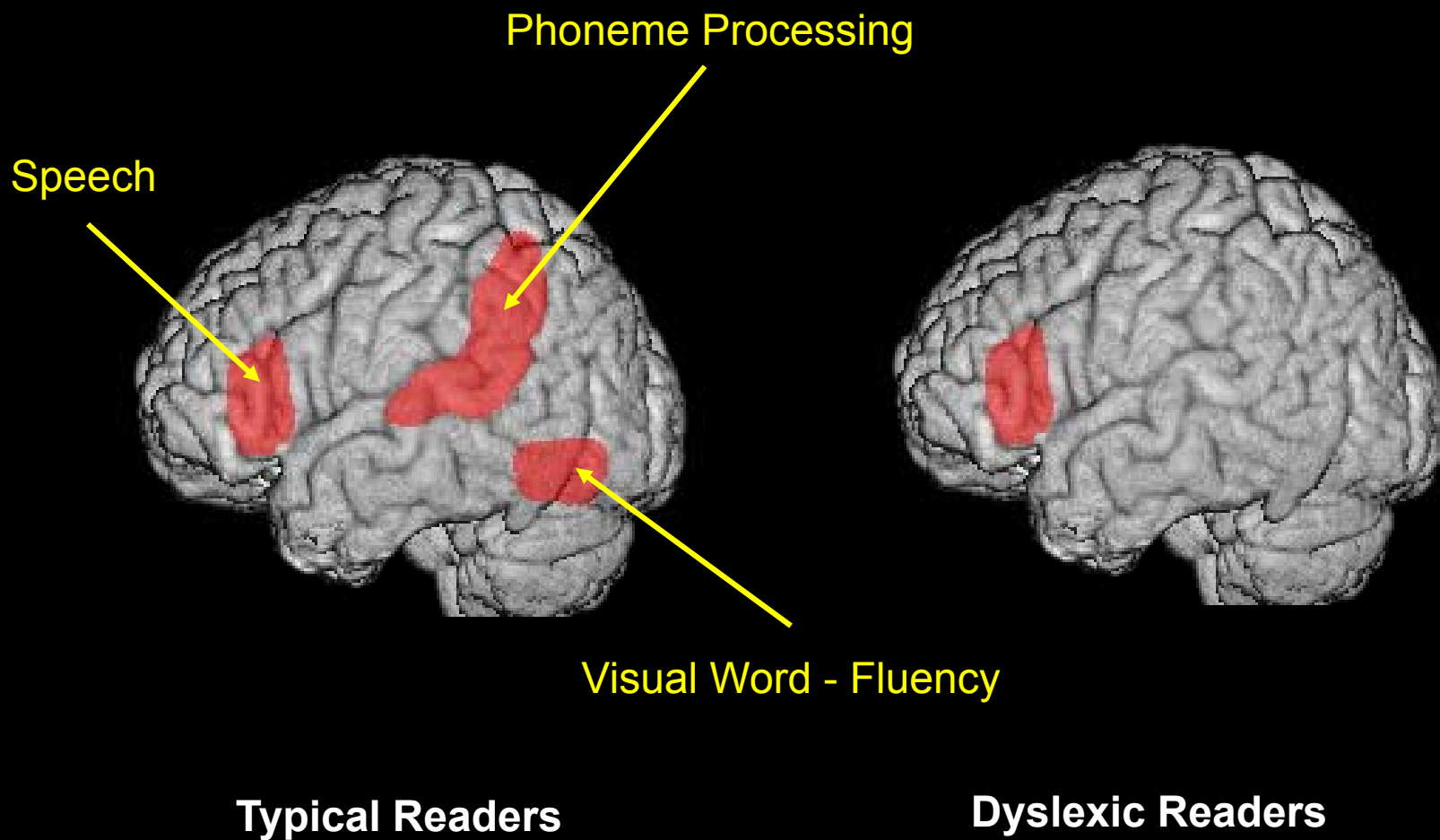
Fluency

- 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

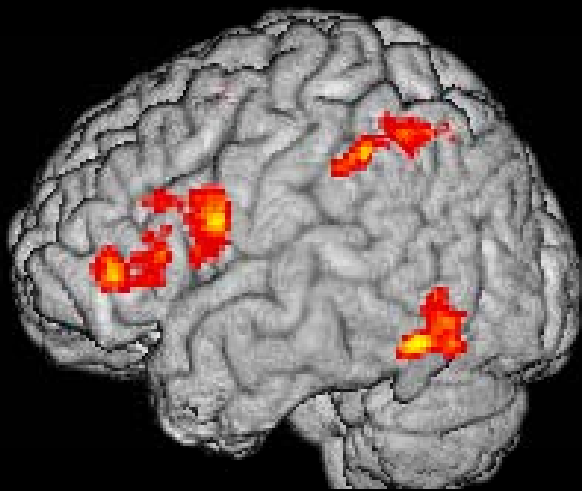
Dyslexia Etiology

- 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

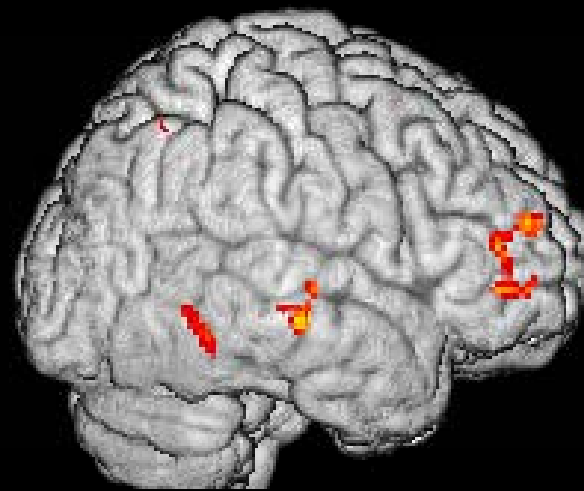
Dyslexia: Neurobiology



Typical Readers: Elision versus Repetition

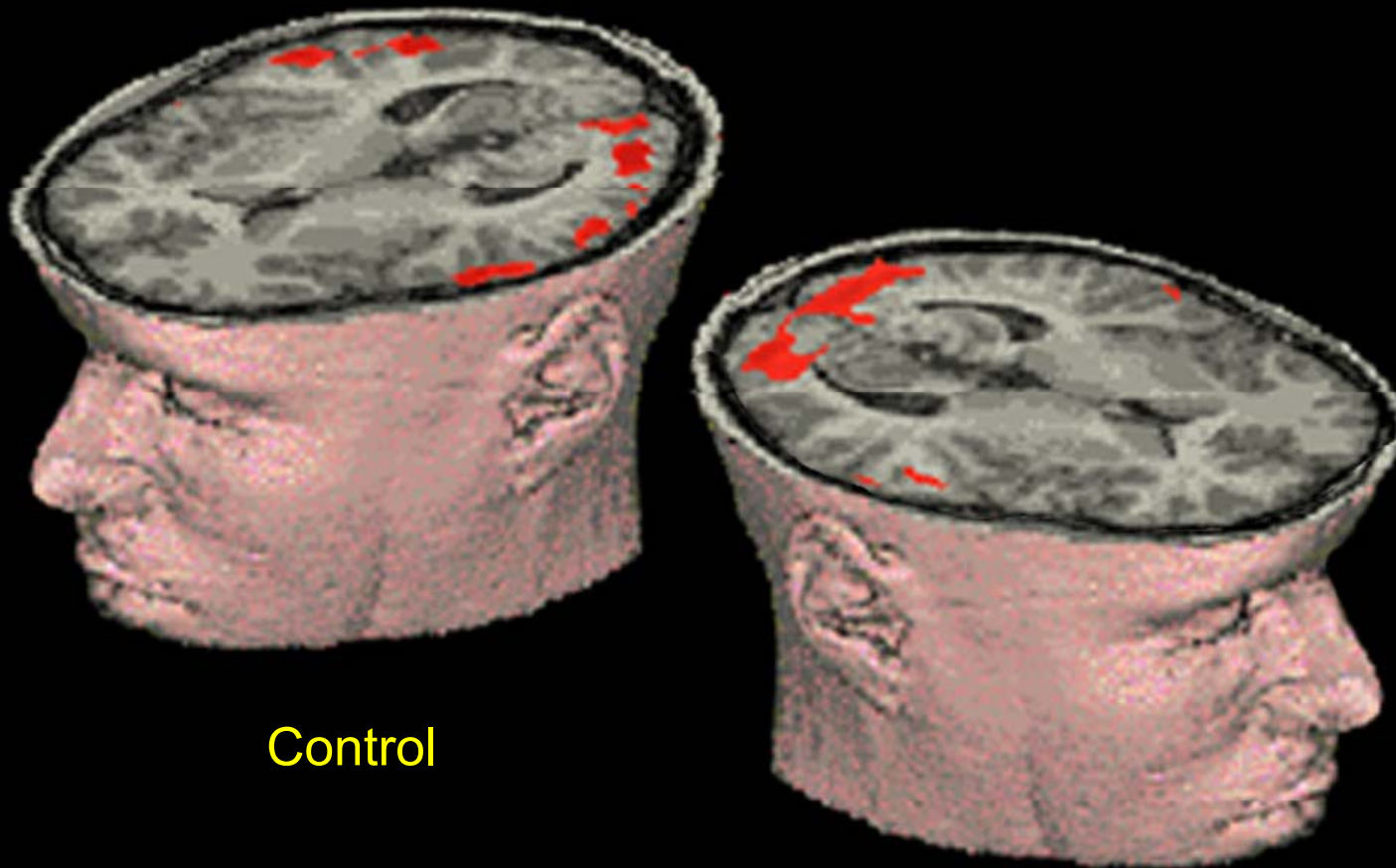


left



right

Dyslexia: Neurobiology



Control

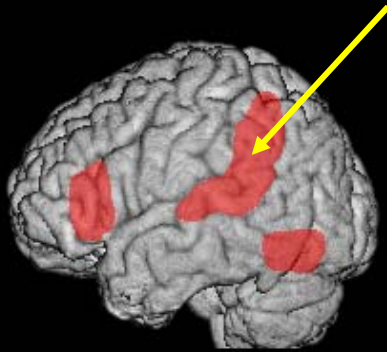
Dyslexic

Eden et al. Nature 1996

Reading: Neurobiology

Phonological processing

Phoneme Processing



cat



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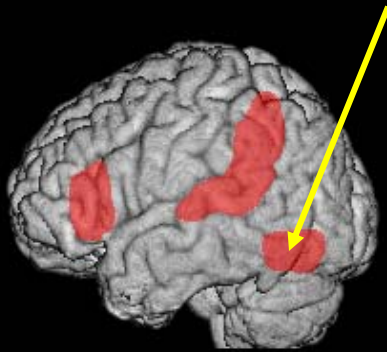
t



Reading: Neurobiology

Visual - Fluency

Visual Word - Fluency



cat



Reading Disability

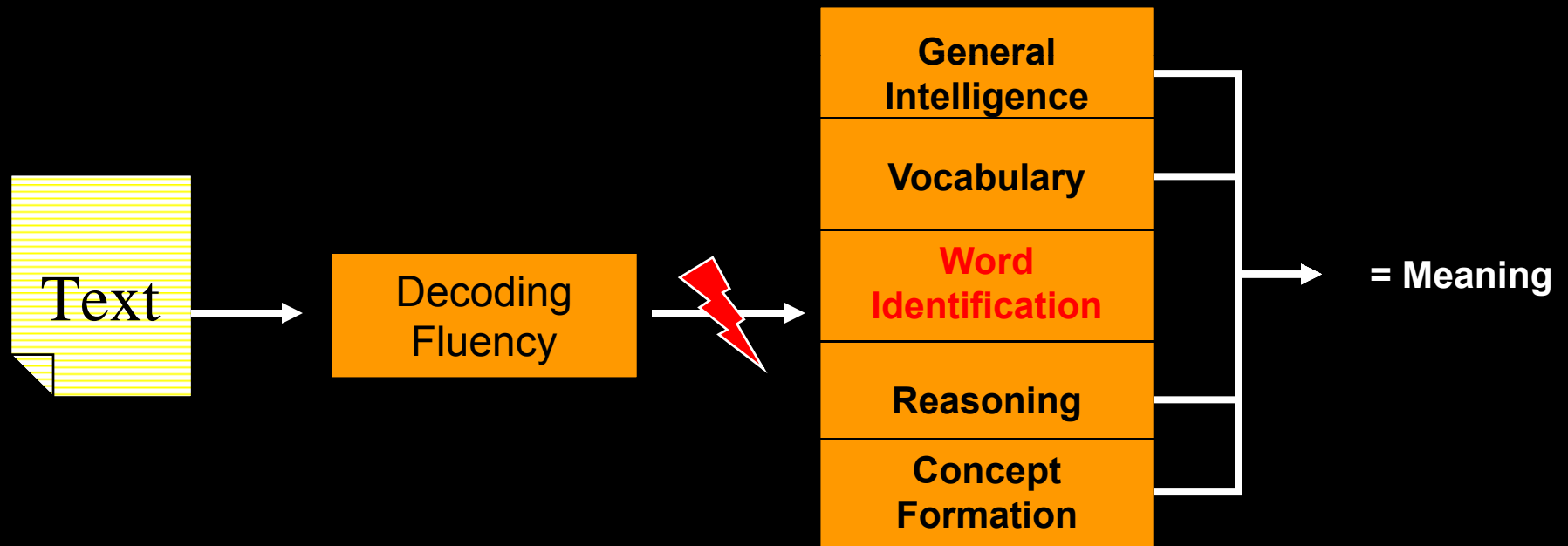
$$(D \times F) + C = \text{Reading}$$

D = Decoding

F = Fluency

C = Comprehension

Reading Disability



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

	Y	N
• Single words by 1 yr	<input type="checkbox"/>	<input type="checkbox"/>
• Phrases by 2 yrs	<input type="checkbox"/>	<input type="checkbox"/>
• Family history of language or reading problems	<input type="checkbox"/>	<input type="checkbox"/>

History Screening: Preschool

End of K – 4

	Y	N
• Omission of sounds – Eliminates initial sounds (i.e., lephant for elephant)	■	■
• Inverts sounds (aminal for animal)	■	■
• Insensitivity to rhyme – Can't memorize nursery rhymes – Can't tell if words rhyme	■	■
• Does not know lower case alphabet	■	■

History Screening: Kindergarten

By the end of year <u>CAN NOT:</u>	Y	N
• Name upper and lower case alphabet	<input type="checkbox"/>	<input type="checkbox"/>
• Name most letter sounds	<input type="checkbox"/>	<input type="checkbox"/>
• Match beginning sounds to words	<input type="checkbox"/>	<input type="checkbox"/>
• Pronounce beginning sounds of words	<input type="checkbox"/>	<input type="checkbox"/>

History Screening: 1st Grade

By the end of year CAN NOT:

- Can separate and / or count sounds in a word
- Find the right words

Y

N



Screening Test: End of 1st Grade

• Alphabetic principle	P	F
– 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

	P	F
• Rhyming		
– Say a word that rhymes with		
• Food	■	■
• Walk	■	■
– Can recite a rhyme	■	■

History Screening: Infancy

	Y	N
• Single words by 1 yr	<input type="checkbox"/>	<input type="checkbox"/>
• Phrases by 2 yrs	<input type="checkbox"/>	<input type="checkbox"/>
• Family history of language or reading problems	<input type="checkbox"/>	<input type="checkbox"/>

History Screening: Preschool

End of K – 4

	Y	N
• Omission of sounds – Eliminates initial sounds (i.e., -lephant for elephant, chi-en for chicken)	■	■
• Inverts sounds (aminal for animal)	■	■
• Insensitivity to rhyme – Can't tell if words rhyme	■	■
• Does not know lower case alphabet	■	■

History Screening: Kindergarten

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

Y

N

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



History Screening: 1st Grade

By the end of year CAN NOT:

- Can separate and / or count sounds in a word
- Find the right words

Y

N



Screening Test: End of 1st Grade

- | | P | F |
|------------------------------------|-----------------------|-----------------------|
| • Alphabetic principle | | |
| – Reads the words accurately | <input type="radio"/> | <input type="radio"/> |
| – Names beginning letters of words | <input type="radio"/> | <input type="radio"/> |
| – Names beginning sounds of words | <input type="radio"/> | <input type="radio"/> |
| – Names ending letters of words | <input type="radio"/> | <input type="radio"/> |
| – Names ending sounds of words | <input type="radio"/> | <input type="radio"/> |
| – Can tell # of sounds in a word | <input type="radio"/> | <input type="radio"/> |

Screening Test: K.5 and 1st Grade

- | | P | F |
|-------------------------------|-----------------------|-----------------------|
| • Rhyming | | |
| – Say a word that rhymes with | | |
| • Food | <input type="radio"/> | <input type="radio"/> |
| • Walk | <input type="radio"/> | <input type="radio"/> |

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 and 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

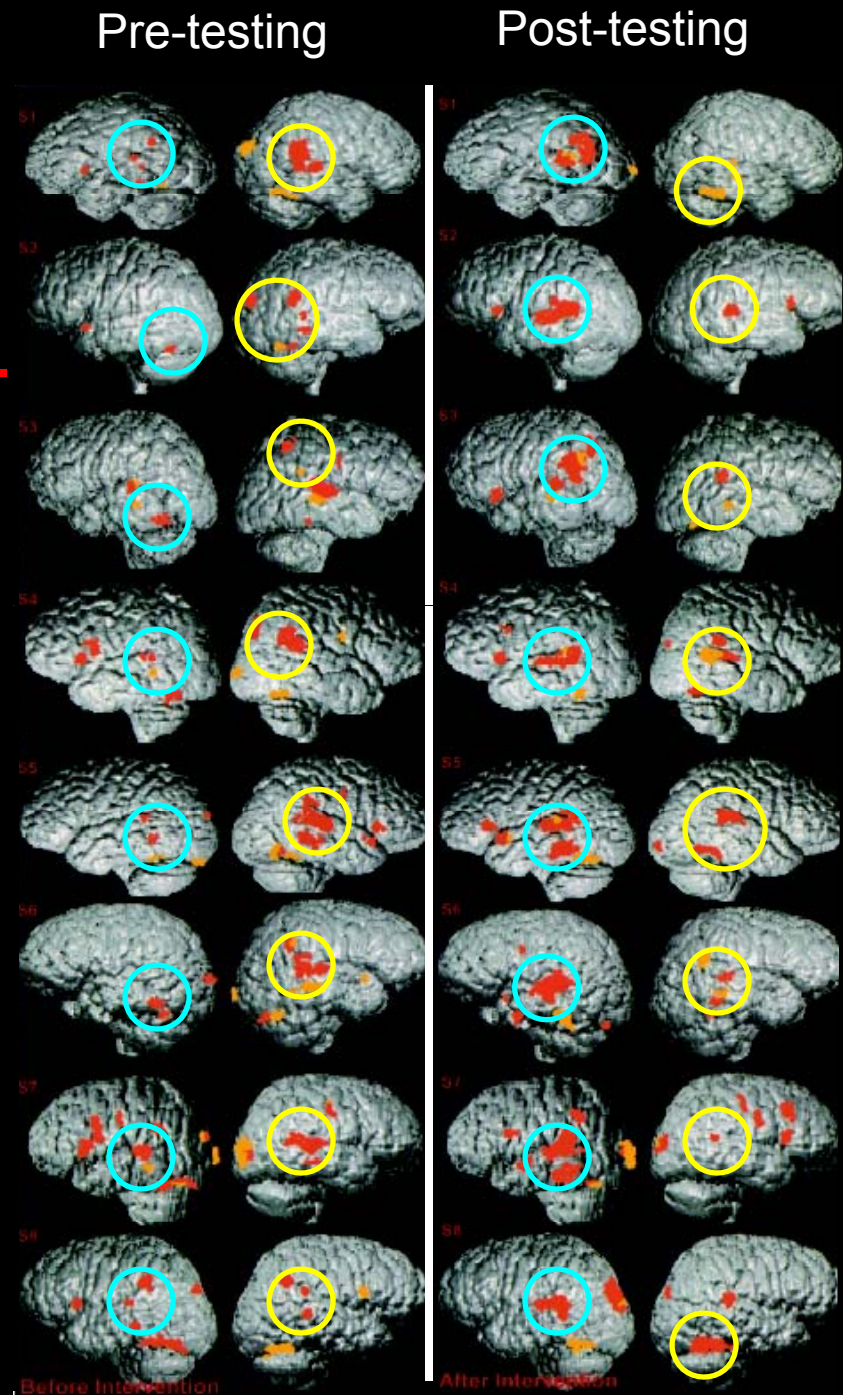
Early Intervention IS Urgent

- **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**

Percentile Rank	Minutes Per Day		Words Read Per Year	
	Books	Text	Books	Text
98	65.0	67.3	4,358,000	4,733,000
90	21.2	33.4	1,823,000	2,357,000
80	14.2	24.6	1,146,000	1,697,000
70	9.6	16.9	622,000	1,168,000
60	6.5	13.1	432,000	722,000
50	4.6	9.2	282,000	601,000
40	3.2	6.2	200,000	421,000
30	1.8	4.3	106,000	251,000
20	0.7	2.4	21,000	134,000
10	0.1	1.0	8,000	51,000
2	0	0	0	8,000

Dyslexia: Management

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



What About Attention?

ADHD:

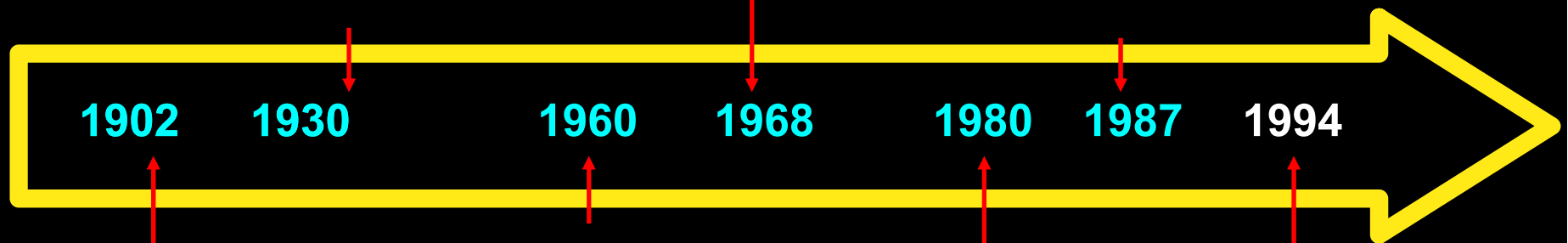
What it is and what is not!

ADHD: Historical Timeline

Hyperkinetic Reaction
of Childhood (DSM-II)

Attention Deficit Hyperactivity
Disorder (DSM-III-R)

Minimal Brain Damage



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

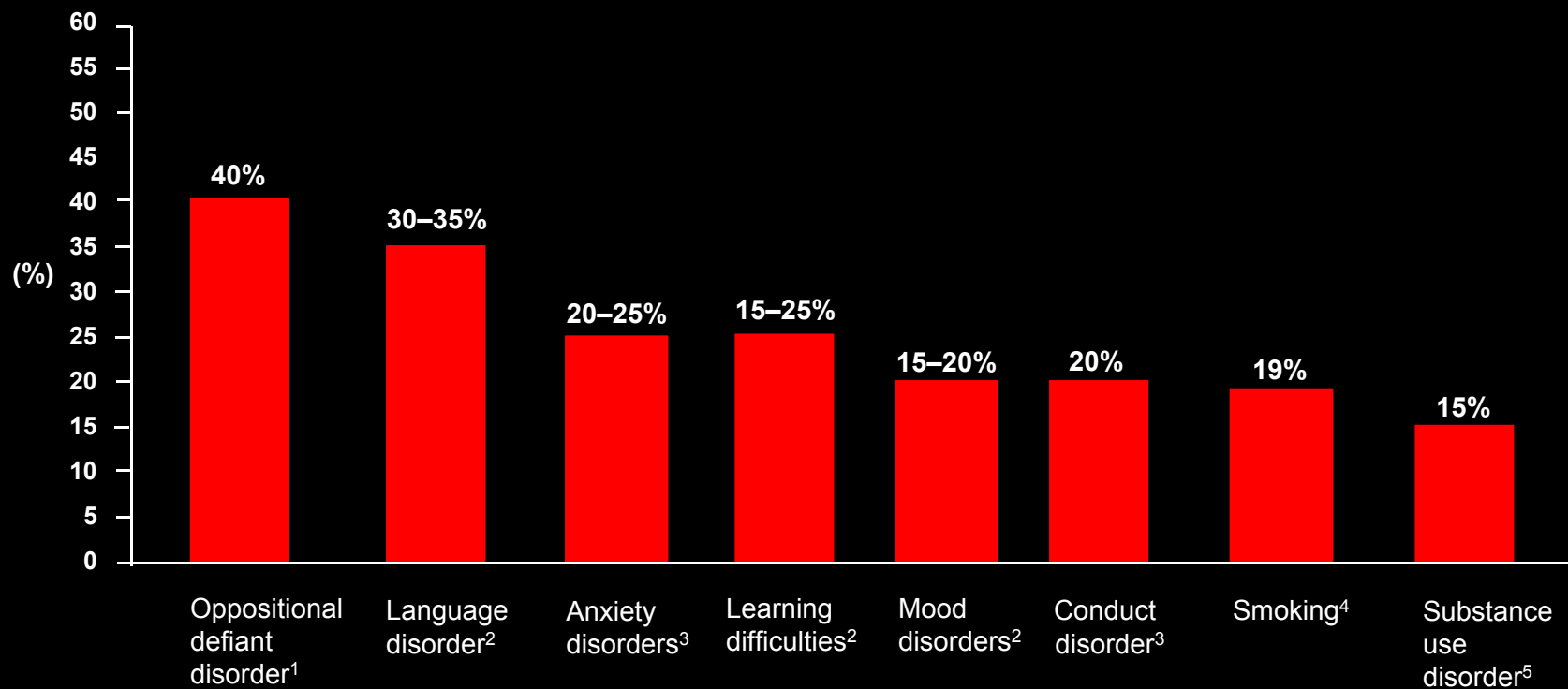
Symptoms for ADHD (cont'd)

- 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 (≥ 6 of each)
- ADHD **Inattentive Type**
 - Criteria met for inattention but not for impulsivity/hyperactivity (≥ 6)
- ADHD **Hyperactive-Impulsive Type**
 - Criteria met for impulsivity/hyperactivity but not for inattention (≥ 6)

ADHD: Comorbid Conditions



¹MTA Cooperative Group. *Arch Gen Psychiatry* 1999; 56:1076–1086.

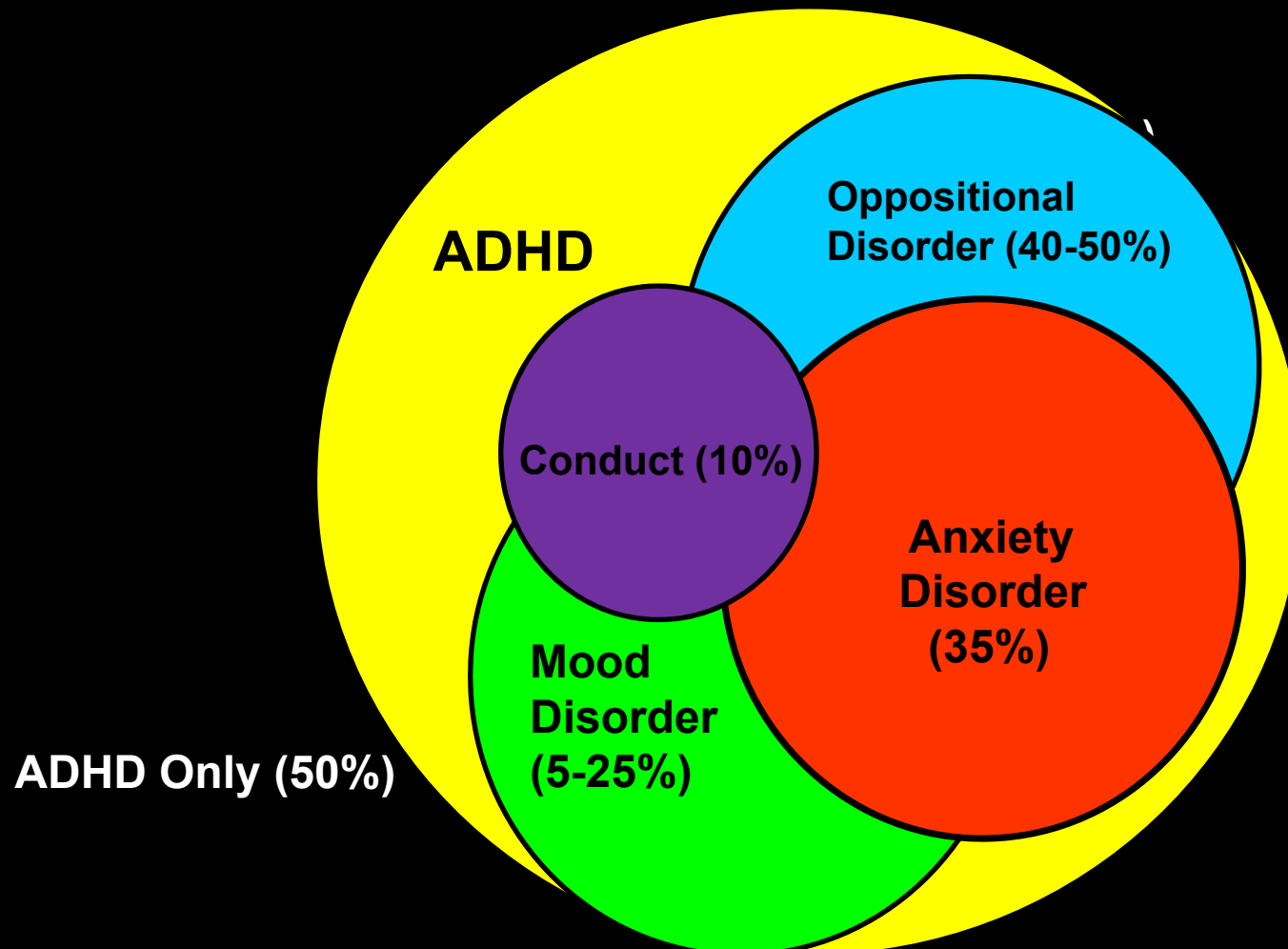
²Barkley R. *Attention-deficit Hyperactivity Disorder. A Handbook for Diagnosis and Treatment*, 2nd ed. New York: Guilford Press, 1993.

³Biederman J, et al. *Am J Psychiatry* 1991; 148:565–577.

⁴Milberger S, et al. *J Am Acad Child Adolesc Psychiatry* 1997;36:37–44.

⁵Biederman J, et al. *J Am Acad Child Adolesc Psychiatry* 1997;36:21–29.

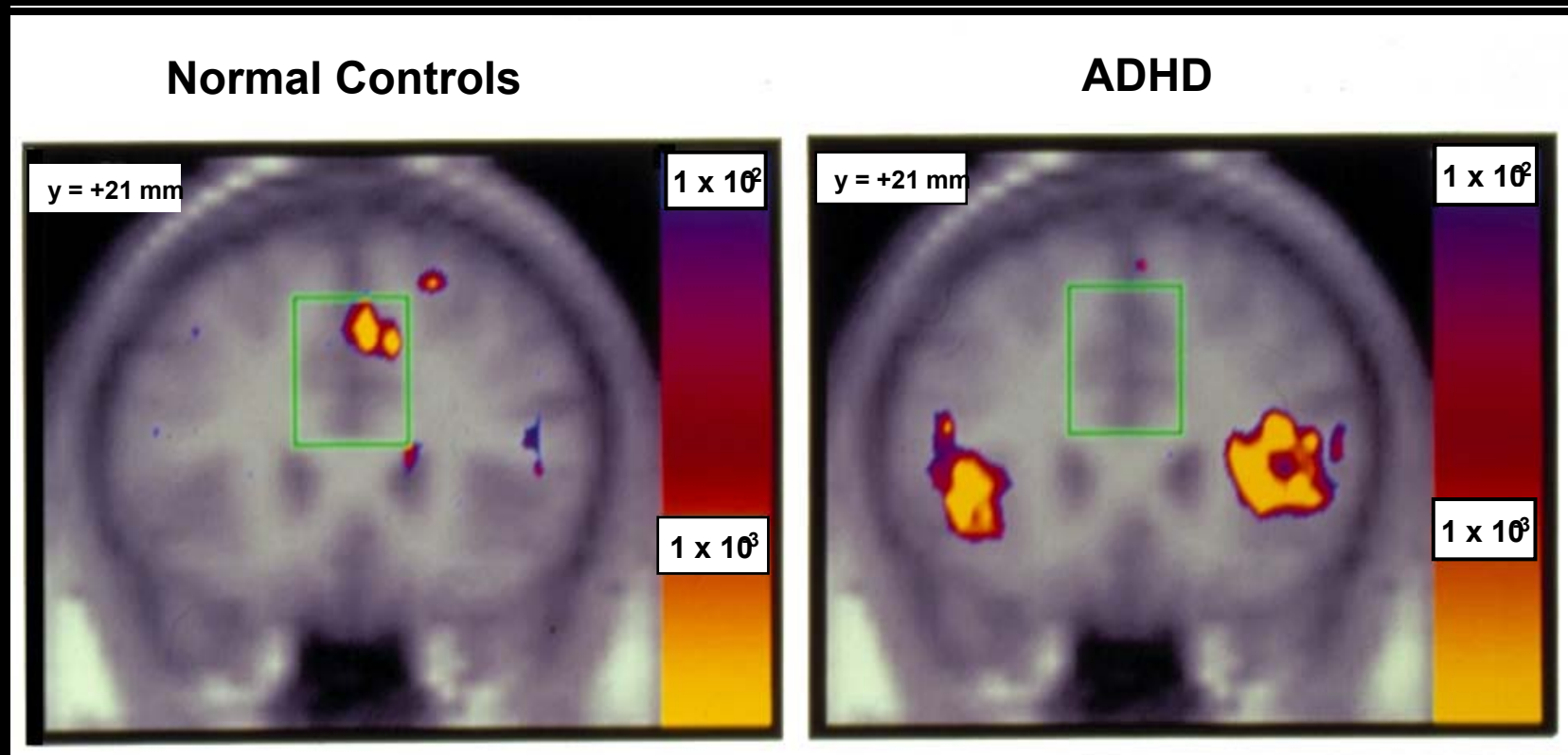
Comorbiditys Common With ADHD





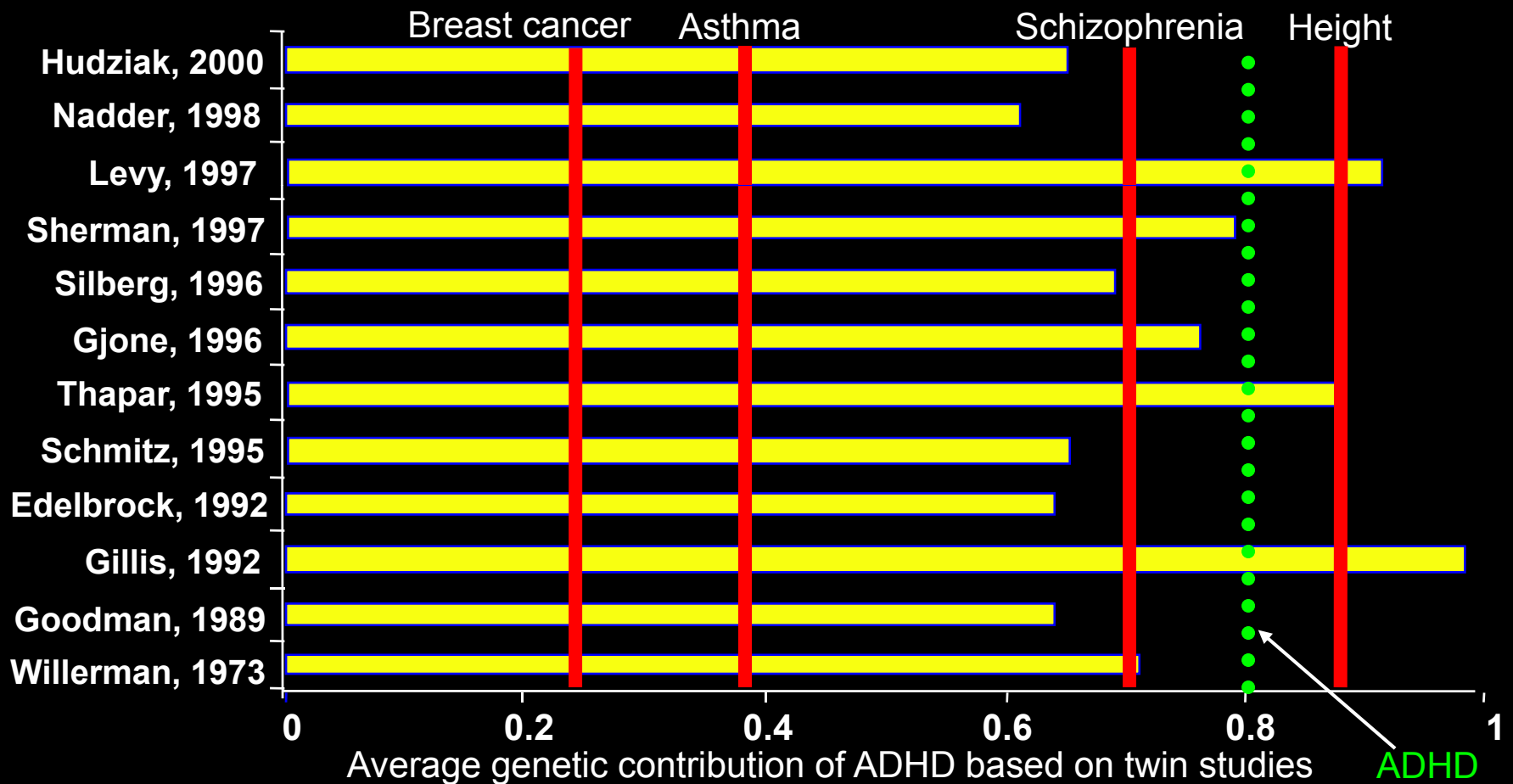
Etiology

A Variety of Functional & Structural Differences Appear in the ADHD Brain



MGH-NMR Center & Harvard- MIT CTP Reprinted by permission of Elsevier Science from Anteriorcingulate cingulate cortex dysfunction in ADHD revealed by fMRI and the Counting Stroop , by Bush G, Frazier JA, Rauch SL, et al., *Biological Psychiatry* 45(12), Copyright 1999 by the Society of Biological Psychiatry.

Twin Studies Show ADHD Is a Genetic Disorder



Faraone. *J Am Acad Child Adolesc Psychiatry*. 2000;39:1455-1457. Hemminki. *Mutat Res*. 2001;25:11-21.
 Palmer. *Eur Resp J*. 2001;17:696-702.

Impairment Caused by ADHD

How does it present?
Impact on quality of life

Impairment

Academic
Behavioral/Emotional
Socialization
Medical

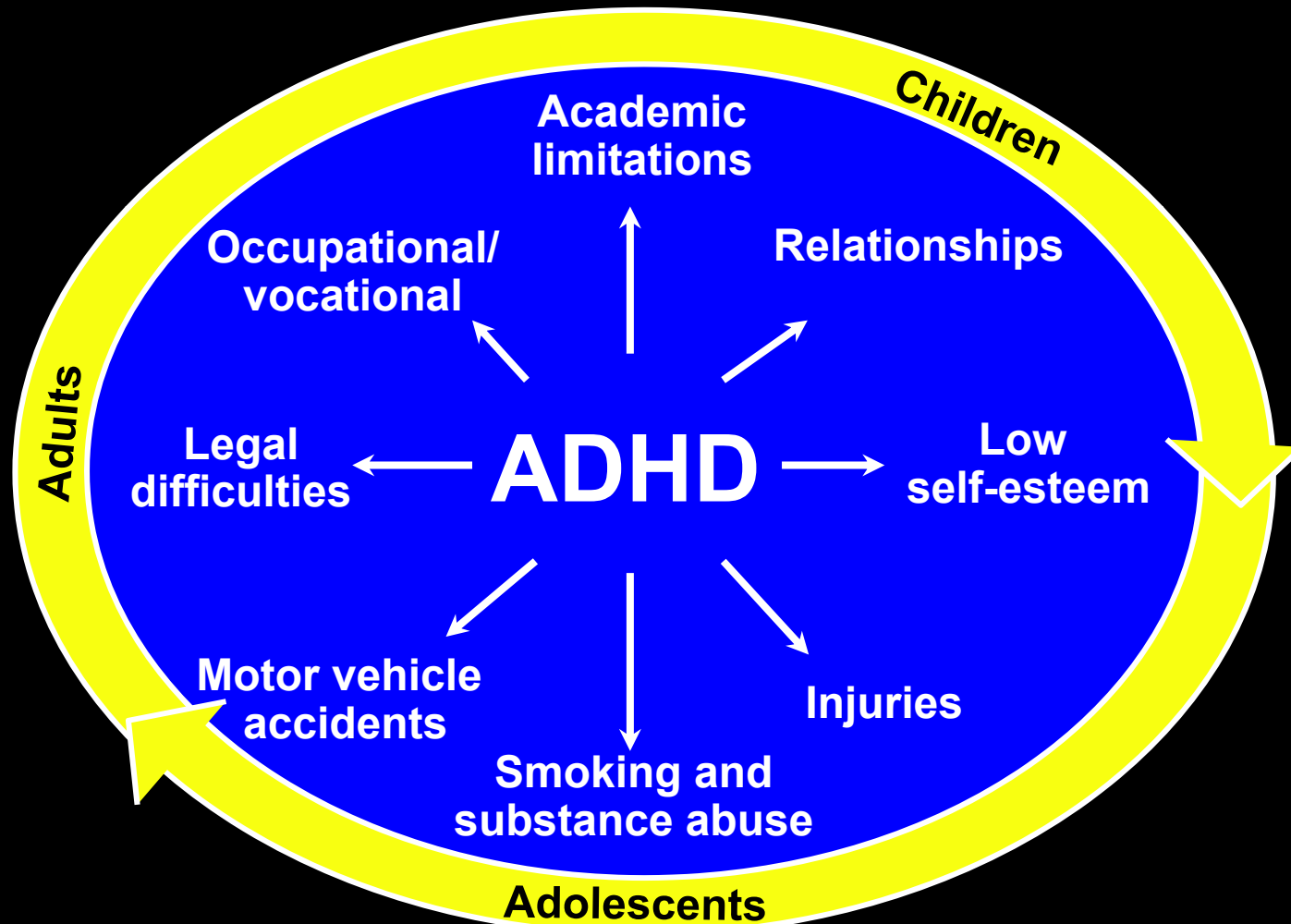
Impairment

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

Impairment

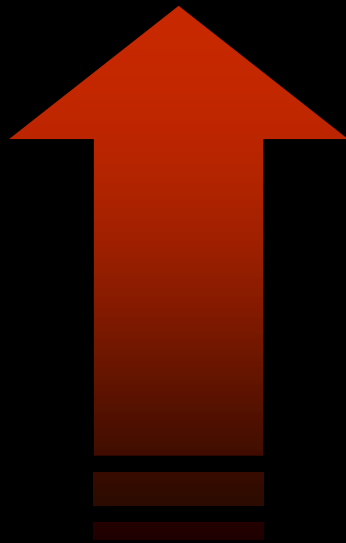
- ACADEMIC
 - *Production vs. Knowledge*
- BEHAVIOR - EMOTIONAL
 - *Spacey/Over-Reactive vs. Defiant*
- SOCIALIZATION
 - *Insatiable vs. Malicious*
- MEDICAL
 - *Cigarette smoking, Car accidents, SUD*

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

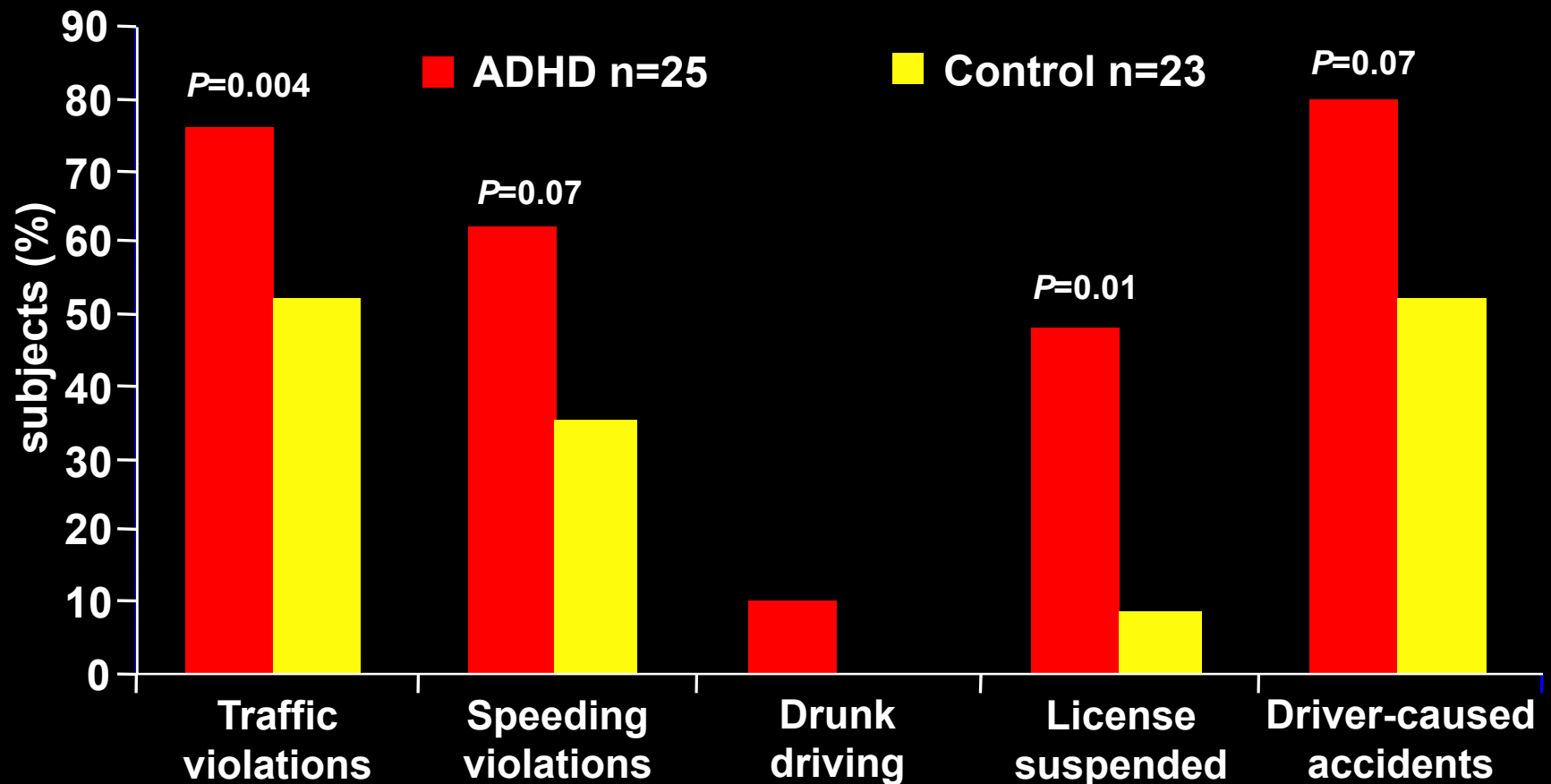
Performance Limitations

- 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

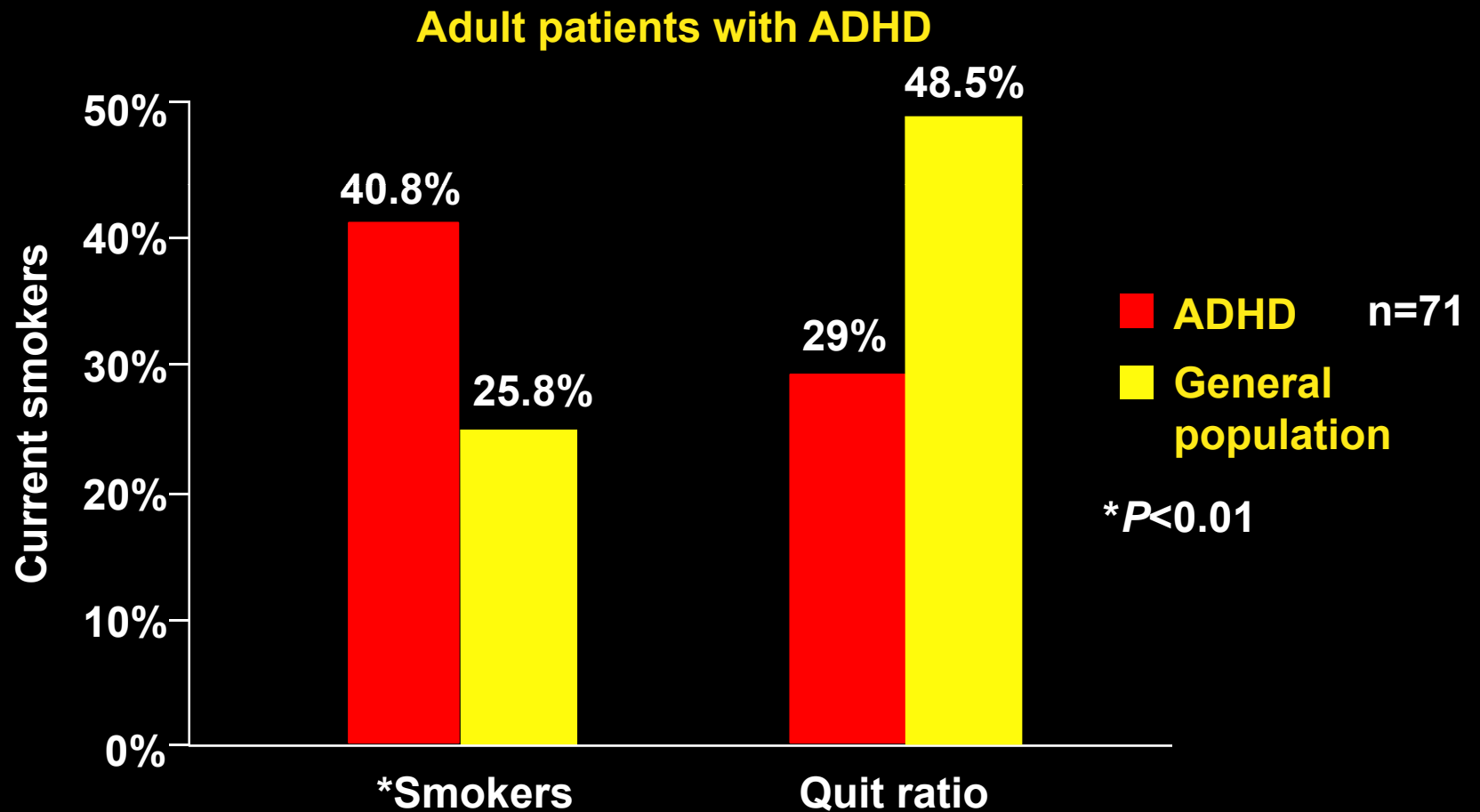
ADHD Affects Socialization

- 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

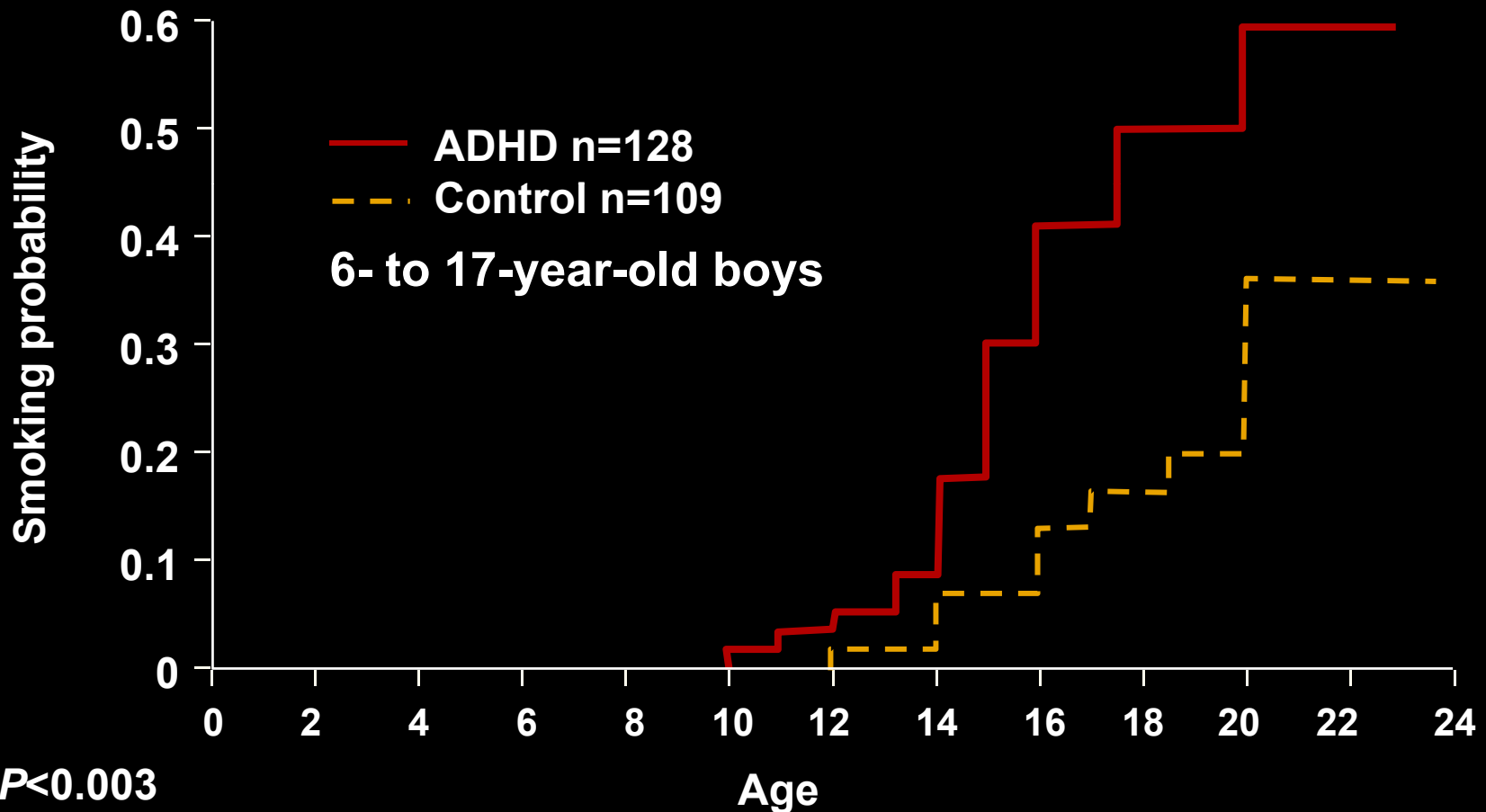
Increased Traffic Violations and Motor Vehicle Accidents in Adolescents and Adults with ADHD



Increased Smoking with ADHD

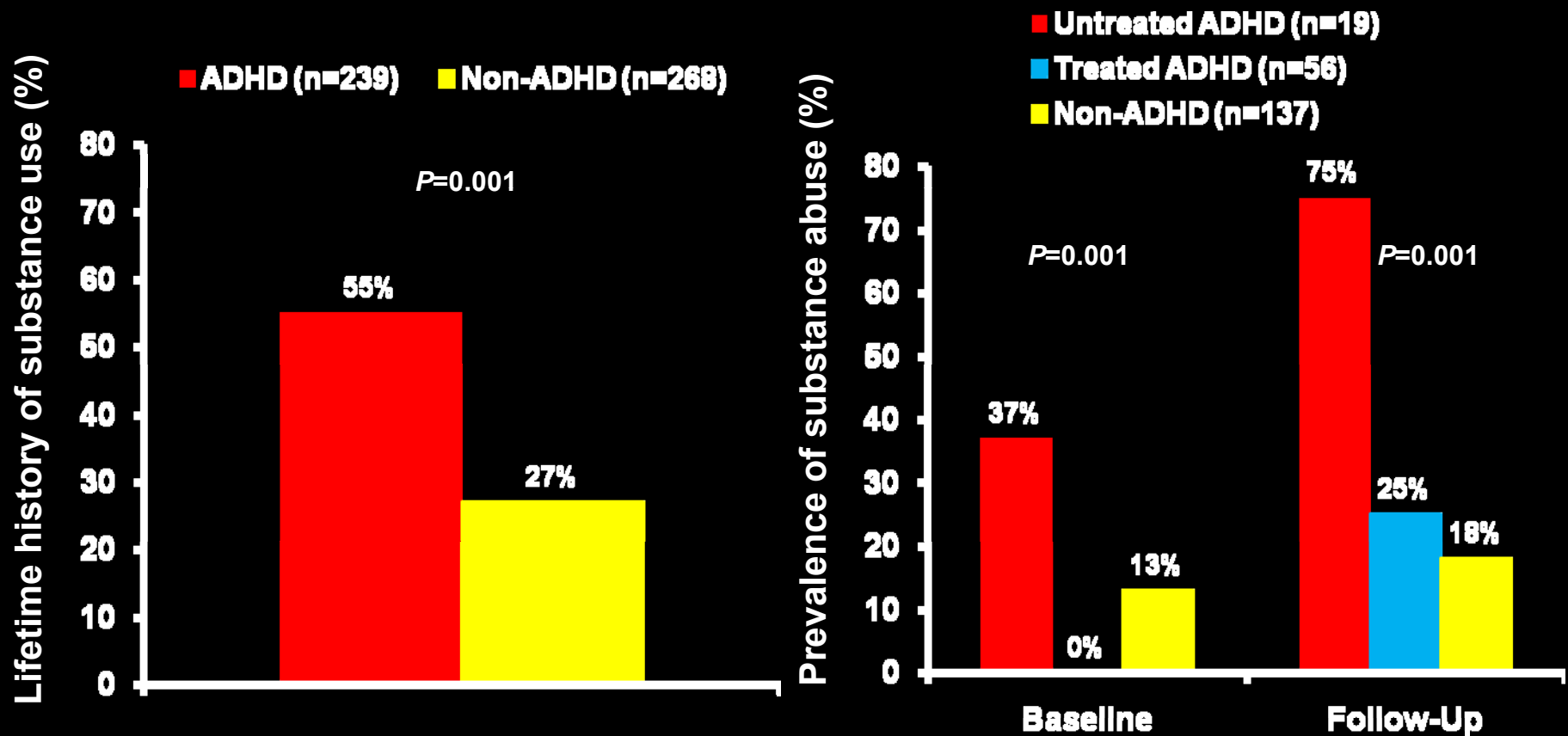


Earlier Initiation of Smoking with ADHD



Milberger S, et al. *J Am Acad Child Adolesc Psychol.* 1997;36:37-44.

Untreated ADHD Is Associated With Higher Risk of Substance Abuse



Biederman J, et al. *Biol Psychiatry*. 1998;44:269-273.
Biederman J, et al. *Pediatrics*. 1999;104:e20-e25.

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

```
graph TD; A[Multimodal Therapy] --> B[Medication]; A --> C[Psychosocial Therapy]; B --> D[Normalization in Many Areas]; C --> D;
```

Medication

Stimulants

Antidepressants

SNRI's

Psychosocial Therapy

Parent Training

Child-Focused Treatment

School-Based Intervention

Normalization in Many Areas

MTA Study Objective and Design

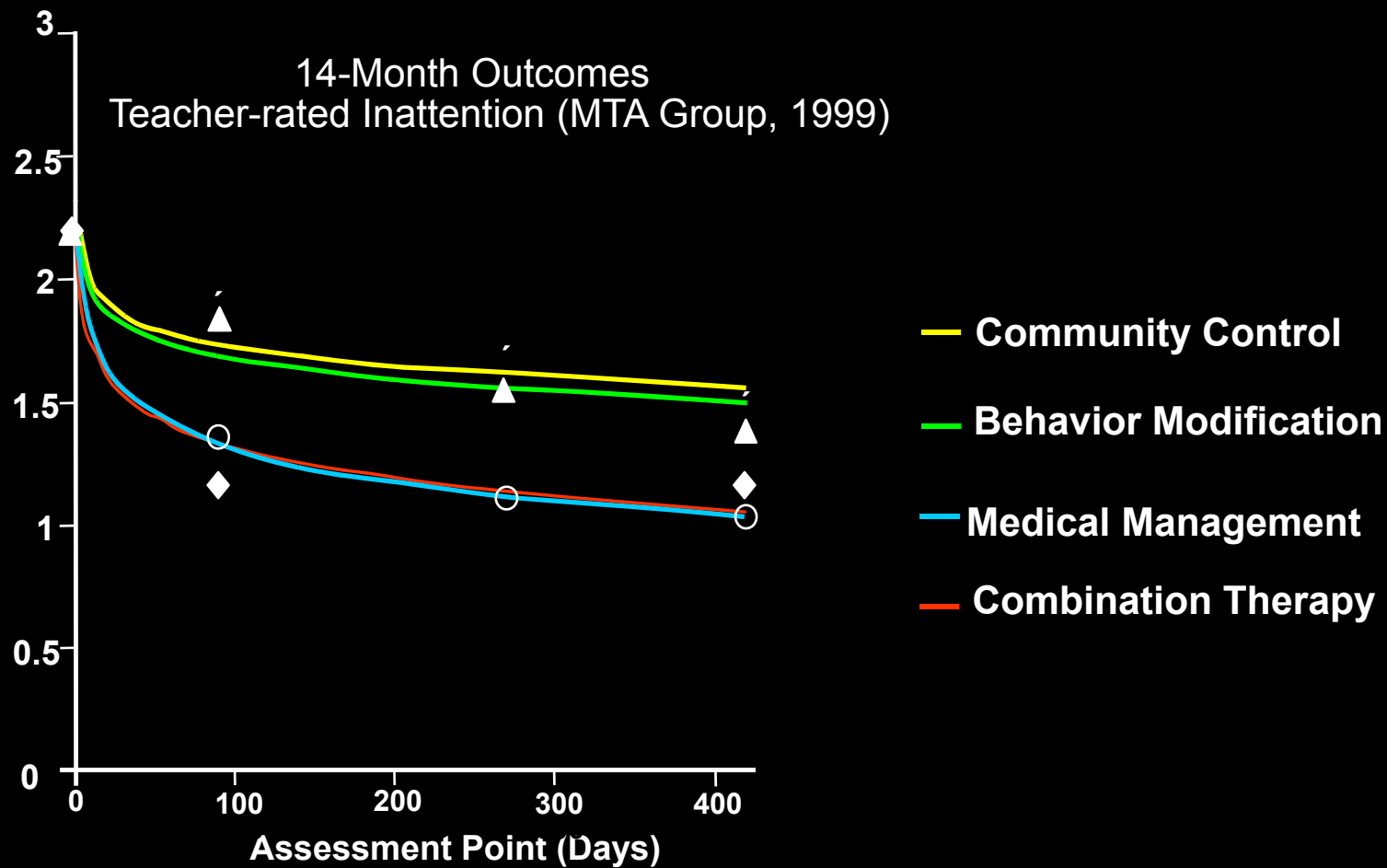
Objective:

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

Protocol:

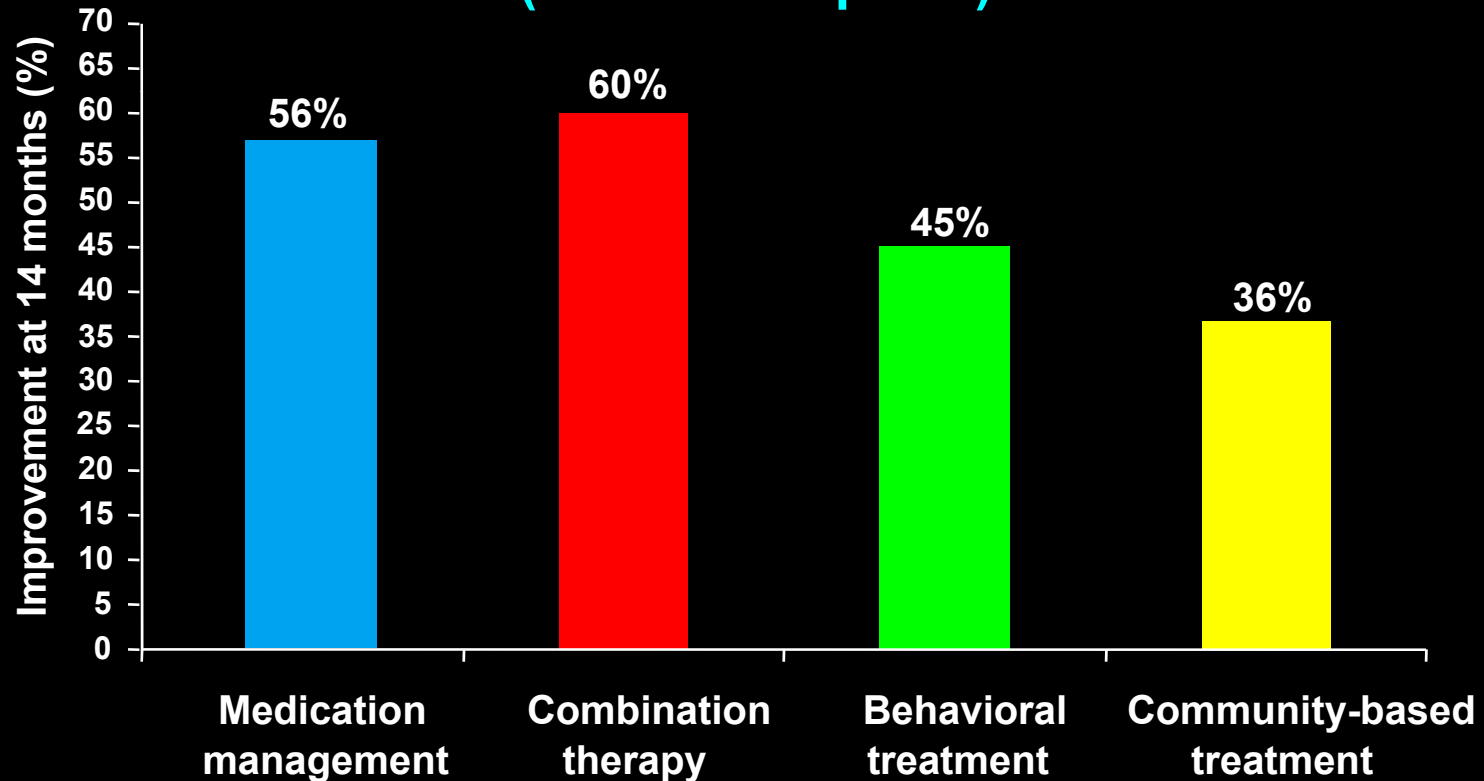
- Population: 579 children with ADHD combined type, aged 7-9.9 years
- In a 4-group parallel design, children randomly assigned to:
 - Medication alone (primarily methylphenidate)
 - Behavioral therapy alone
 - Combination of medication and behavioral treatment
 - Routine community care (medication and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

MTA Study: Treatment Outcome: Teacher-Rated Inattention

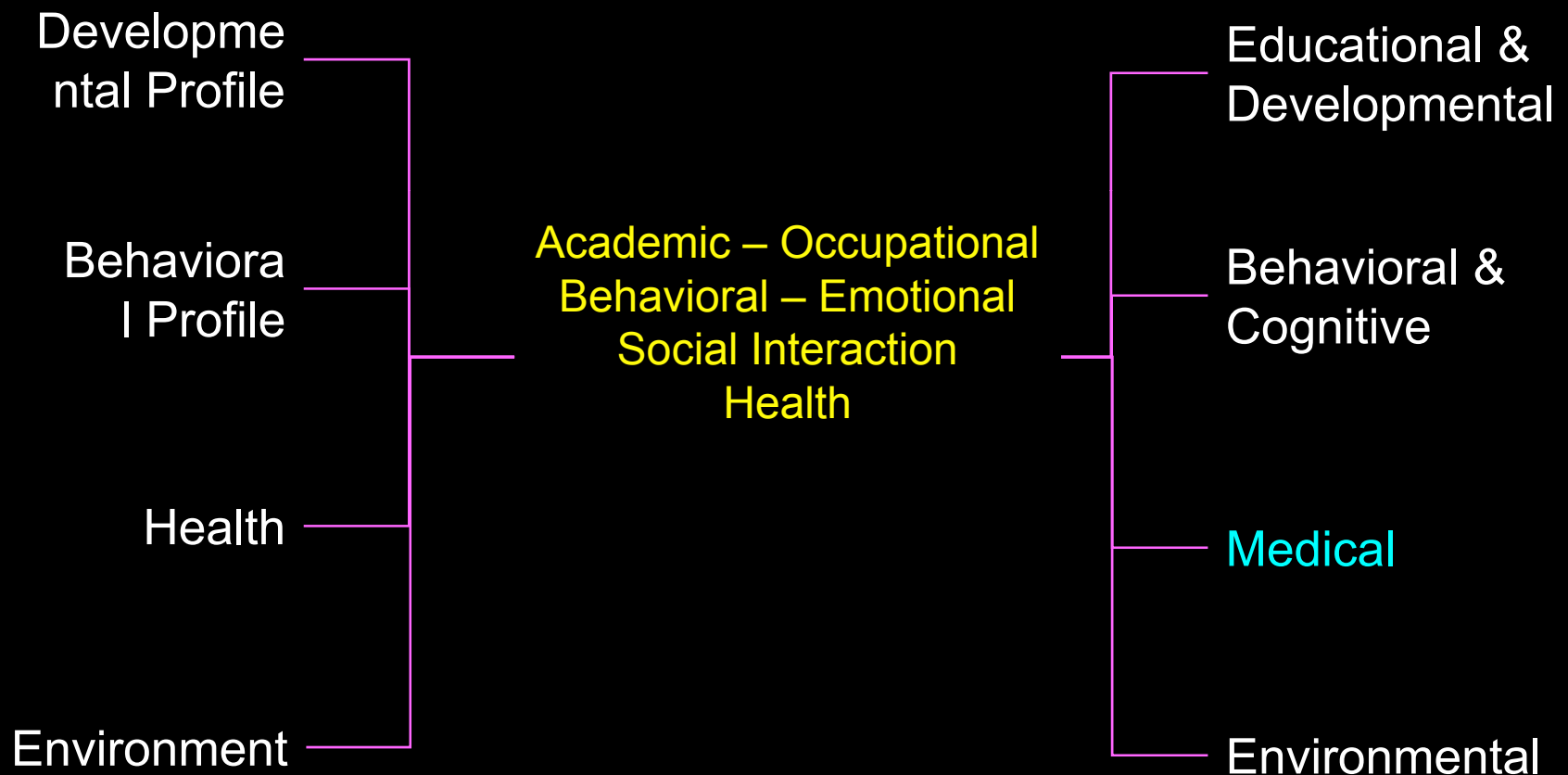


Long-term Outcomes of Therapies for ADHD in the MTA Study

Hyperactive Impulsive Symptoms (Teacher Reports)



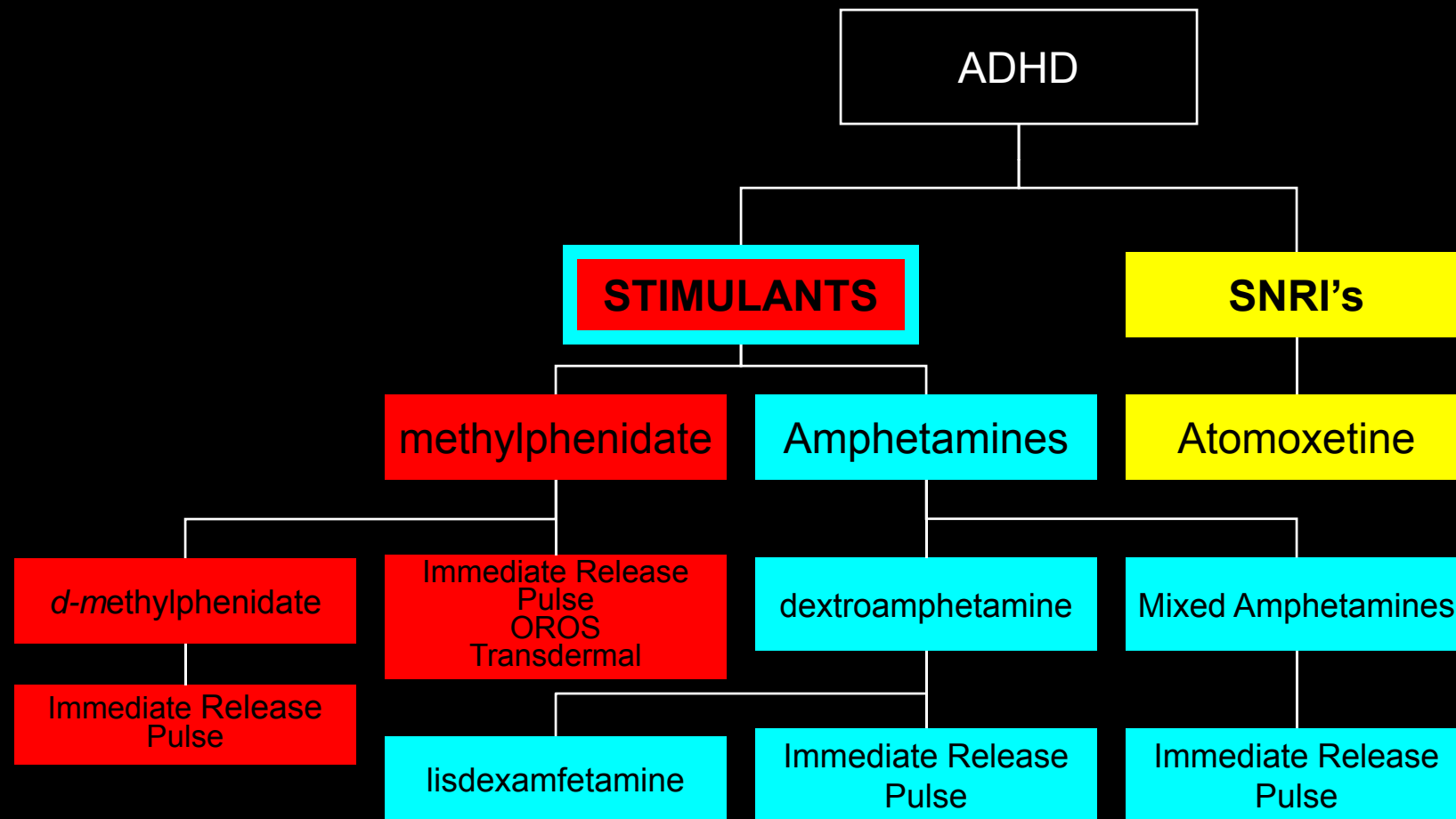
The Developmental Web



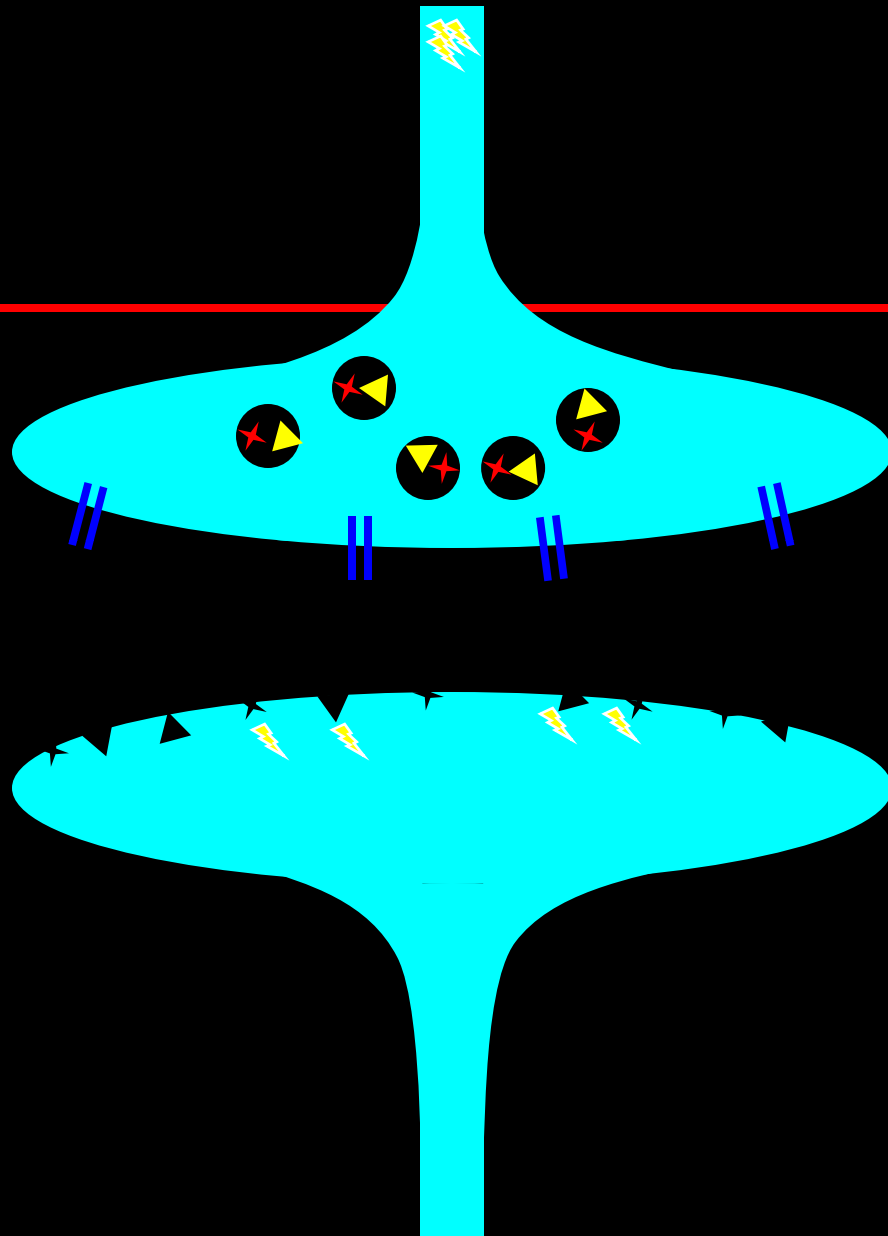
American Academy of Pediatrics: Guidelines for the Treatment of ADHD

- 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

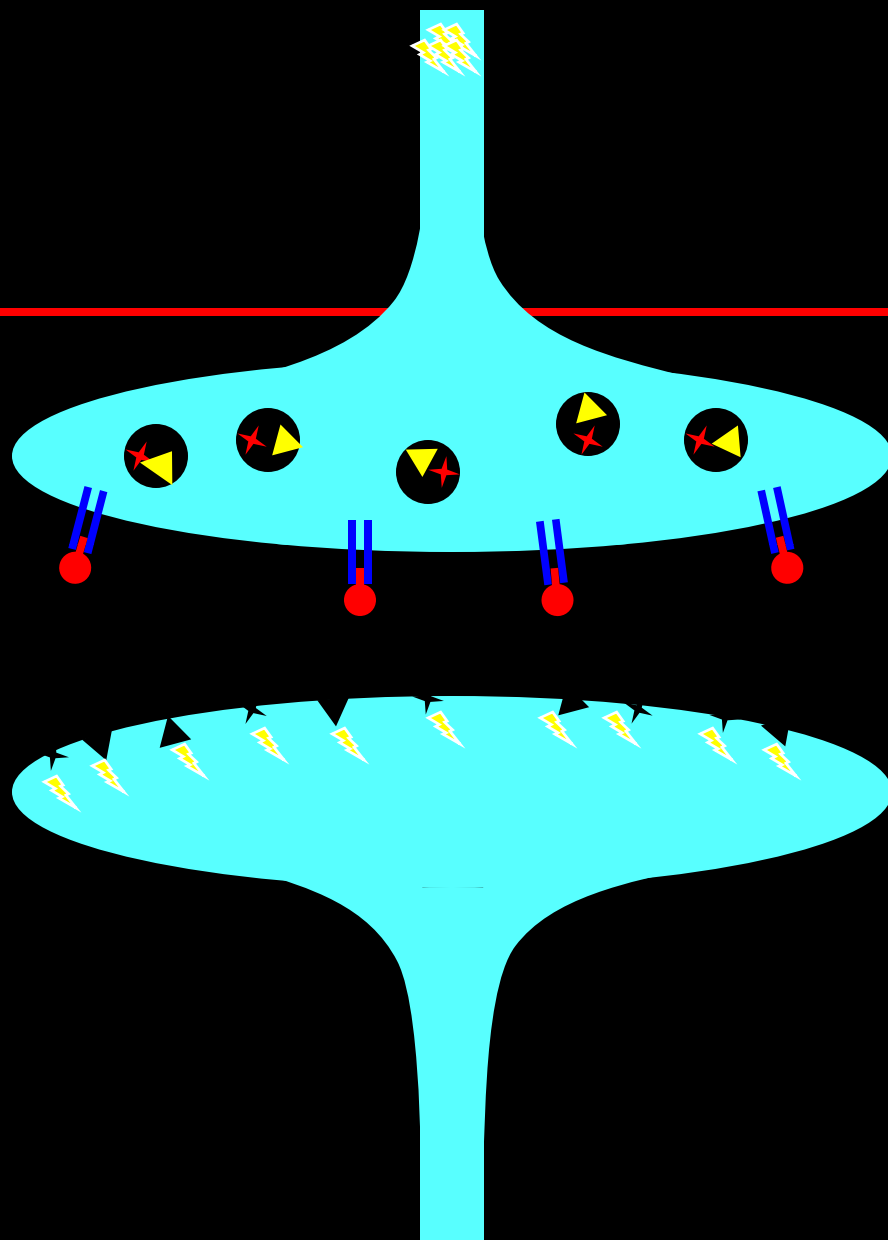
Types of Medications Used In Managing ADHD



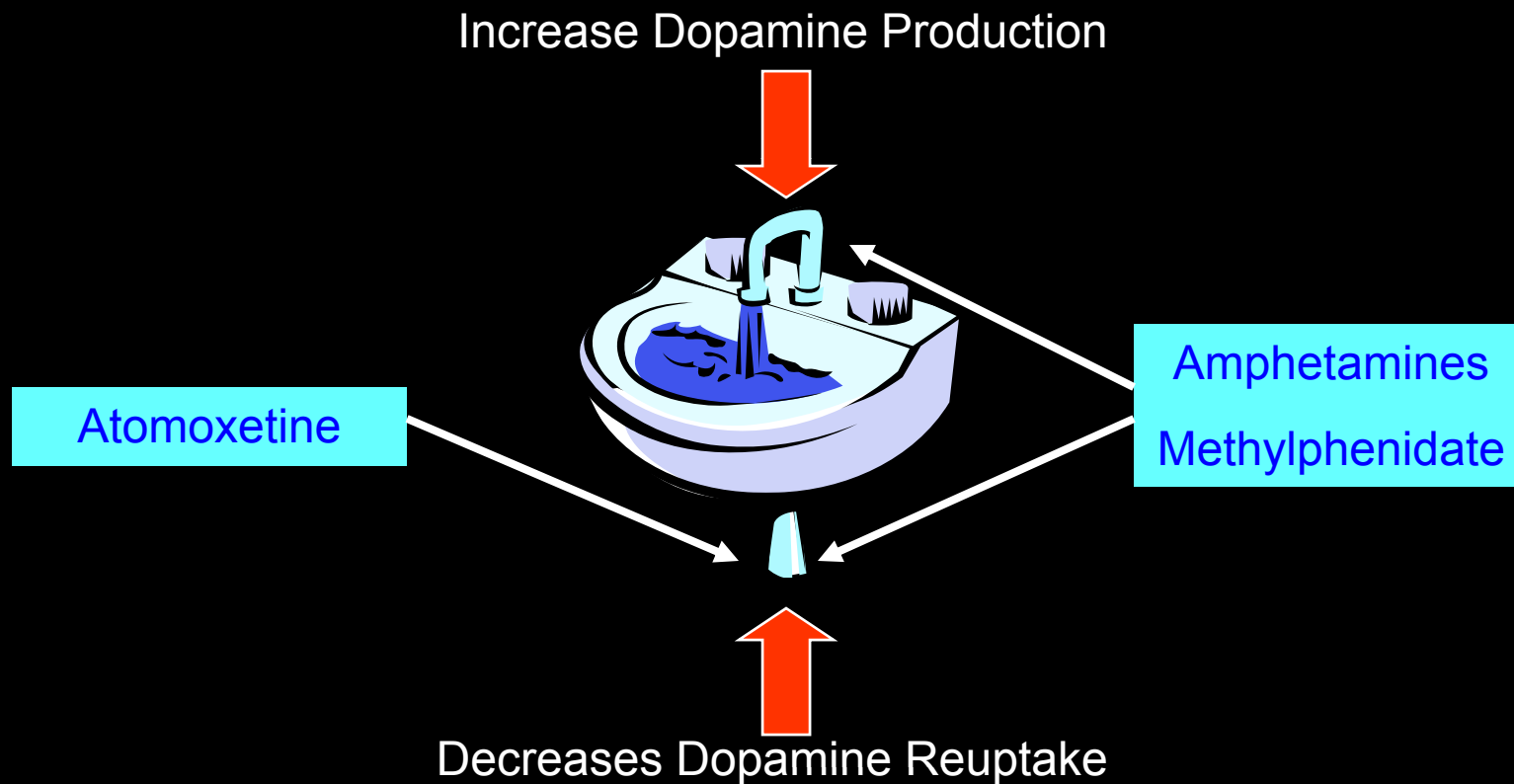
- ▲ Dopamine
- + Norepinephrine
- || Reuptake pumps
- Medication
- ⌋ Receptors



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Proposed Effect of Stimulants



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*

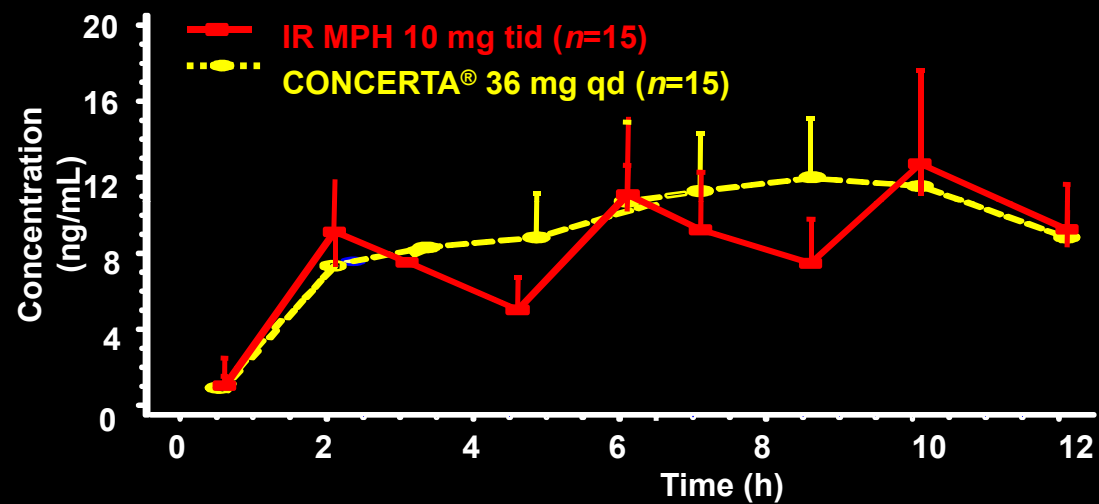
Medications: Duration of Action

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

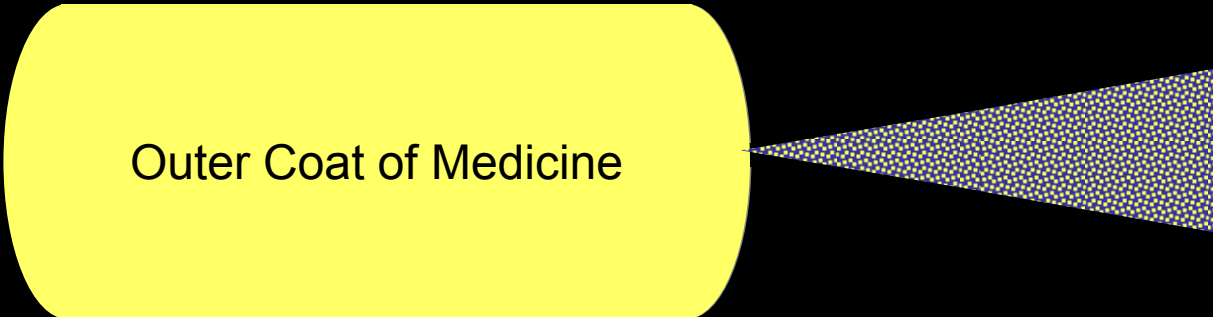
Medications

- Short-Acting
 - Ritalin, Dexedrine, DextroStat, Focalin Methylin (Tablet, Chewable & Liquid)
- Intermediate-Acting
 - Ritalin SR, Metadate ER, Adderall, Ritalin LA, Metadate-CD, Methylin ER, Focalin XR
- Long-Acting
 - Dexedrine Spansules, Cylert, Adderall-XR, Concerta, Daytrana, Vyvanse
- 24 hours
 - Strattera

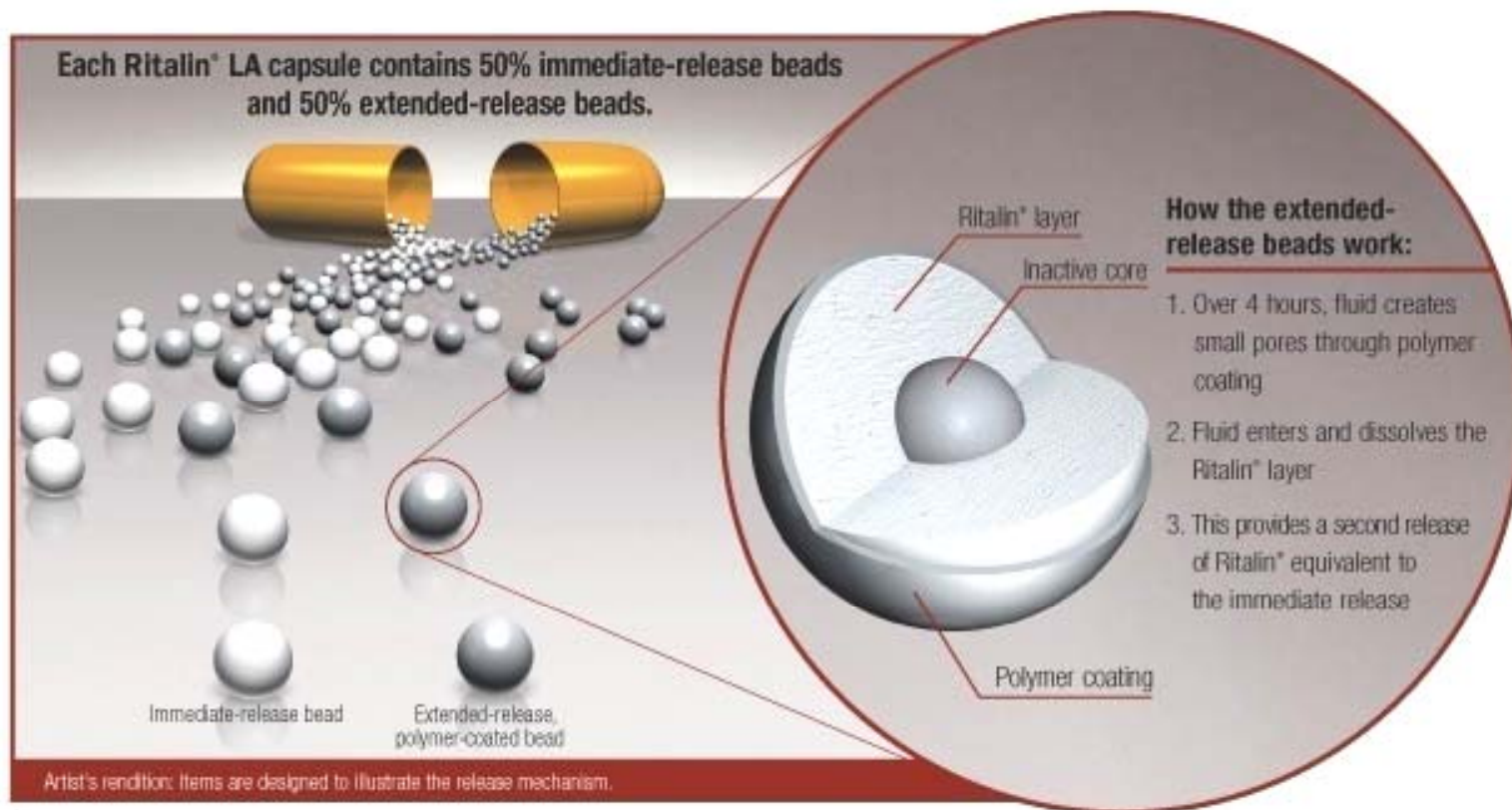
MPH OROS (Concerta[®])



Outer Coat of Medicine

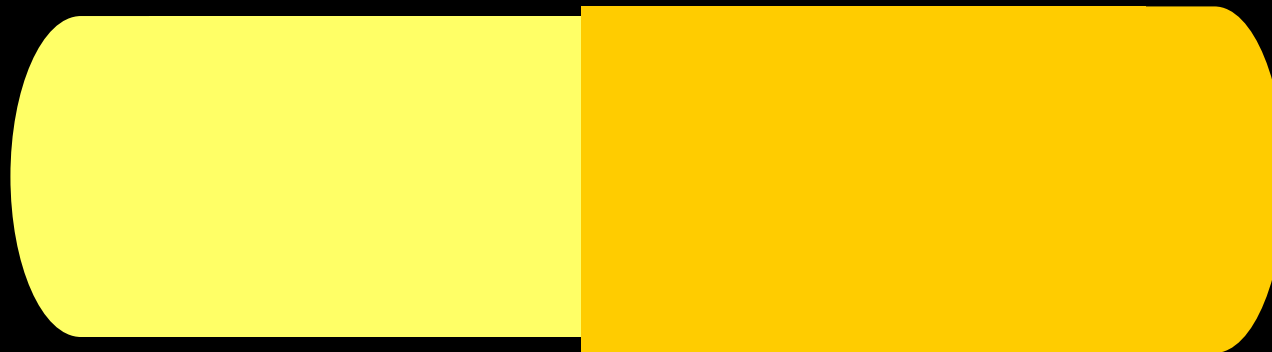
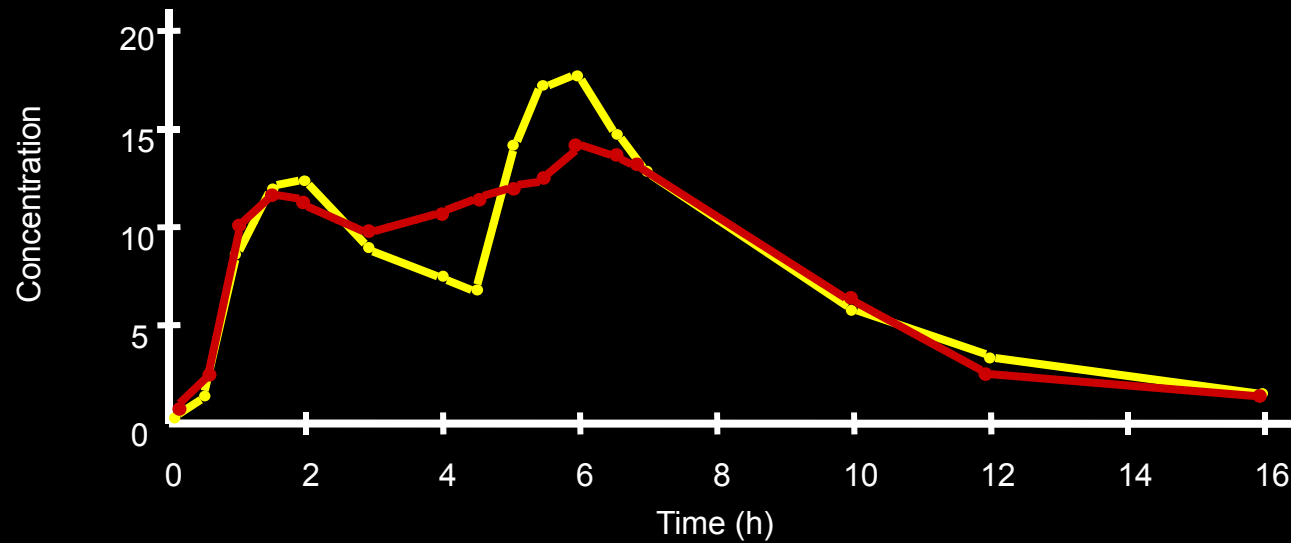


MPH SODAS™ (Ritalin® LA) Pulse Release



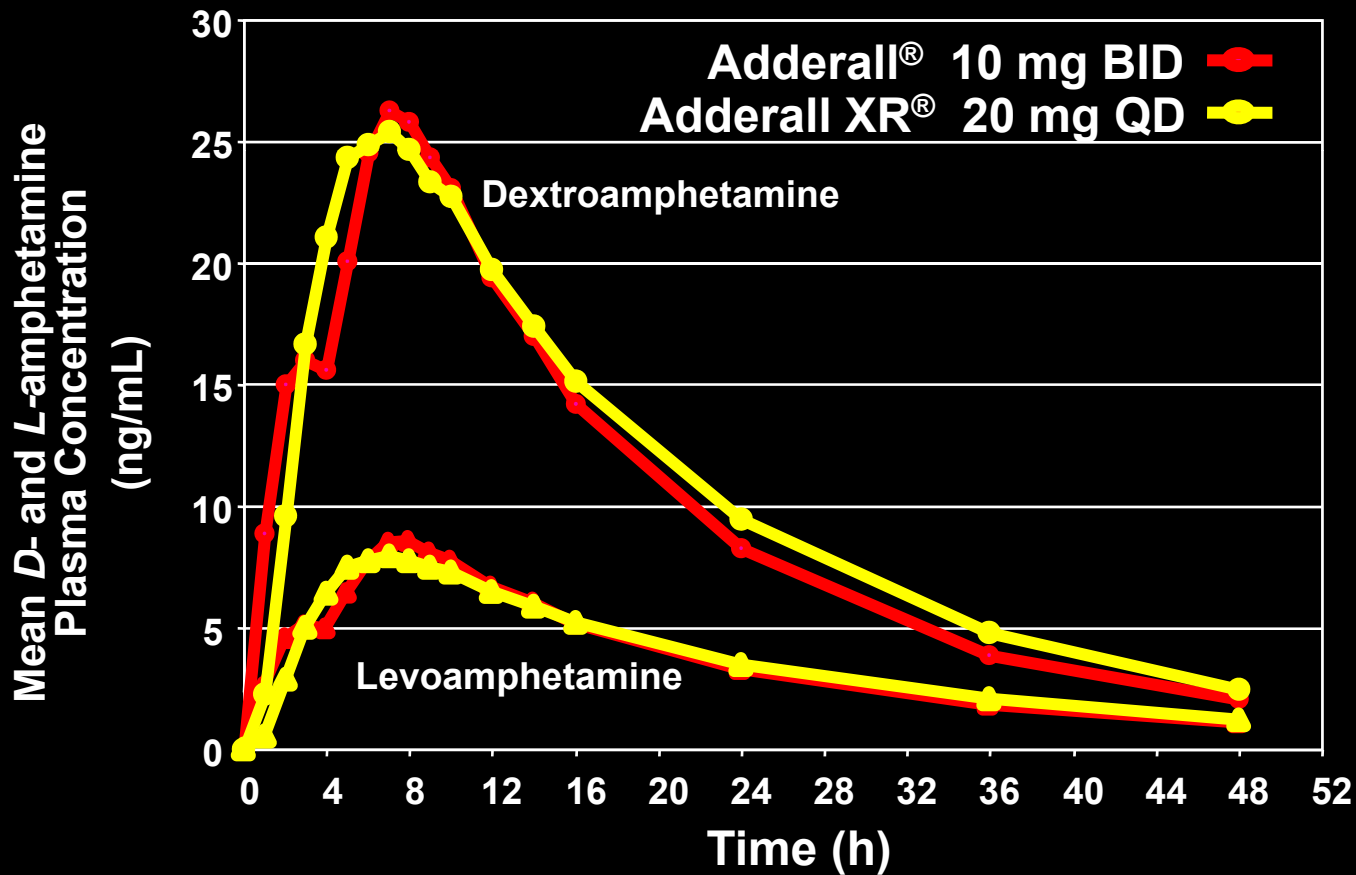
*Spheroidal Oral Drug Absorption System.

Pulse Delivery System (SODAS, Difucaps)



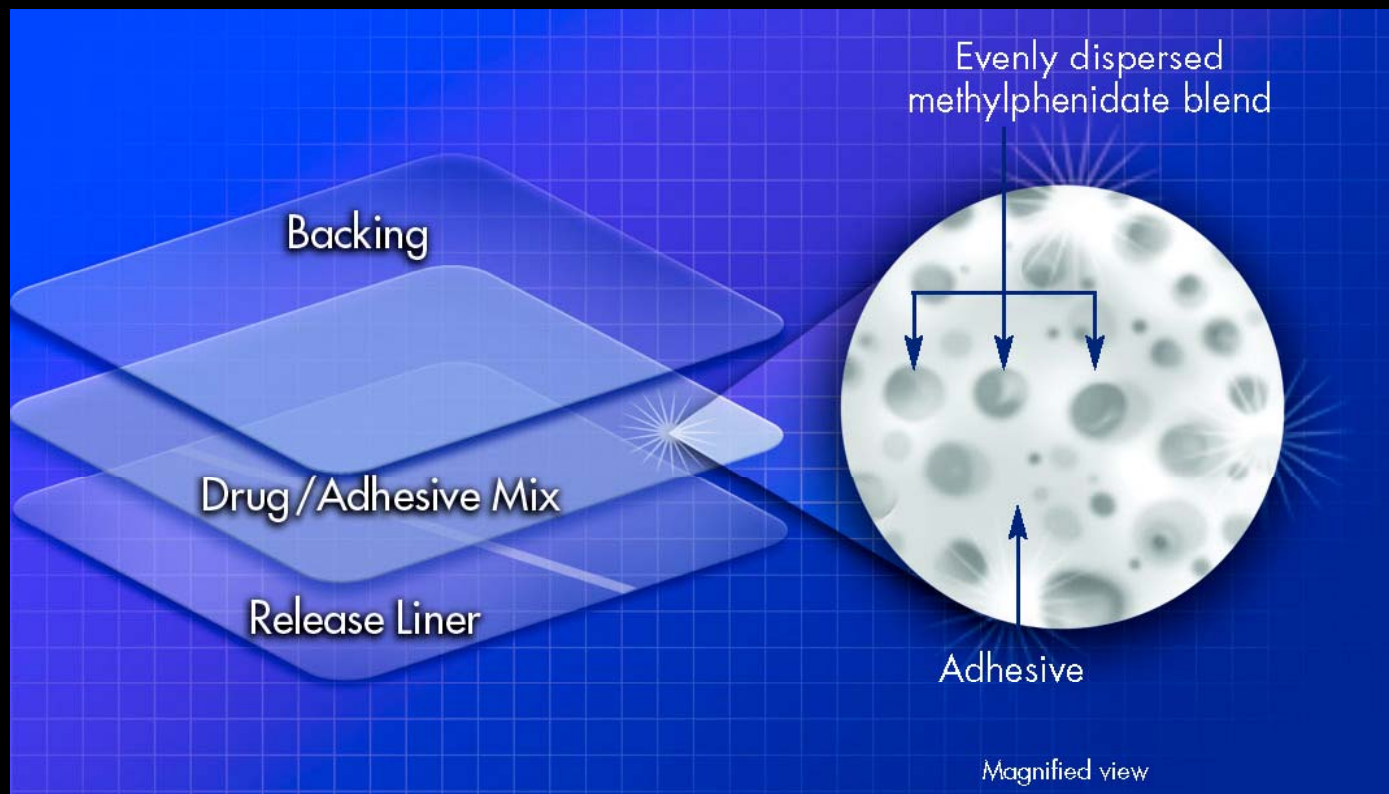
Mixed Amphetamine Salts (Adderall XR[®]) Formulation Study

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



Daytrana DOT Matrix™ Transdermal Technology

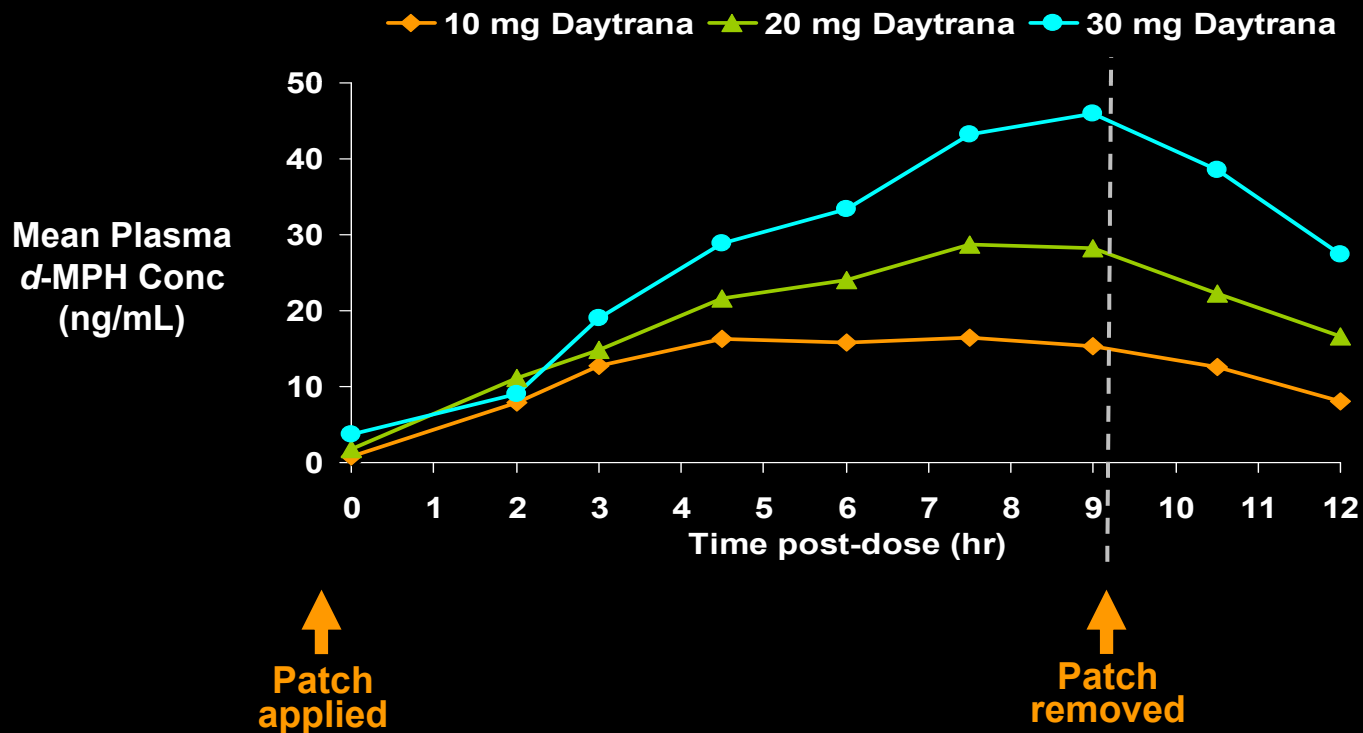
- Methylphenidate is mixed with adhesive



DOT Matrix is a trademark of Noven Pharmaceuticals, Inc.

Pharmacokinetics with Daytrana

Mean Plasma Concentration of *d*-methylphenidate



Lower limit of quantification 0.25 ng/mL.

Pierce et al. Poster presented at the AACAP Annual Meeting. Toronto. October 20, 2005.

Application and Removal/Disposal



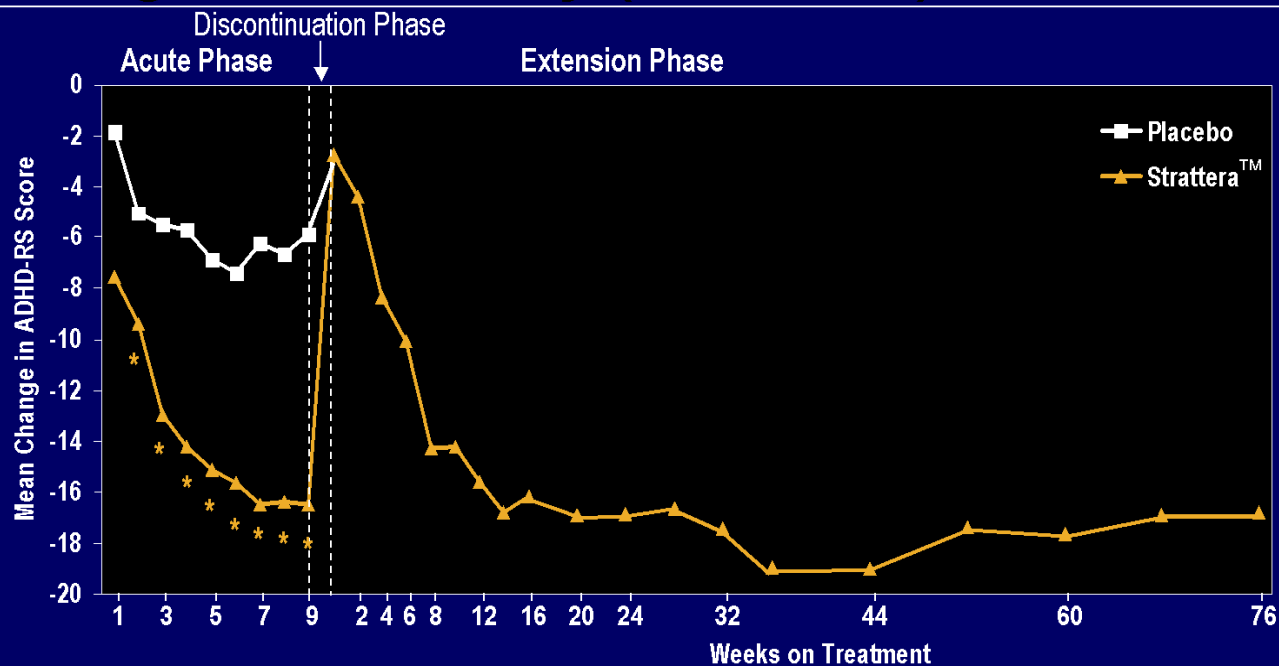
- Holding the patch down, the rest of the liner should be removed slowly and the exposed half should be pressed against the skin
- The patch should be pressed down with the palm of the hand for 30 seconds
- Upon removal, the patch should be folded in half, with sticky sides together, and discarded immediately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

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



* $p < .01$ for Strattera vs placebo.
 $p < .001$ for Strattera within-group change.
Spencer T, et al. Manuscript in preparation.

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