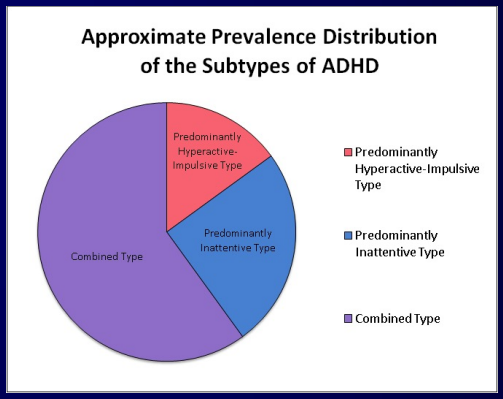
I principali sistemi classificatori forniscono criteri precisi per porre la diagnosi di ADHD ma differiscono tra loro in quanto:

il DSM (*American Psychiatric Association*) permette di distinguere tre forme cliniche:

a) iperattiva-impulsiva;
b) inattentiva;
c) combinata



mentre

l'ICD-10 (*World Health Organization*) prevede solo la forma combinata

I SINTOMI CARATTERISTICI

Iperattività motoria
Impulsività
Inattenzione

causano spesso

Difficoltà relazionali
Difficoltà scolastiche
Bassa autostima
Disturbi del comportamento

Iperattività

- Incapacità di star fermi (movimenti delle mani e dei piedi, impossibilità a star seduti)
- Attività motoria spesso incongrua e afinalistica
- Gioco rumoroso e disorganizzato
- Eccessive verbalizzazioni
- Sentimenti soggettivi di irrequietezza (adolescenti ed adulti)
- Limitate possibilità di inibizione motoria

Impulsività

- Difficile controllo sui propri comportamenti
- Incapacità a differire la risposta automatica ad uno stimolo (es., una domanda)
- Difficoltà ad attendere il proprio turno
- Tendenza ad interrompere gli altri e ad essere invadenti
- Scarsa capacità di riflessione
- Difficoltà nel valutare le conseguenze delle proprie azioni

❑ Hyperactivity-Impulsivity Symptoms (at least 6 symptoms required)

- Difficulty playing or engaging in activities quietly
- Always "on the go" or acts as if "driven by a motor”
- Talks excessively
- Blurts out answers
- Difficulty waiting in lines or awaiting turn
- Interrupts or intrudes on others
- Runs about or climbs inappropriately
- Fidgets with hands or feet or squirms in seat
- Leaves seat in classroom or in other situations in which remaining seated is expected

APA, 2000

Disattenzione

- Difficoltà a mantenere l'attenzione sui compiti scolastici o le attività di gioco
- Facile distraibilità per stimoli banali
- Difficoltà ad organizzarsi nelle diverse attività quotidiane
- Rapidi passaggi da un'attività all'altra
- Difficoltà nel seguire un discorso
- Evitamento di attività che richiedono sforzo mentale protratto

DSM Diagnostic Criteria

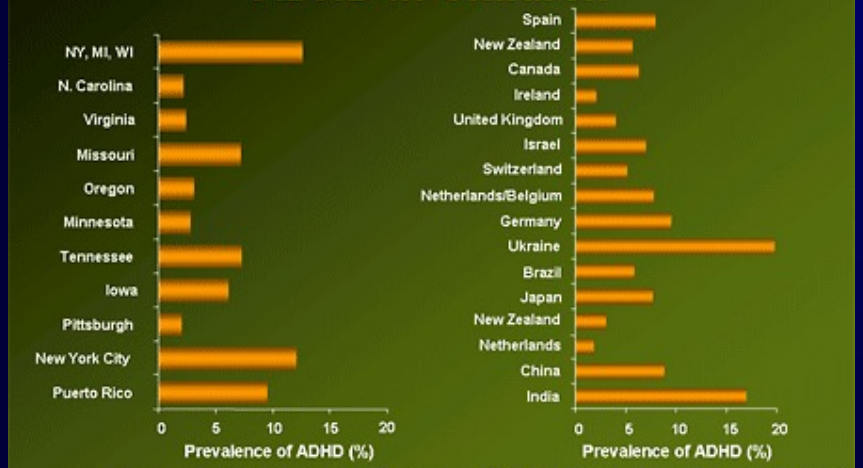
- Inattention Symptoms (at least 6 symptoms required)
  - Fails to give close attention to details or makes careless mistakes in schoolwork, work, etc.
  - Difficulty sustaining attention
  - Does not seem to listen when spoken to directly
  - Does not follow through on instructions and fails to finish schoolwork, chores, etc.
  - Difficulty organizing tasks and activities
  - Avoids tasks requiring sustained mental effort
  - Loses things necessary for tasks or activities
  - Easily distracted by extraneous stimuli
  - Forgetful in daily activities

APA, 2000

ADHD: Prevalence

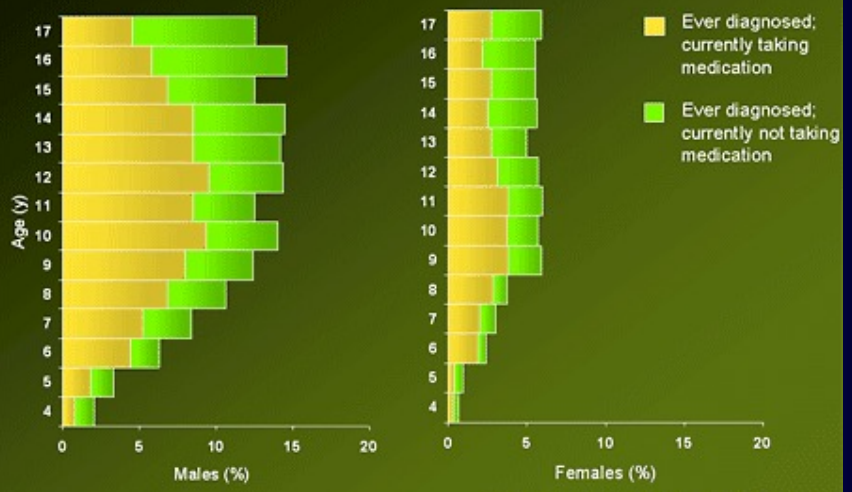
- Affects 3-5% school-aged children[1]
  - Recent data suggest rates of up to 7.5% in school-aged children[2]
  - Diagnosed in boys 3 to 4 times more than in girls[3,4]
- Accounts for 30-50% of mental health referrals for children[5]
- Resulted in 9.7 million physician-office visits in 2001[4]
- Persists in some patients into adolescence and adulthood[6]

Worldwide Prevalence of ADHD in Children



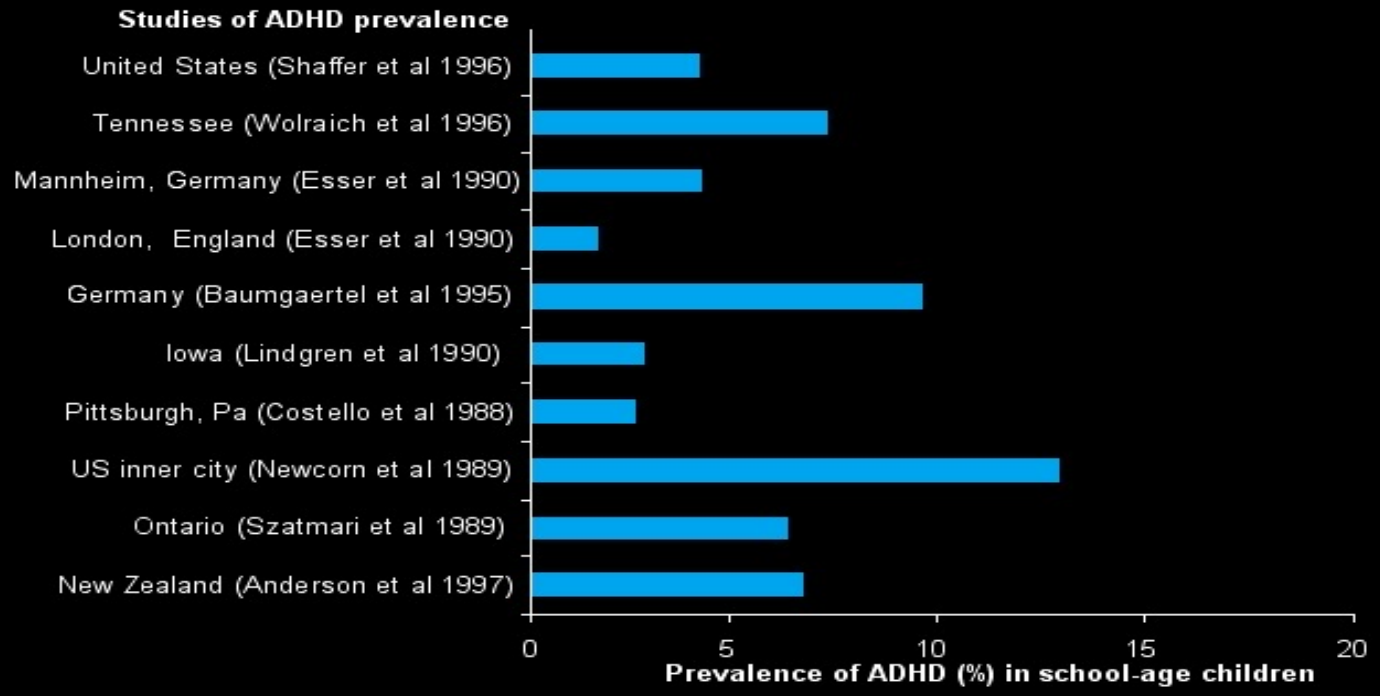
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, text revision. Washington, DC: American Psychiatric Association; 2000:85-93; Biederman J et al. *J Nerv Ment Dis*. 2004;192:453-454. Faraone SV et al. *World Psychiatry*. 2003;2:104-113.

ADHD: Prevalence and Treatment



MMWR Morb Mortal Wkly Rep. 2005;54:842-847.

Worldwide Prevalence of ADHD Is 3% to 7%



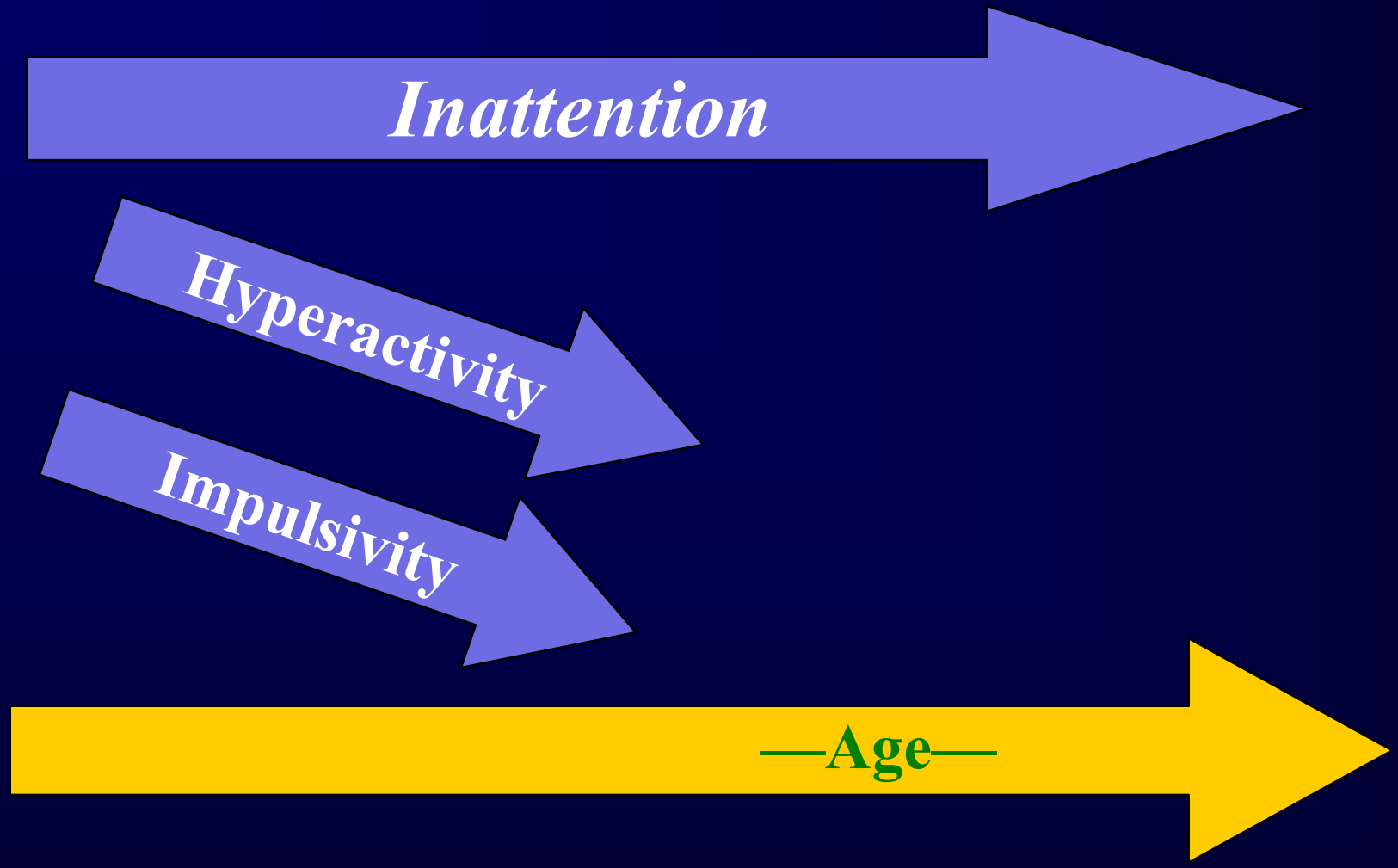
Goldman, et al. *JAMA*.1998;279:1100-1107.

- Clinically significant impairment in social or academic/occupational functioning
- Some symptoms that cause impairment are present in 2 or more settings (e.g., school/work, home, recreational settings)
- Not due to another disorder (e.g., Autism, Mood Disorder, Anxiety Disorder)

Neuropsychological Testing

- Nigg (2005) in a meta-analysis identified the most common abnormalities in various neuropsychological tasks in ADHD (listed by Effect Size):
  - Spatial working memory (0.75)
  - Continous Performance Test (CPT) d-prime (0.72)
  - Stroop Naming Speed (0.69)
  - Stop Task Response Suppression (0.61)
  - Full Scale IQ (0.61)
  - Mazes, a planning measure (0.58)
  - Trails B Time (0.55)

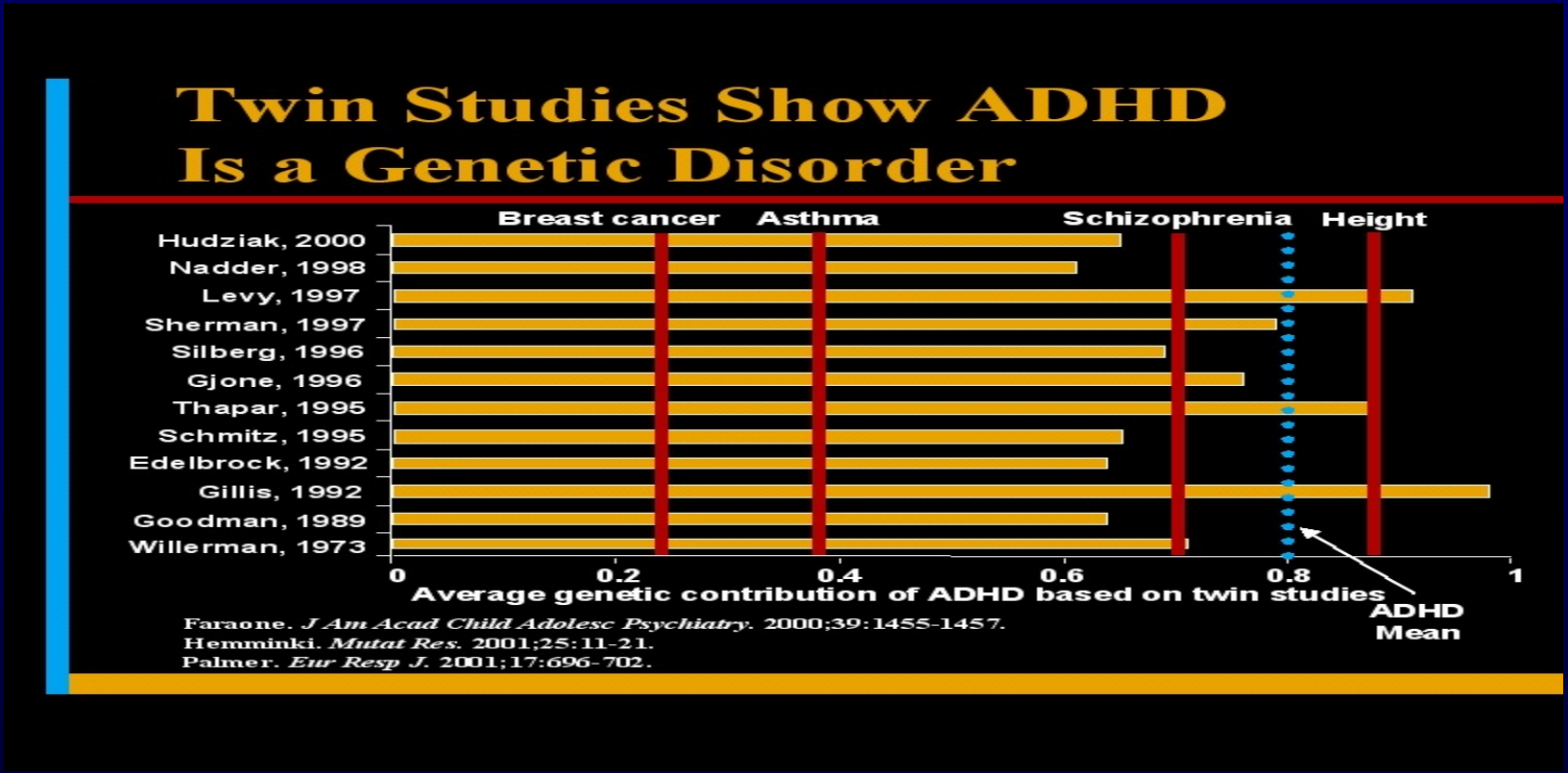
ADHD: Course of the Disorder



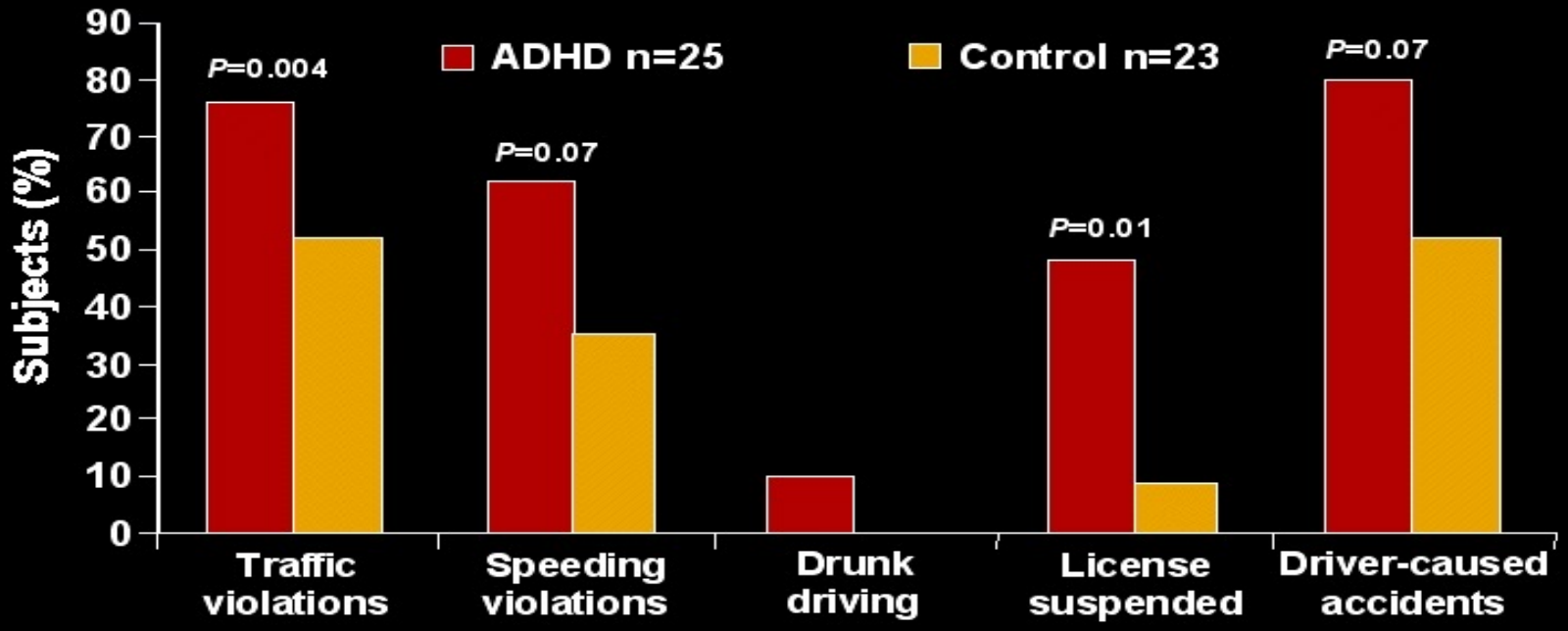
- Adult use of these medications increased 90% between March 2002 and June 2005…can you say *Strattera*?!
- Use of meds to treat ADHD in adults aged 20 – 44 rose 19% in 2005
- An estimated 1.7 million adults aged 20 – 64 and 3.3 million children under 19 took medication for ADHD in 2005
  - Use increased 2% for those 10 – 19
  - Use decreased by 5% for those under 10

ADHD is Familial

- Family studies: (1) sibling risk increases 2-5x; (2) 3-5x increased likelihood that parent is affected (9 – 35%)

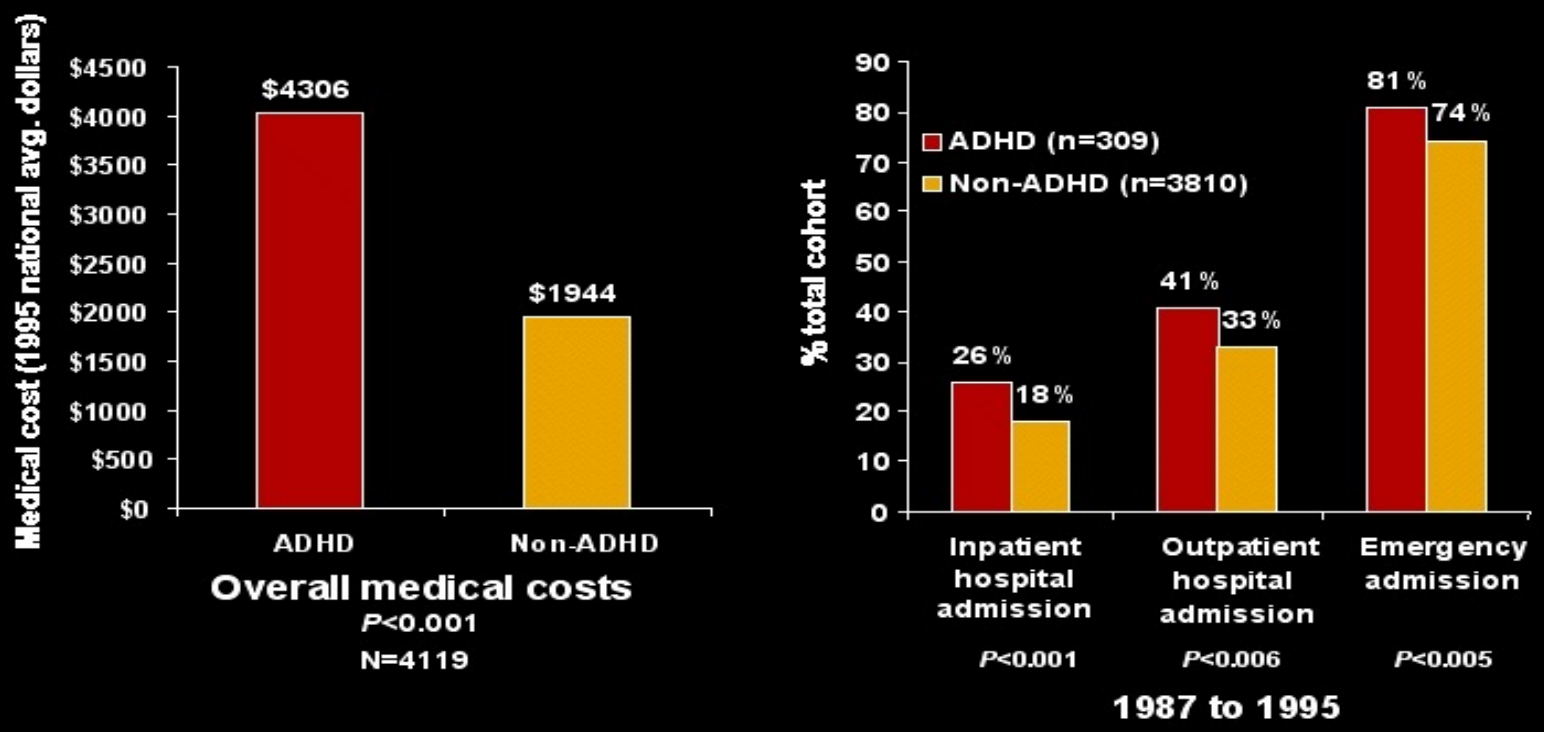


Increased Traffic Violations and Motor Vehicle Accidents in Adolescents and Adults with ADHD



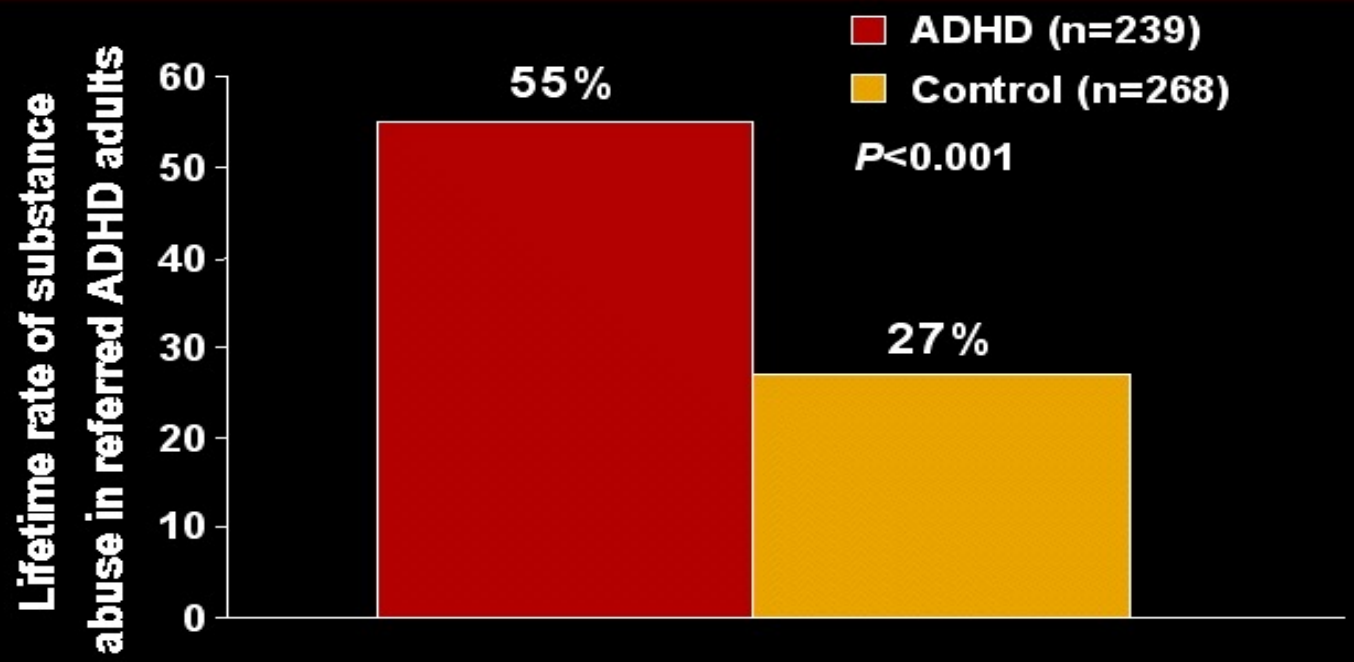
Barkley RA, et al. *Pediatrics*. 1996;98:1089-1095.

ADHD Is Associated with Increased Medical Costs



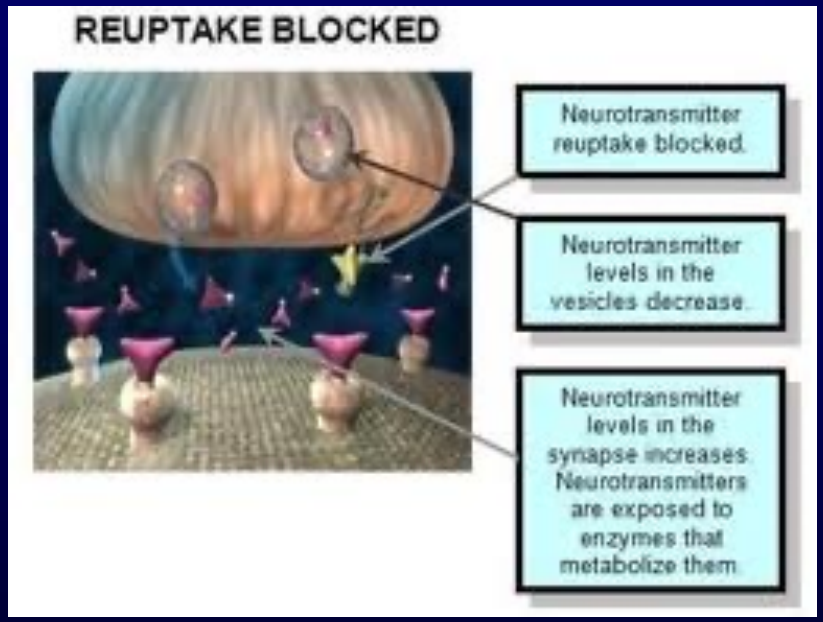
Leibson CL, et al. *JAMA*. 2001;285:60-66.

Increased Lifetime Substance Abuse in Untreated Adults with ADHD



Biederman, et al. *Biol Psychiatry.* 1998;44:269-273.

Ritalin (metilfenidato): agonista dopaminergico



Stimulant medications, doses and pharmacological activity

Medication	Tablets/Dosages	Dose Range	Administration	Peak Effect	Duration of Action
Amphetamines					
Dexedrine®	5 mg	10–40 mg/d	b.i.d. or t.i.d.	1–3 h	5 h
Adderall®	5, 7.5, 10, 12.5, 15, 20, 30 mg	10–40 mg/d	b.i.d. or t.i.d.	1–3 h	5 h
Dextrostat® (generic)	5, 10 mg	10–40 mg/d	b.i.d. or t.i.d.	1–3 h	5 h
Long-duration type					
Dexedrine Spansule®	5, 10, 15 mg spansule	10–45 mg/d	once-daily	1–4 h	6–9 h
Adderall XR®	10, 20, 30 mg capsules	10–40 mg/d	once-daily	1–4 h	9 h
Methylphenidates					
Ritalin®	5, 10, 20 mg	10–60 mg/d	t.i.d.	1–3 h	2–4 h
Methylphenidate	5, 10, 20 mg	10–60 mg/d	t.i.d.	1–3 h	2–4 h
Methylin®	5, 10, 20 mg	10–60 mg/d	t.i.d.	1–3 h	2–4 h
Focalin®	2.5, 5, 10 mg	5–30 mg/d	b.i.d.	1–4 h	2–5 h
Long-duration type					
Ritalin-SR®	20 mg	20–60 mg/d	q.d. in AM or b.i.d.	3 h	5 h
Metadate-ER®	10, 20 mg	20–60 mg/d	q.d. in AM or b.i.d.	3 h	5 h
Medadate-CD®	20 mg	20–60 mg/d	q.d. in AM	5 h	8 h
Concerta®	18, 36, 54 mg	18–54 mg/d	q.d. in AM	8 h	12 h
Ritalin-LA®	20, 30, 40 mg	20–60 mg/d	q.d. in AM	5 h	8 h
Pemoline (Cylert®)	18.75, 37.5, 75 mg; 37.5 chewable	37.5–112.5 mg/d	q.d. in AM or b.i.d.	2–4 h	7 h

Rates of psychotropic medication use by children in the United States

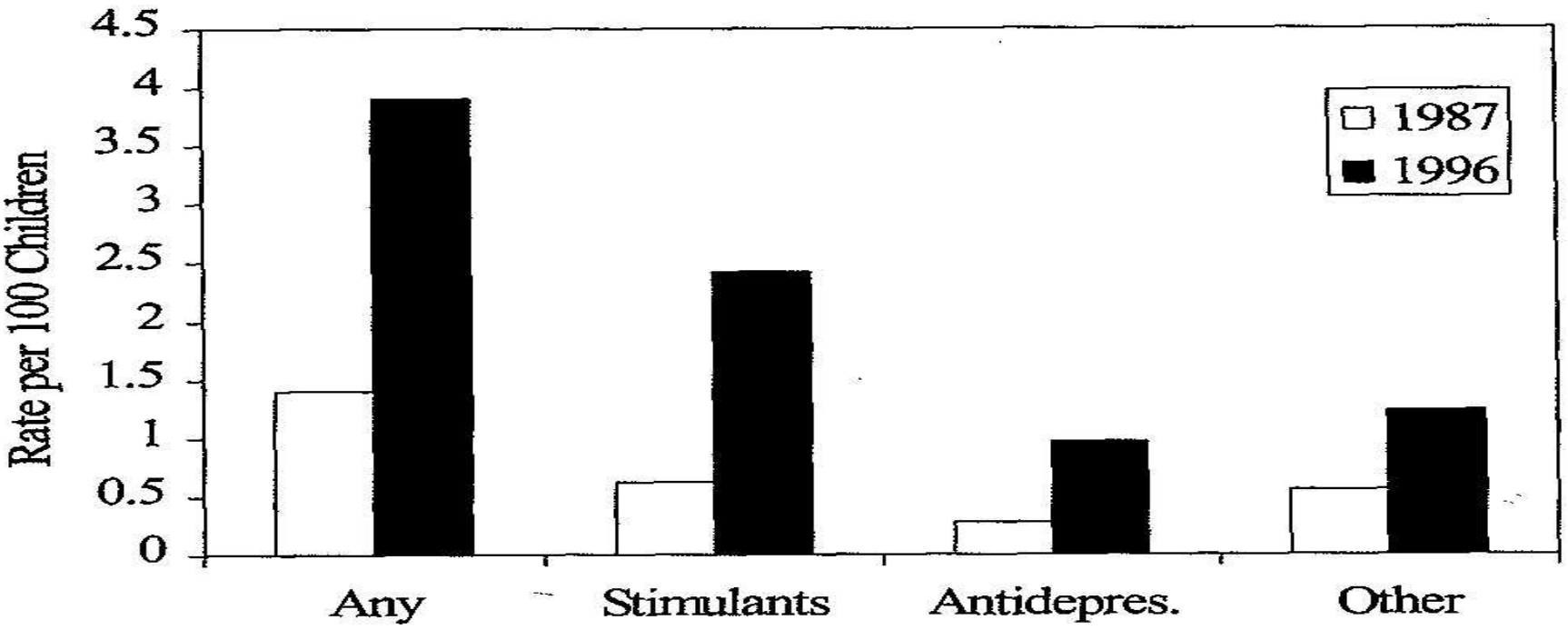


Fig. 1 Rates of psychotropic medication use by children in the United States. Data are from the 1987 National Medical Expenditure Survey (Edwards and Berlin, 1989) and the 1996 Medical Expenditure Panel Survey (Cohen, 1997a,b). Rates are for persons aged 18 years and younger. See text for definition of psychotropic medication groups.

TABLE 3

National Rates of Stimulant Use by Children and Adolescents in 1987 and 1996

	Rates of Stimulant Use per 100 Children and Adolescents (95% CI)	
	1987	1996
Age, years		
<6	0.22 (0.02–0.42)	0.31 (0.04–0.58)
6–14	1.18 (0.81–1.55)	4.14 (3.28–5.00)
15–18	0.15 (0–0.31)	1.56 (0.76–2.36)
Gender		
Female	0.28 (0.10–0.46)	1.23 (0.76–1.70)
Male	0.95 (0.66–1.24)	3.54 (2.68–4.40)
Race		
African American	0.26 (0.04–0.48)	2.02 (1.00–3.04)
Hispanic	0.15 (0–0.33)	0.74 (0.29–1.19)
White	0.80 (0.54–1.05)	3.03 (2.36–3.70)
Insurance		
Private	0.78 (0.51–1.05)	2.41 (1.90–2.92)
Public	0.54 (0.21–0.87)	3.59 (2.32–4.86)
None	0.21 (0–0.45)	0.65 (0.20–1.10)
Region of residence		
Northeast	0.39 (0.08–0.70)	1.66 (0.90–2.42)
Midwest	0.78 (0.43–1.13)	2.60 (1.44–3.76)
South	0.88 (0.45–1.31)	3.48 (2.52–4.54)
West	0.14 (0.02–0.26)	1.28 (0.80–1.76)

Note: Data are from the 1987 National Medical Expenditure Survey (Edwards and Berlin, 1989) and the 1996 Medical Expenditure Panel Survey (Cohen, 1997a,b). CI = confidence interval.

Incidence of ADHD

- In 2003, approximately **4.4 million** children aged 4--17 years were reported to have a history of ADHD diagnosis; of these, **2.5 million** (56%) were reported to be taking medication for the disorder.

- CDC - from the 2003 National Survey of Children's Health (NSCH).

Ritalin Use in the United States

Estimated Number of Children Taking Ritalin

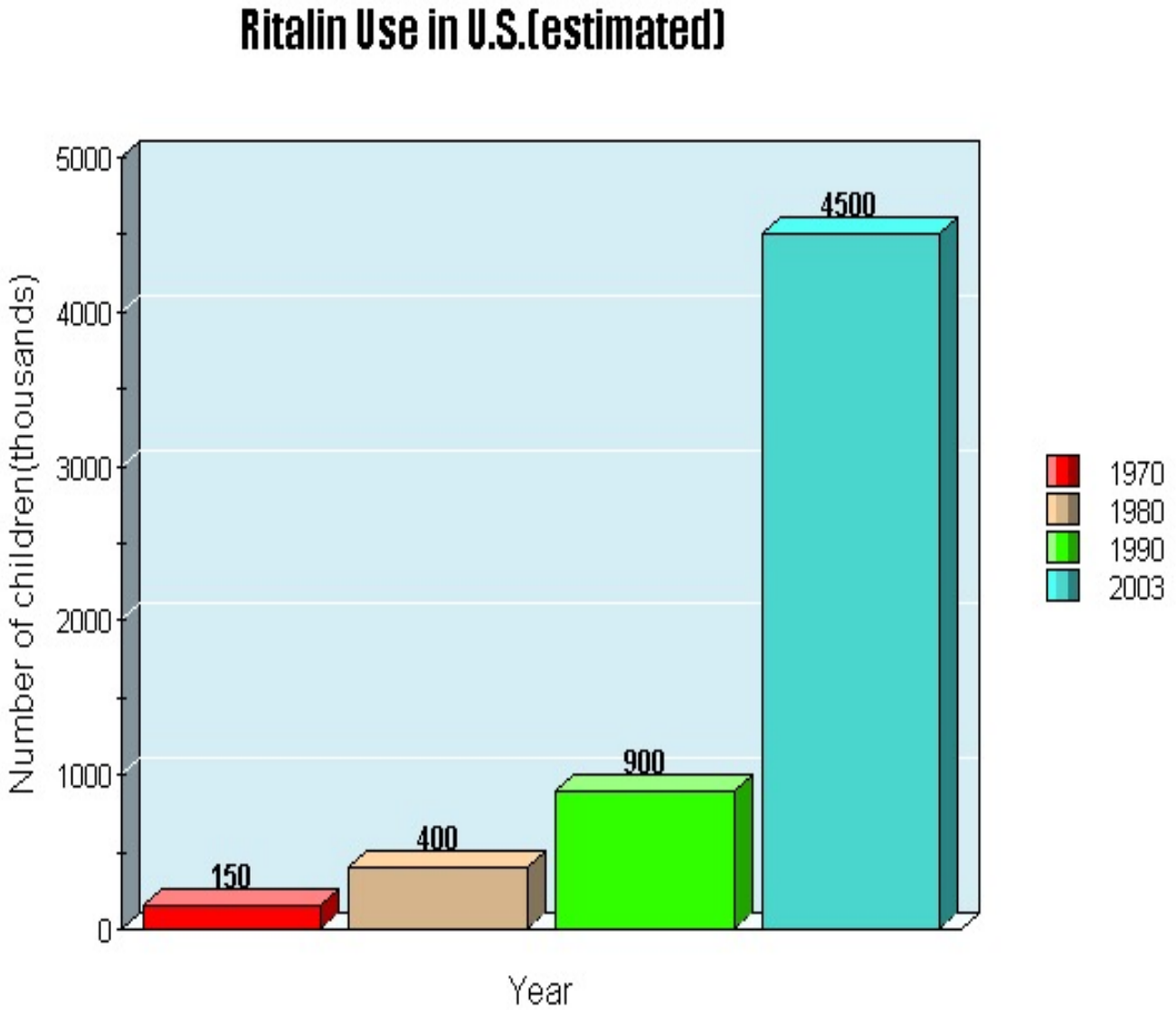
1970 - 150,000

1980 - Between 270,000 and 541,000;

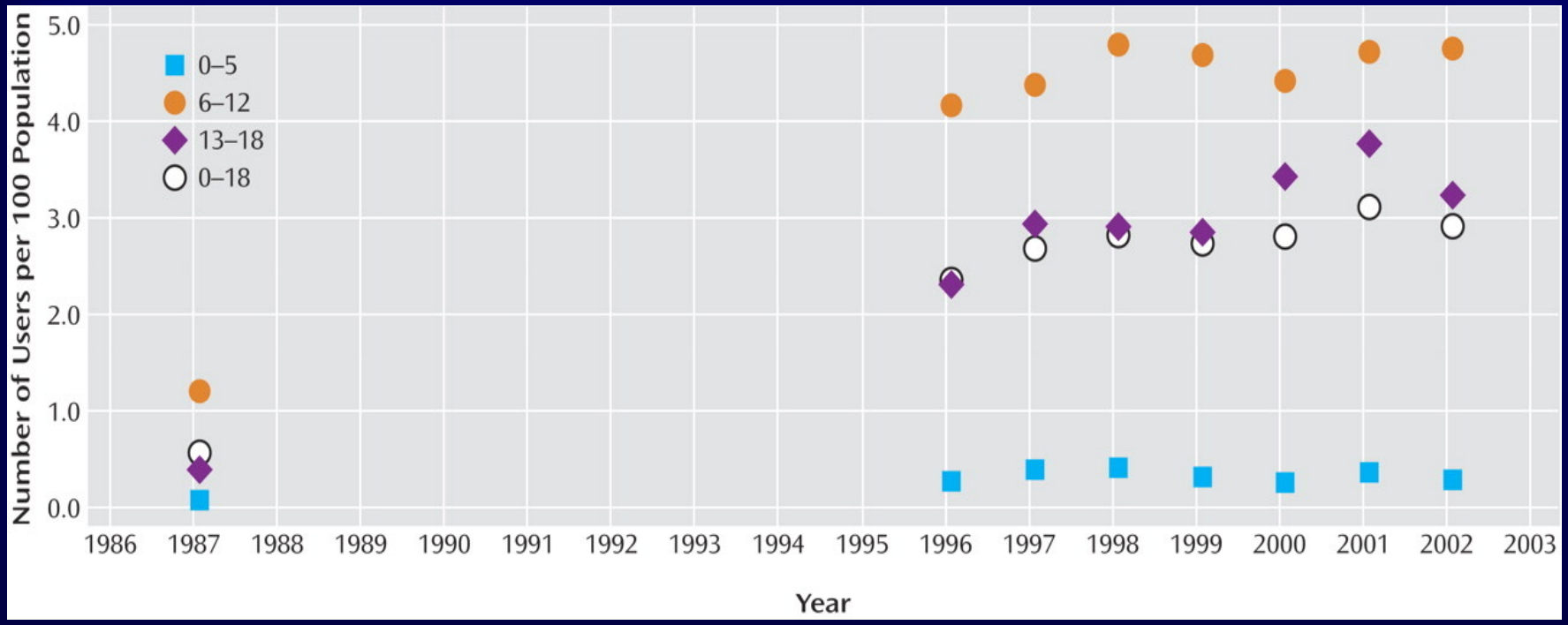
1990 - 900,000,

2003 - 2.5 million

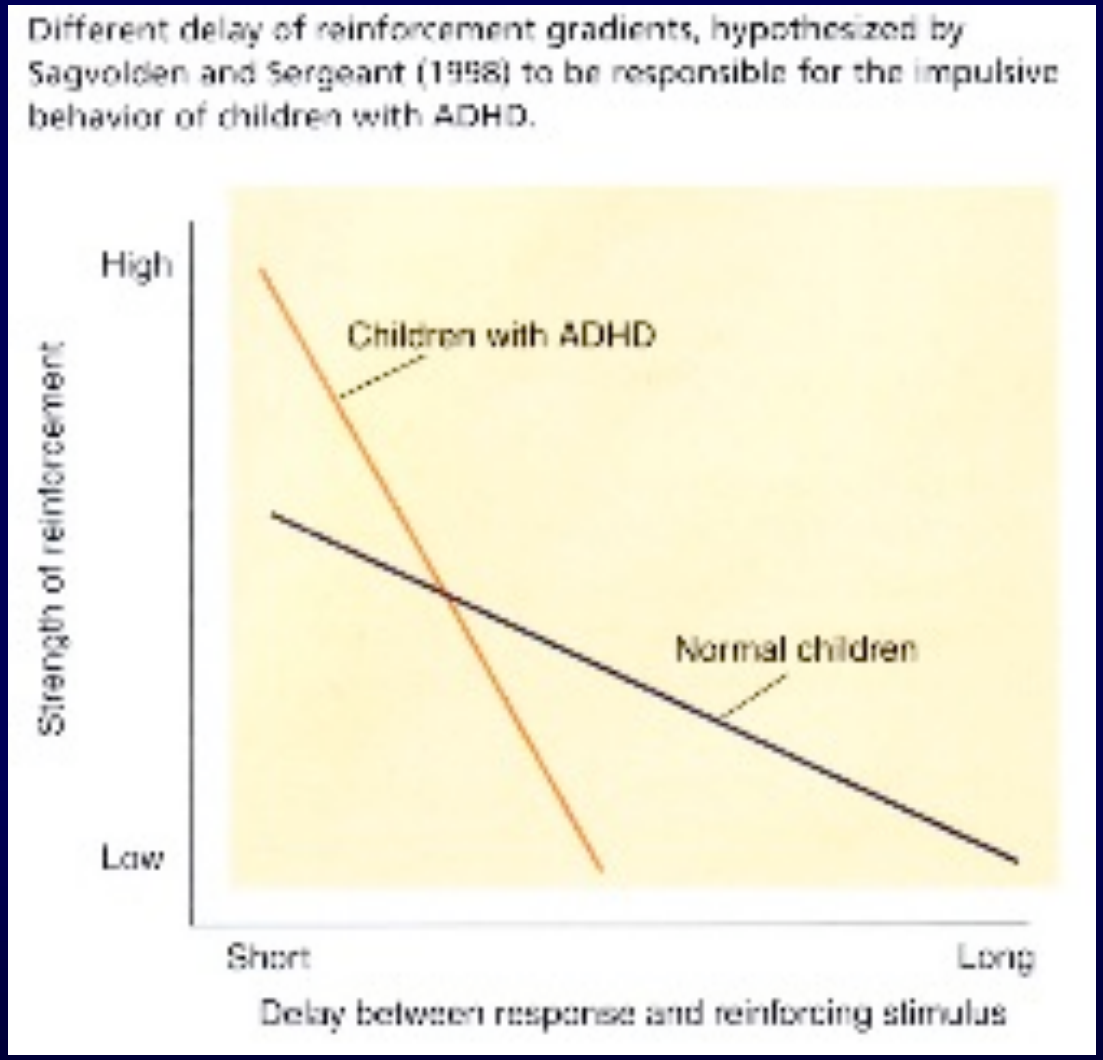
F S

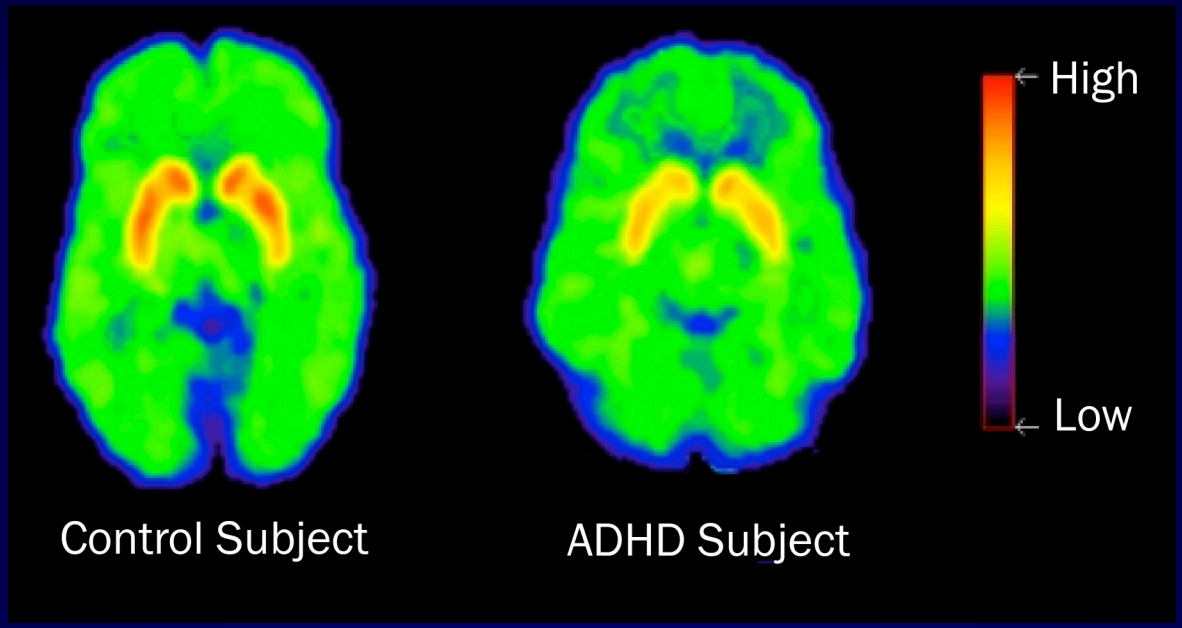

Ritalin Use in U.S.(estimated)
Number of children(thousands)
5000
4000
3000
2000
1000
0
150
400
900
4500
Year
1970
1980
1990
2003

Stimulant Use -Leveling Off Over the Last 5 Years, but Still Very High



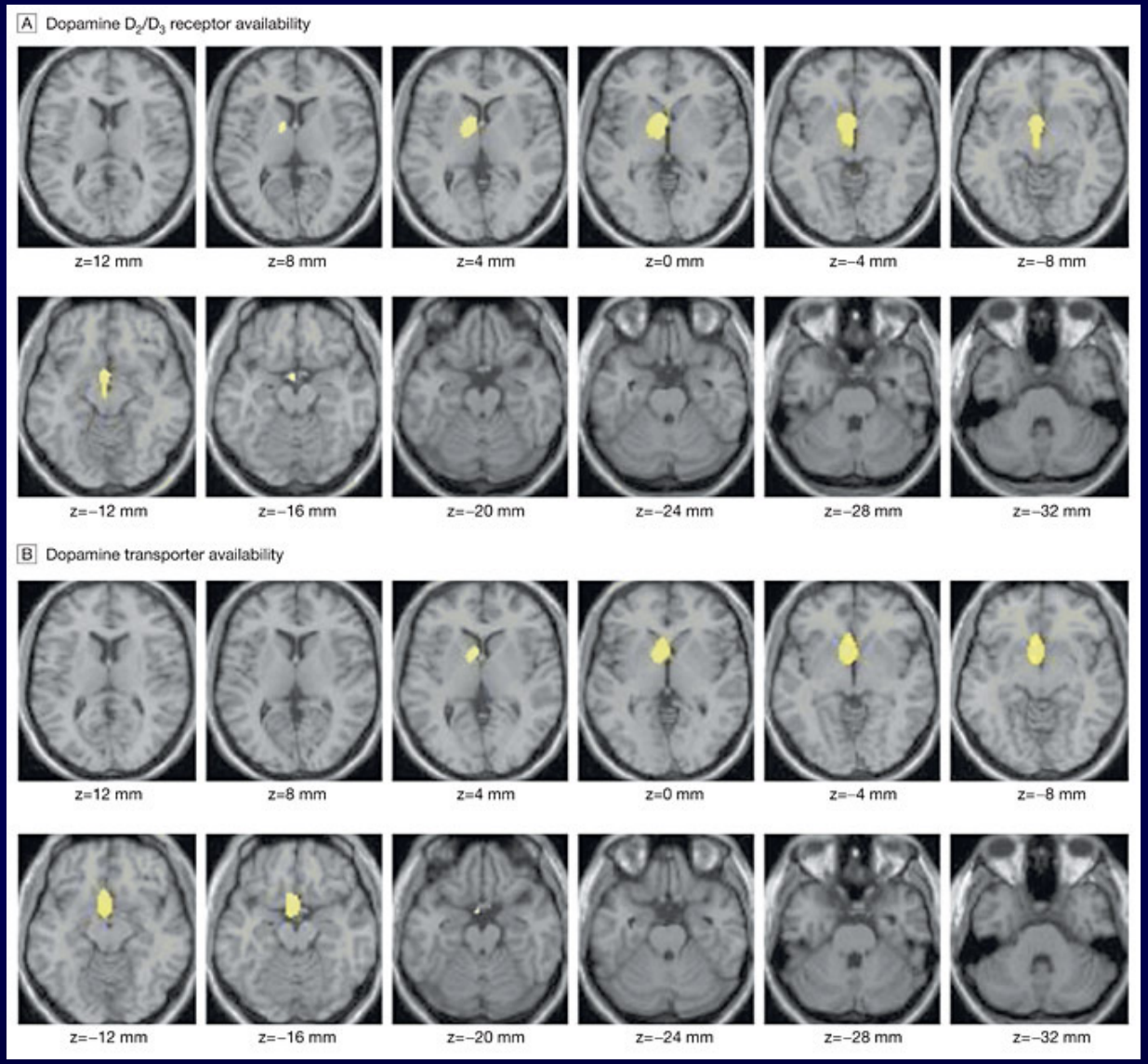
Spiegazione nei termini di riduzione dell'intervallo temporale del gradiente del rinforzo (ipoteticamente legato ad una disfunzione dopaminergica)





These PET scans show that patients with ADHD had lower levels of dopamine transporters in the nucleus accumbens, a part of the brain's reward center, than control subjects

Regions in the Brain in Which Dopamine Measures Were Lower in Participants With ADHD Than in Controls



Volkow, N. D. et al. JAMA 2009;302:1084-1091.

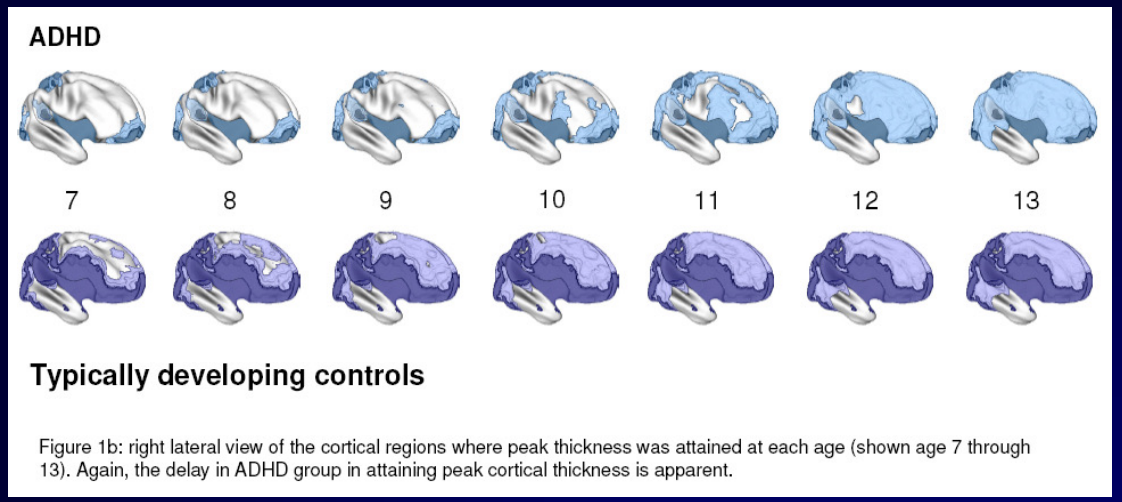
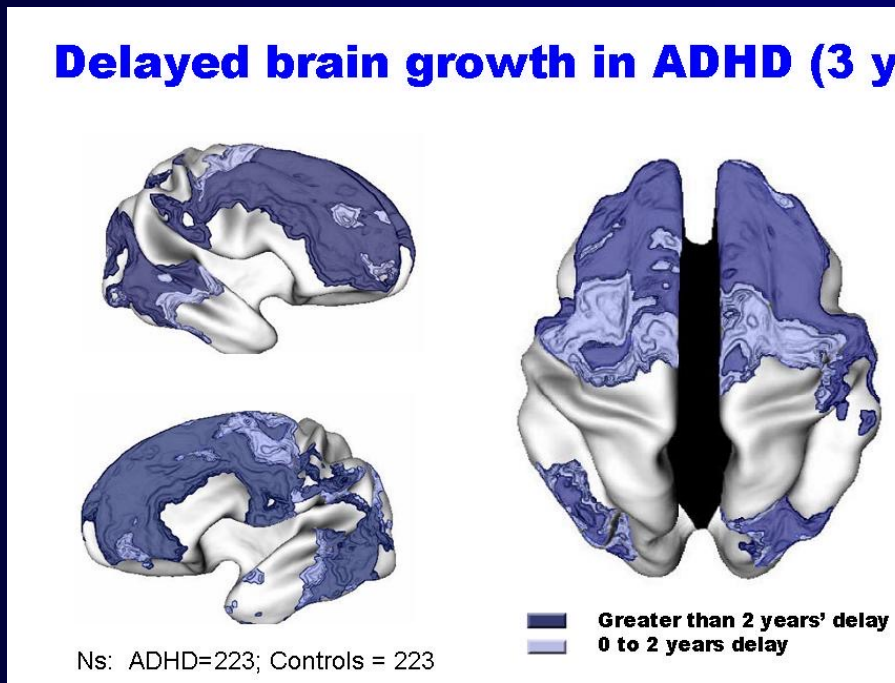
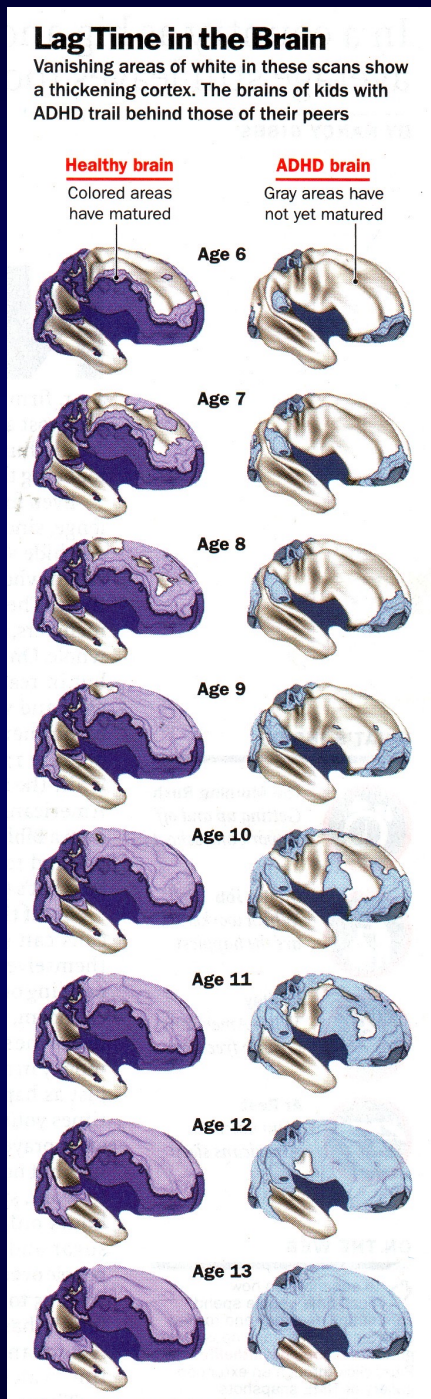


Figure 1b: right lateral view of the cortical regions where peak thickness was attained at each age (shown age 7 through 13). Again, the delay in ADHD group in attaining peak cortical thickness is apparent.



From Shaw, P. et al. (2007). ADHD is characterized by a delay in cortical maturation. *Proceedings of the National Academy of Sciences, 104*, 19649-19654.

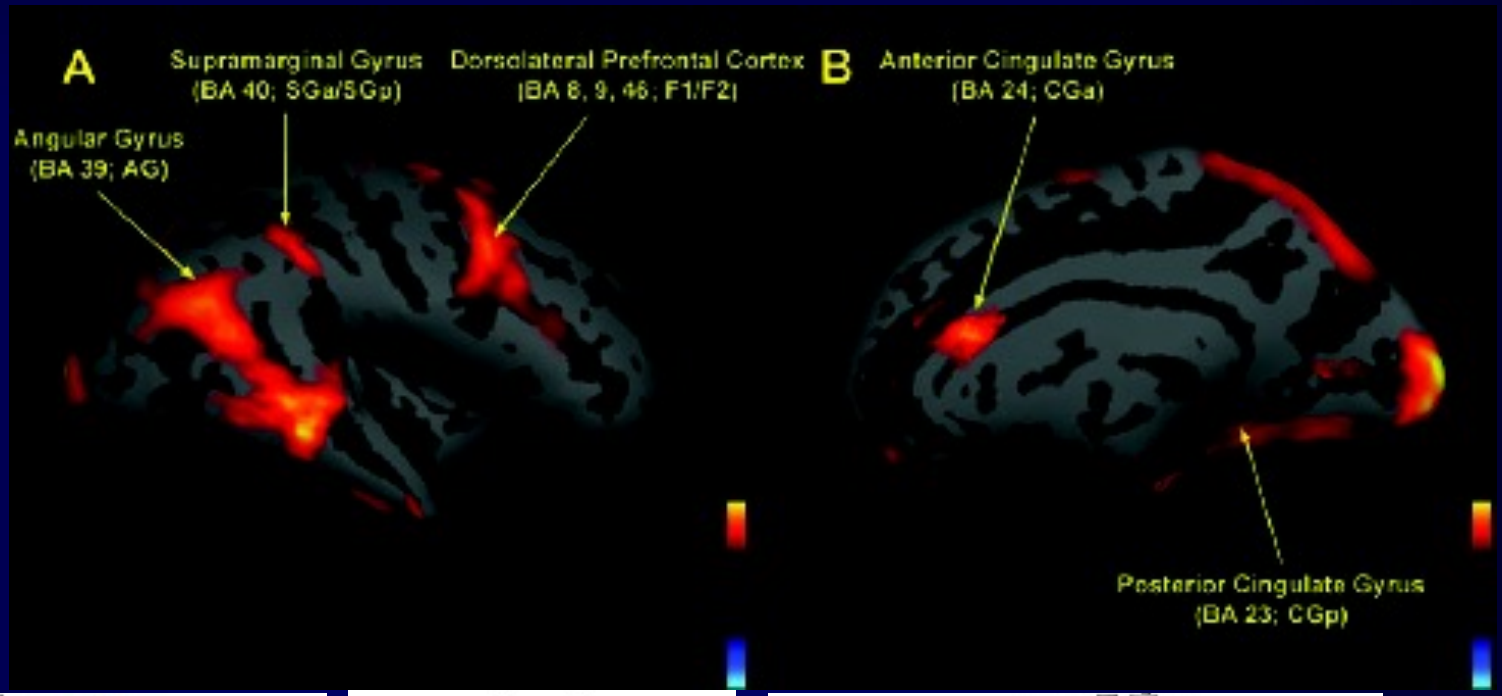


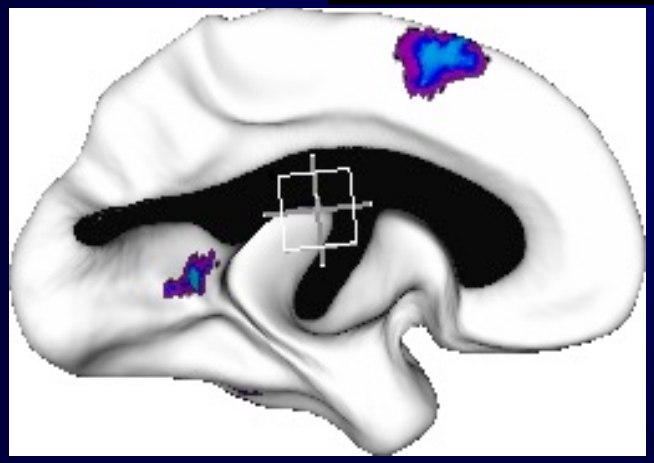
Cortical Thickness in ADHD: Cingulate Cortex

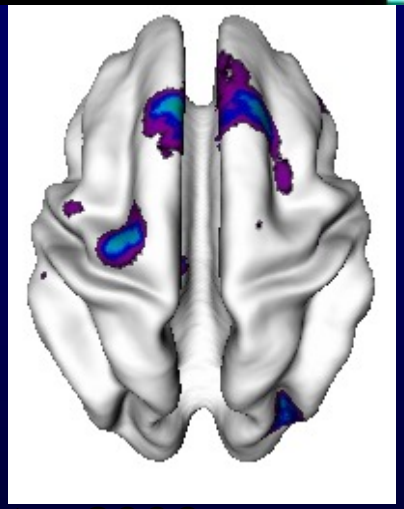
Makris et al.

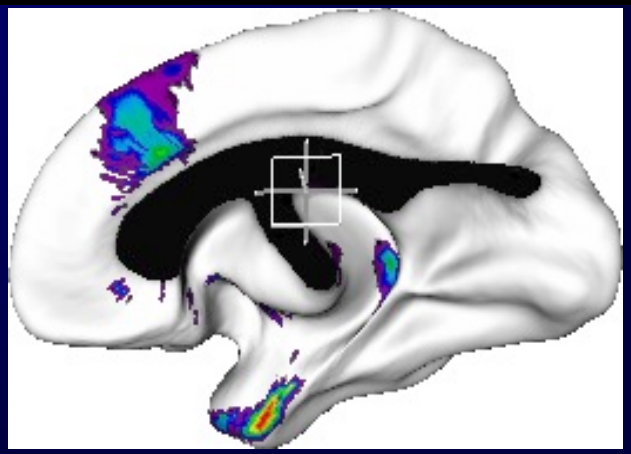
Cerebral Cortex

2006



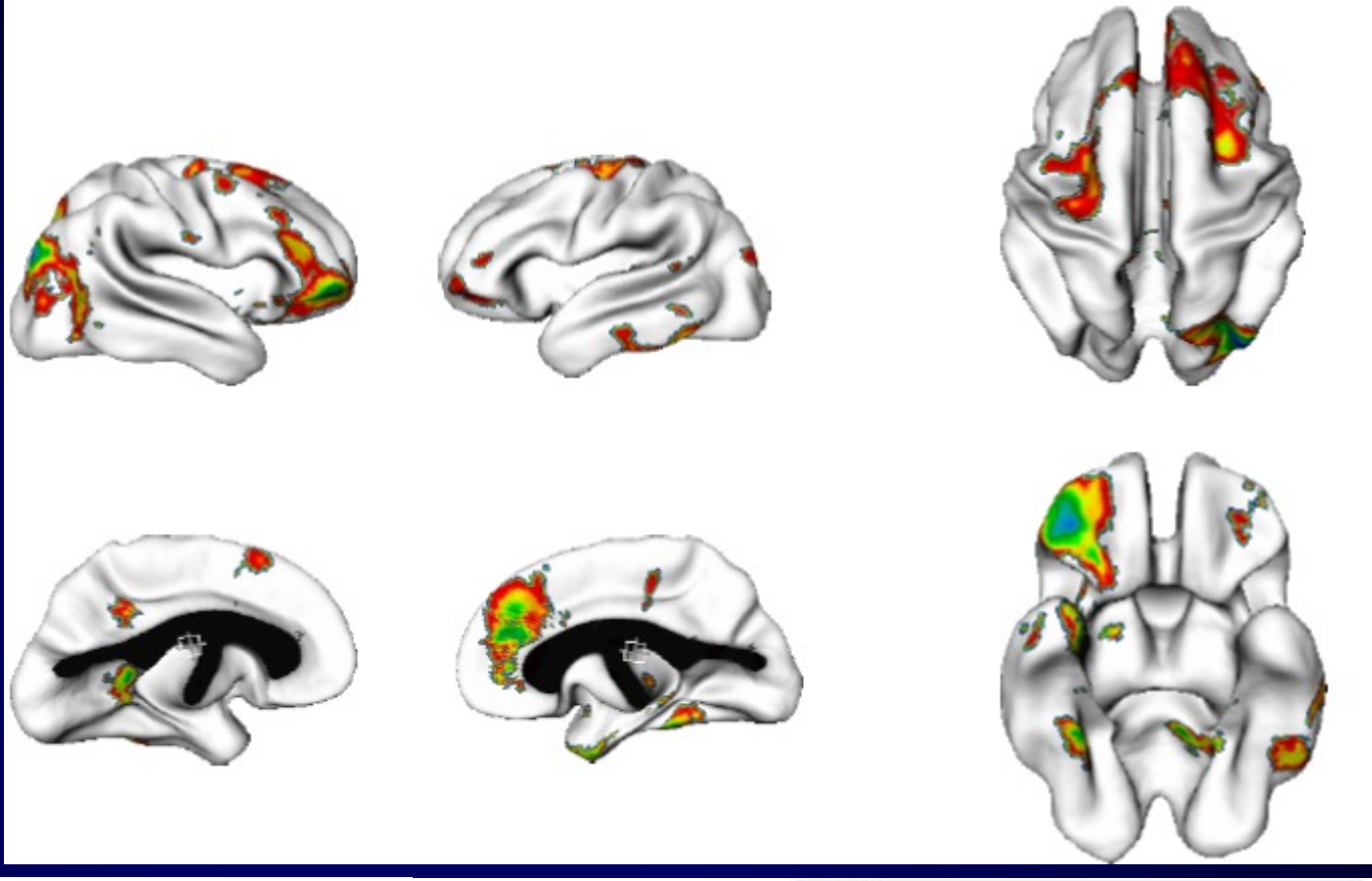


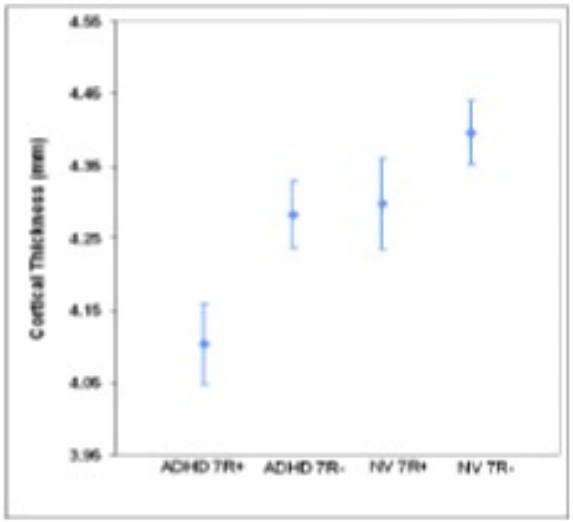


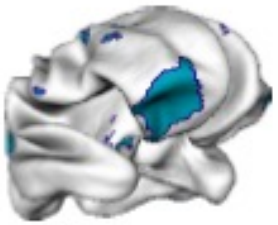


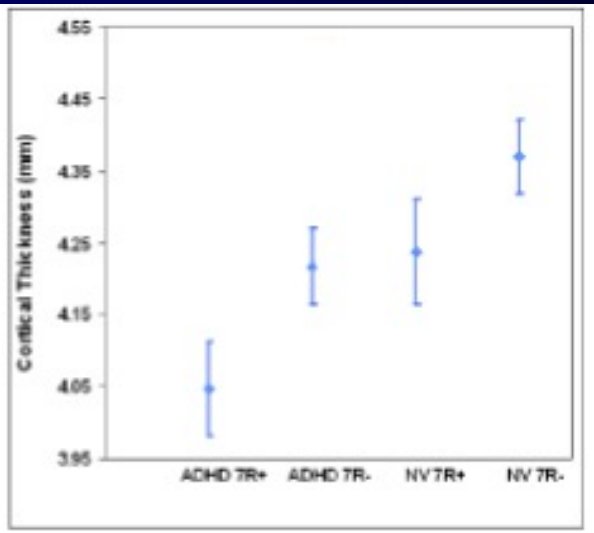
Shaw et al., Arch Gen Psychiatry 2006

Cortical Thickness & DRD4 (gene che codifica il sottotipo recettoriale D4) Shaw et al. AGP 2007









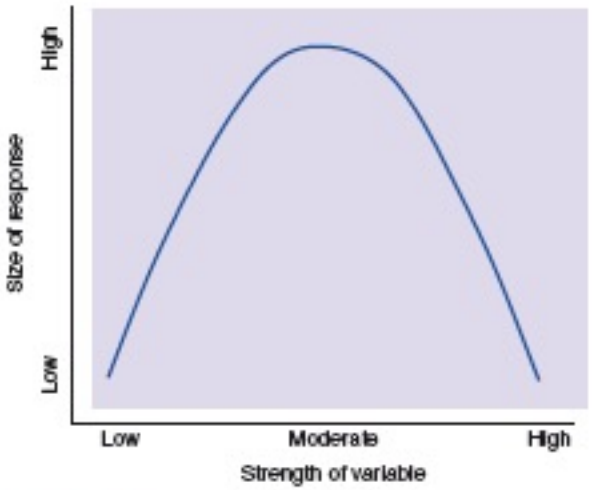


FIGURE 17.9 An Inverted U Curve

The graph illustrates an inverted U-curve function, in which low and high values of the variable on the horizontal axis are associated with low values of the variable on the vertical axis and moderate values are associated with high values. Presumably, the relationship between brain dopamine levels and the symptoms of ADHD follow a function like this one.

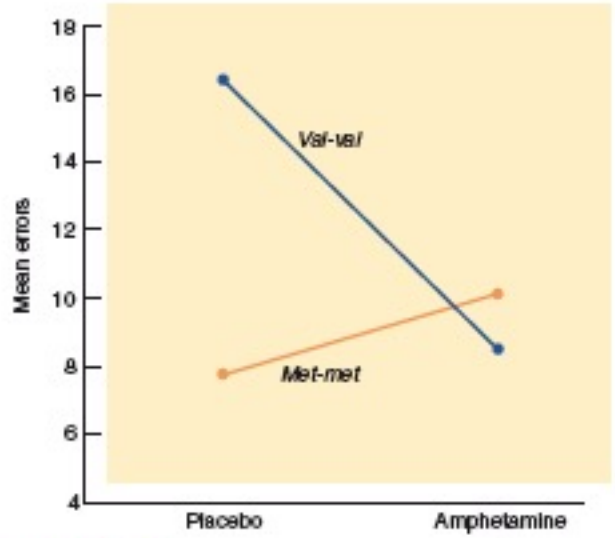


FIGURE 17.10 Interactions Between Amphetamine and COMT Alleles on Working Memory

The graph shows the differential effects of amphetamine on the performance on a working memory task of people with two different variants of the gene for the COMT enzyme. The performance of people with the *val-val* variant was enhanced by amphetamine, and the performance of people with the *met-met* variant was reduced.

(Based on data from Mattay et al., 2003.)

Ruolo del gene per l'enzima COMT

Treatment

- Medication
- Behavioral Therapy
  - Cognitive/Behavioral Therapy
  - Parent Management Training
  - Social Skills Training
- Educational Support

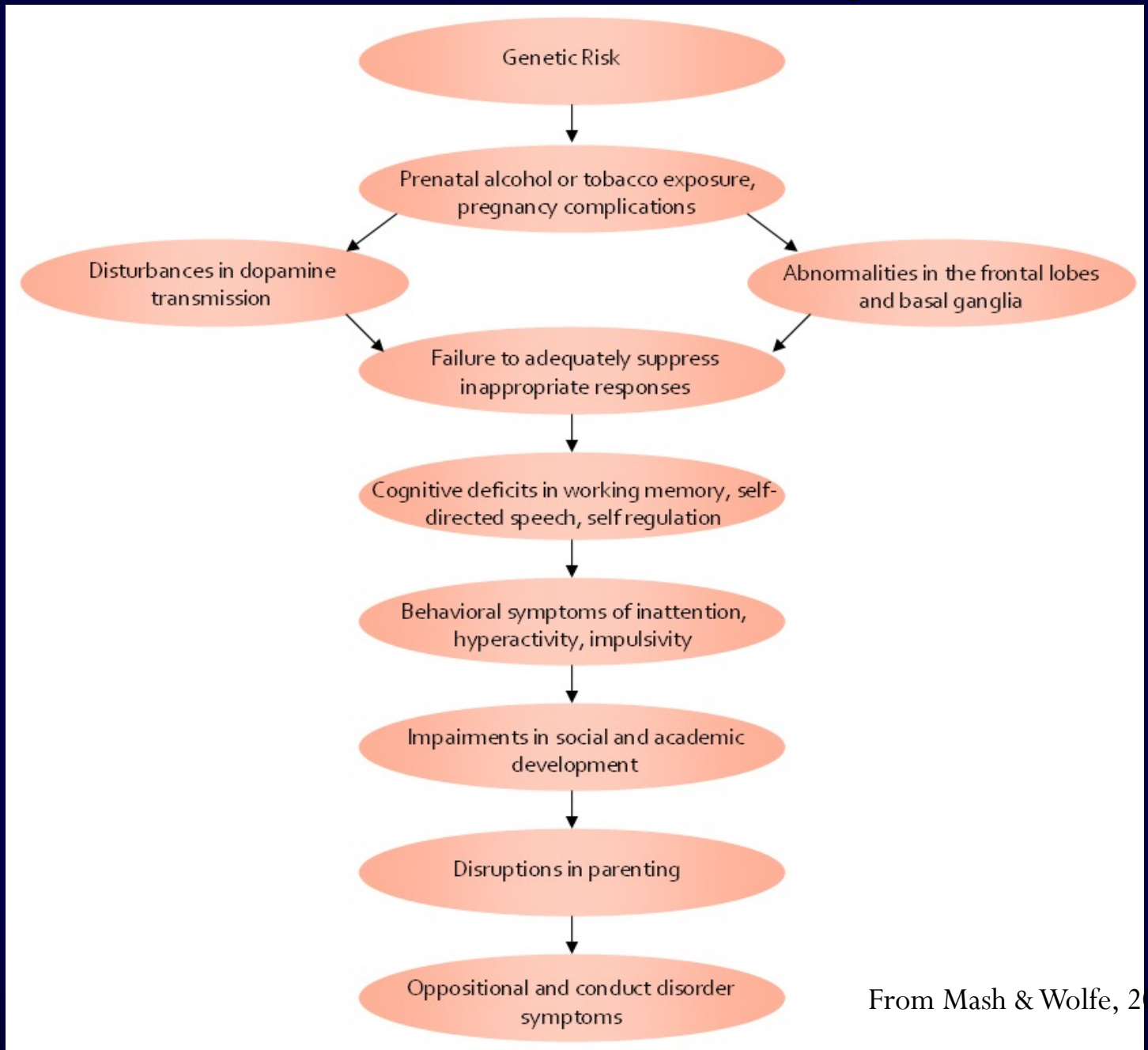
Barkley's Theory

"ADHD is not a problem with knowing what to do; it is a problem of doing what you know."

-Barkley, 2006

- Behavioral disinhibition is the basis of executive functioning deficits in ADHD
- A performance, rather than knowledge, deficit

A Possible Developmental Pathway for ADHD



From Mash & Wolfe, 2007

C'ERA UNA VOLTA

"INVENTORI DI MALATTIE"

Deregistrazione audio, a cura del C.M.S.di Foggia, del documentario mandato in onda su RAI 3 nazionale in data 5 agosto 2009