



Porque **creemos** en la genialidad de cada niño

Trastorno por Déficit de Atención e Hiperactividad *¿Es seguro el tratamiento?*

*"Empieza por hacer lo necesario,
luego haz lo posible
y, de pronto, estarás haciendo lo imposible"*



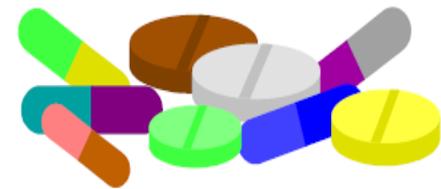
➤ Aprobación para estudio

➤ Estudio en humanos

Fase I: Tolerancia

Fase II: Eficacia (ensayos clínicos)

Fase III: **Farmacovigilancia**



Farmacovigilancia

Seguridad

EEUU,
1936

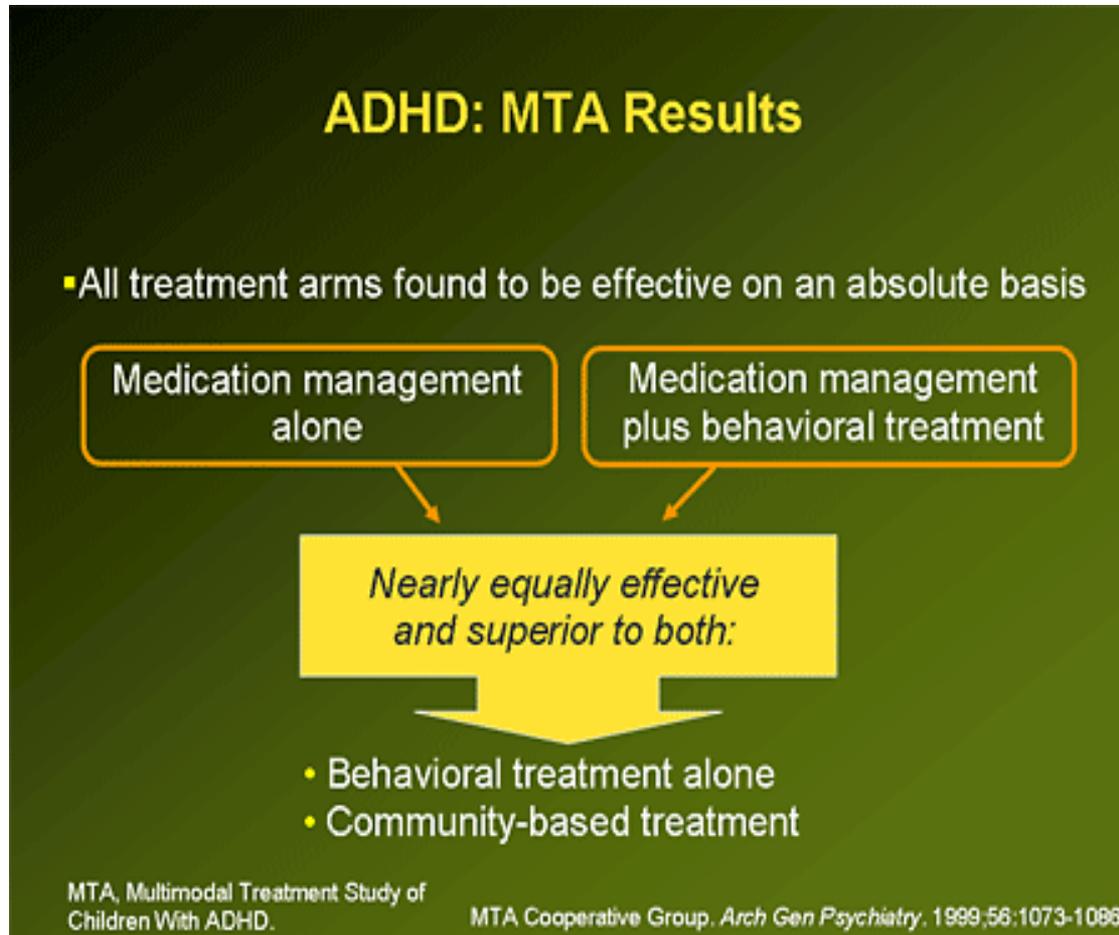
España,
1984

- Disminución de apetito
- Pérdida de peso
- Insomnio

- Irritabilidad
- Cambios de humor

- Inespecíficos.

Indicación del tratamiento



MTA Multimodal Treatment Study of Children With ADHD
MTA Cooperative Group. *Arch Gene Psychiatry*, 1999;56:1073-1066

Clasificación

Estimulantes

Metilfenidato

Liberación inmediata (*Rubifen*)

Liberación bifásica/media
(*medikinet*)

Liberación retardada (*Concerta*)

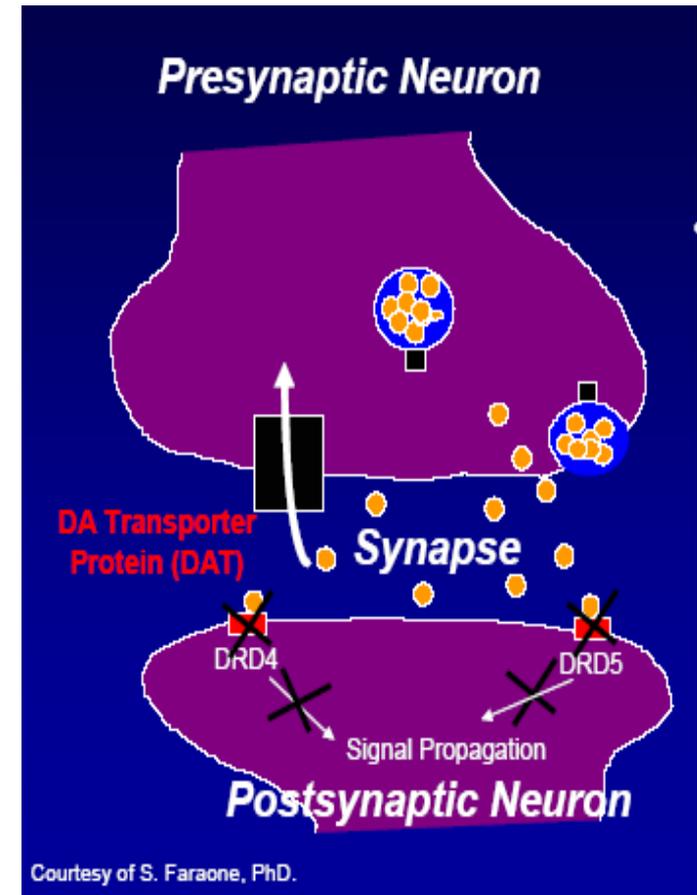
Sales/Derivados anfetamínicos

LDX

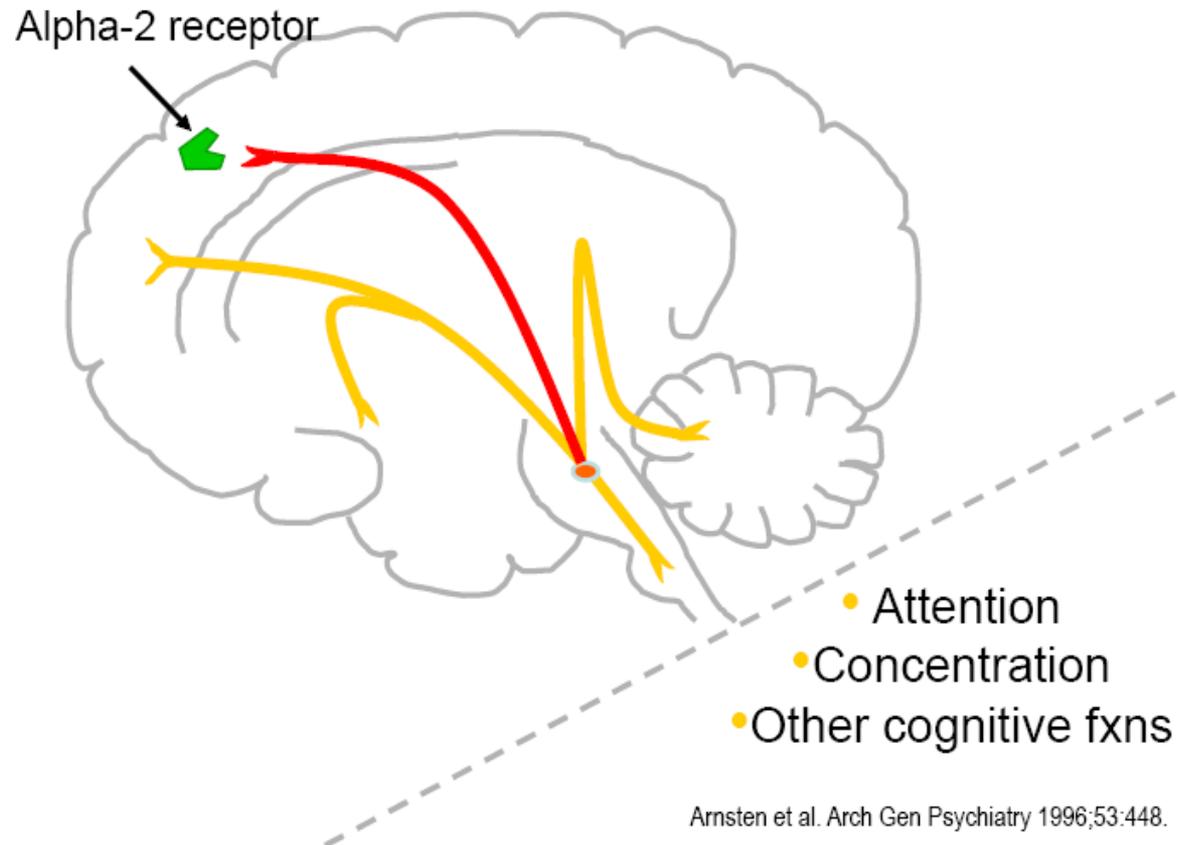
(*FDA aprobado*)

TDAH-Tratamiento

Tratamiento



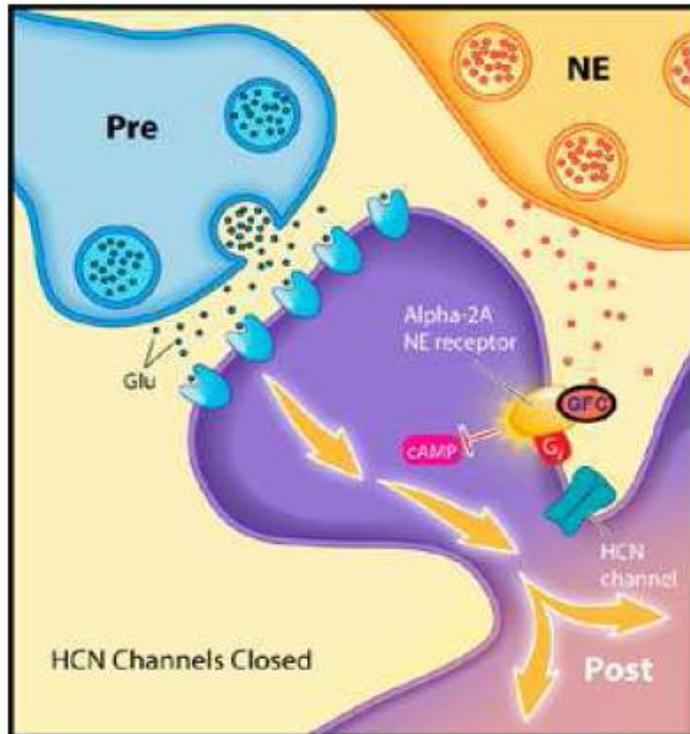
Atamoxetina



Clasificación

**Antihipertensivos
(Guanfacina)**

Tenex (FDA aprobado)



Antidepresivos

Modafinilo

Bupropion (FDA aprobado)

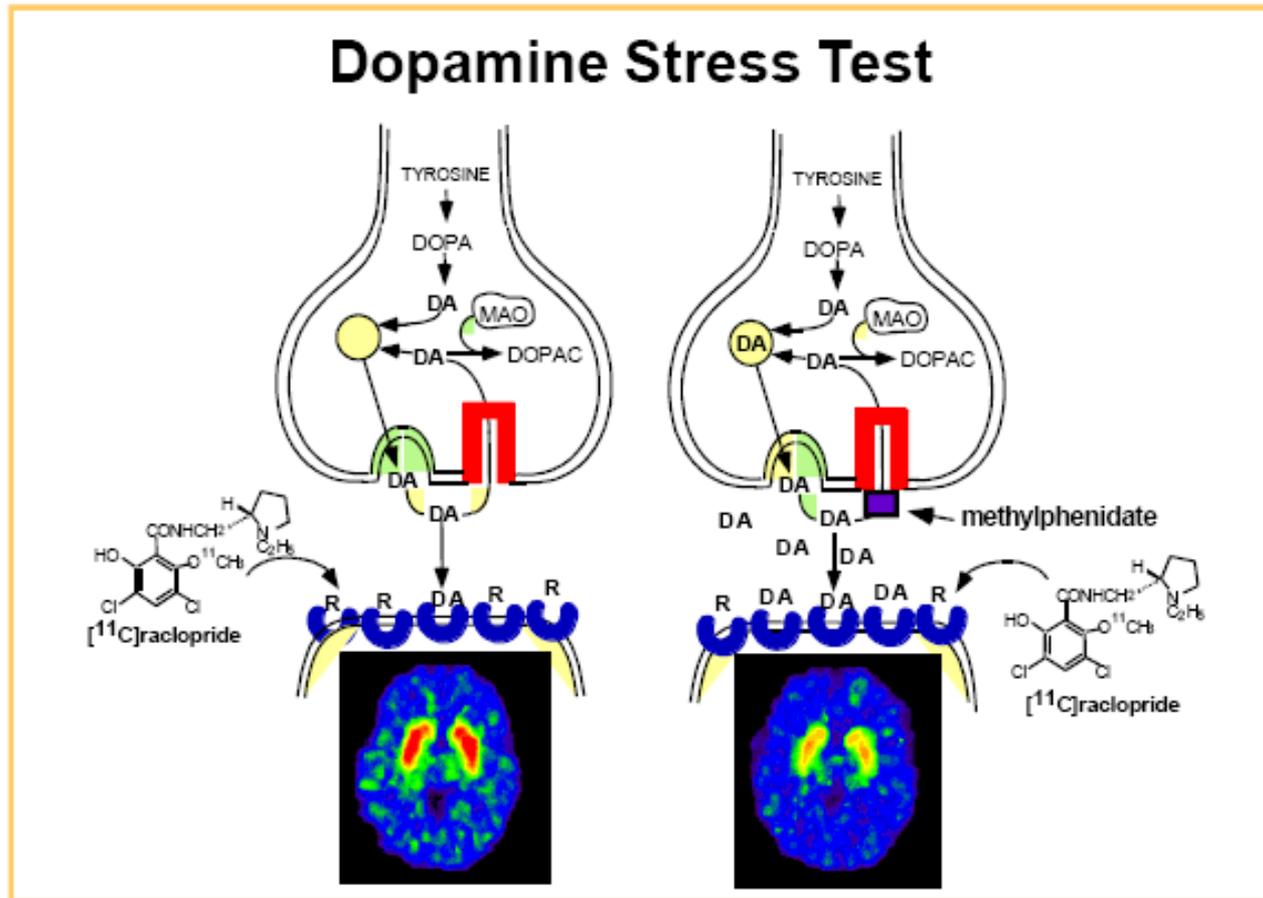
Tricíclicos

En investigación:

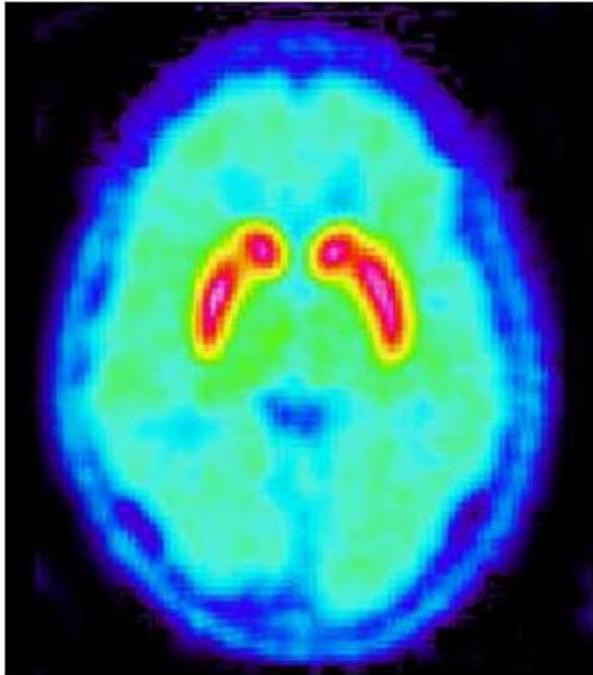
**Agentes colinérgicos
(donepezilo, galantemina)**

**Acidos Omega- 3 (agente natural,
resultados no concluyentes)**

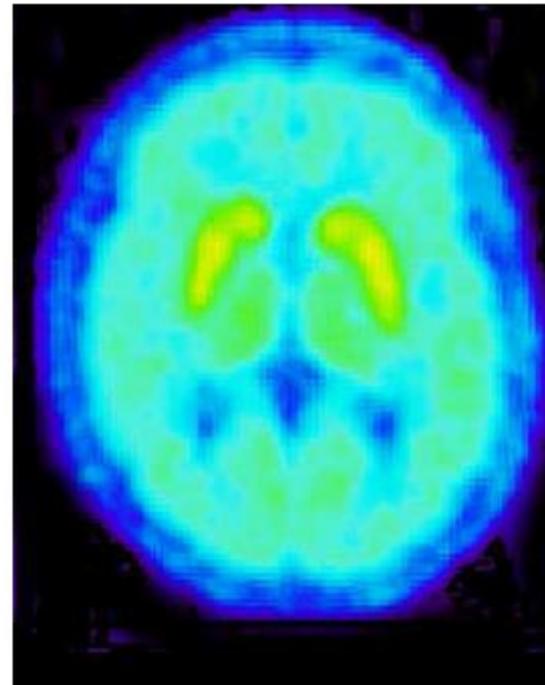
Hallazgos neuroquímicos



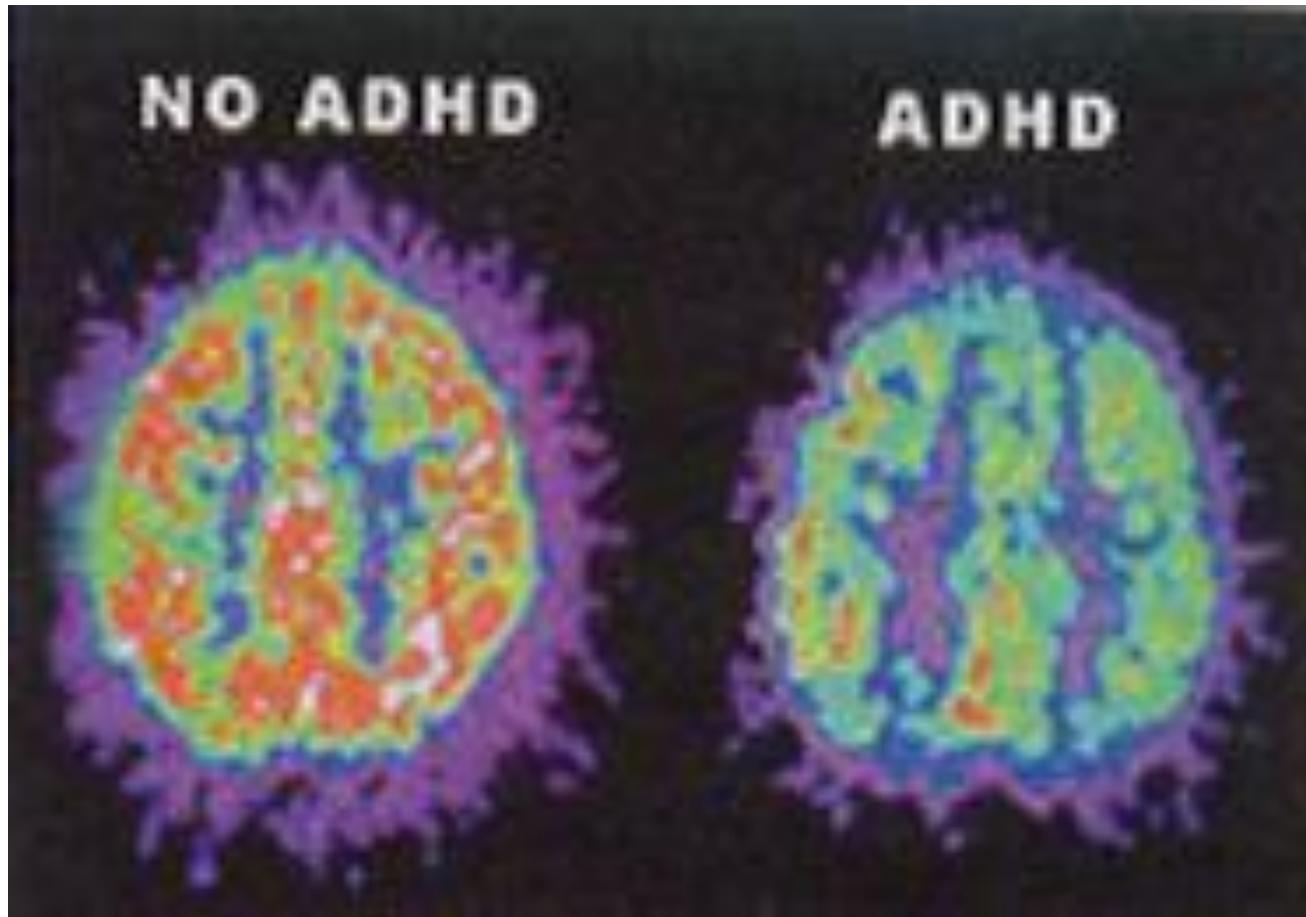
Hallazgos neuroquímicos



Baseline

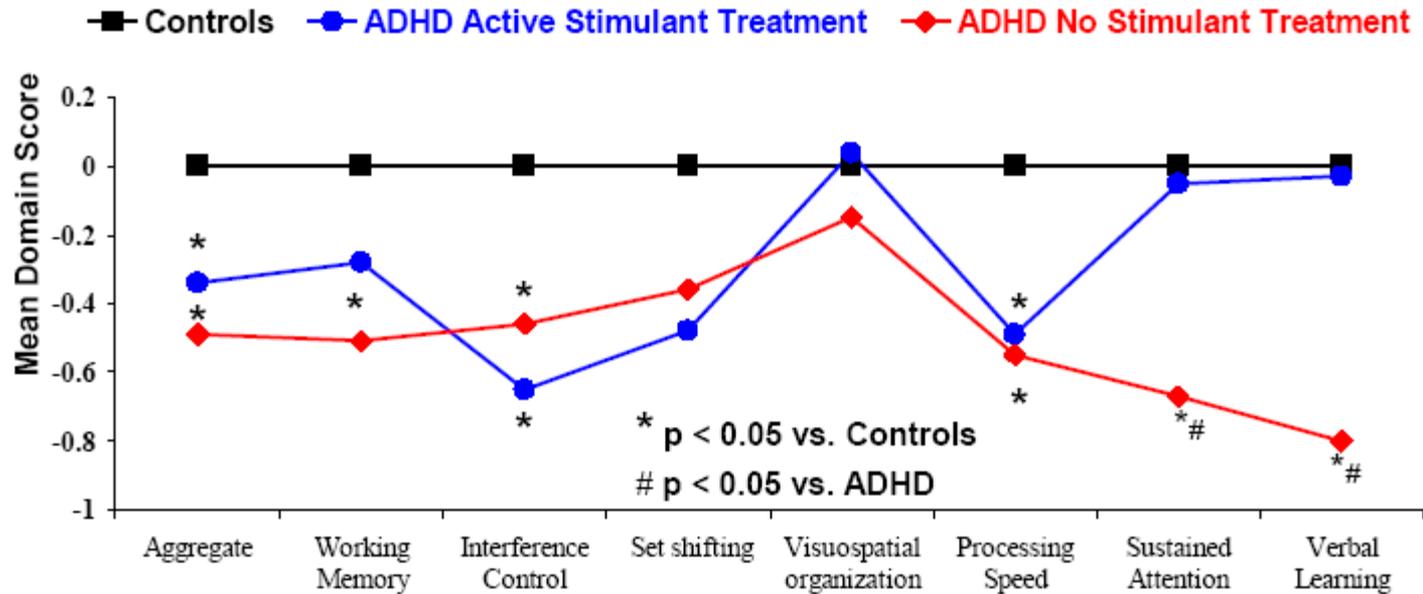


After Oral MPH



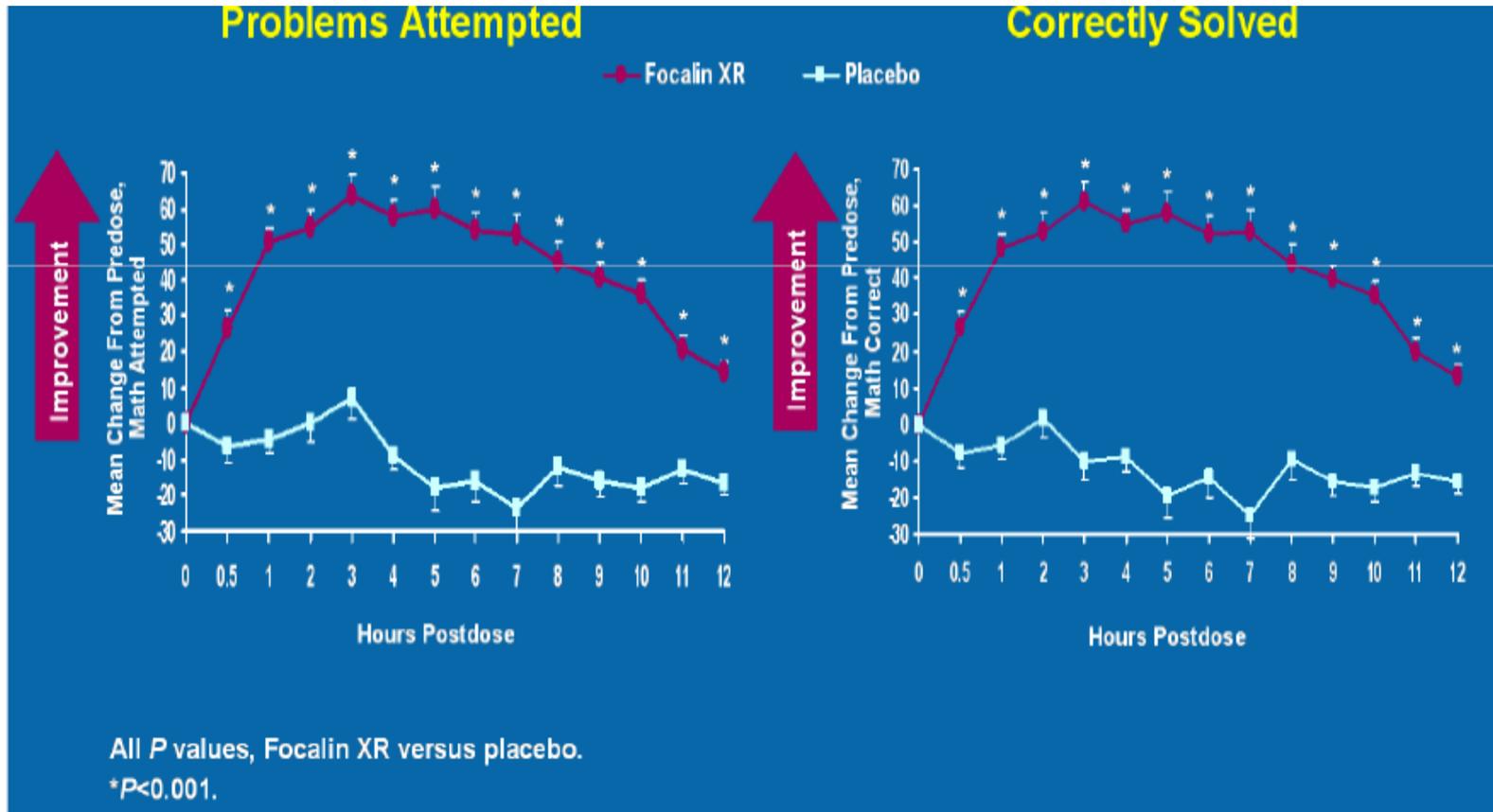
PET- Hipoactivación frontal

Respuesta al tratamiento



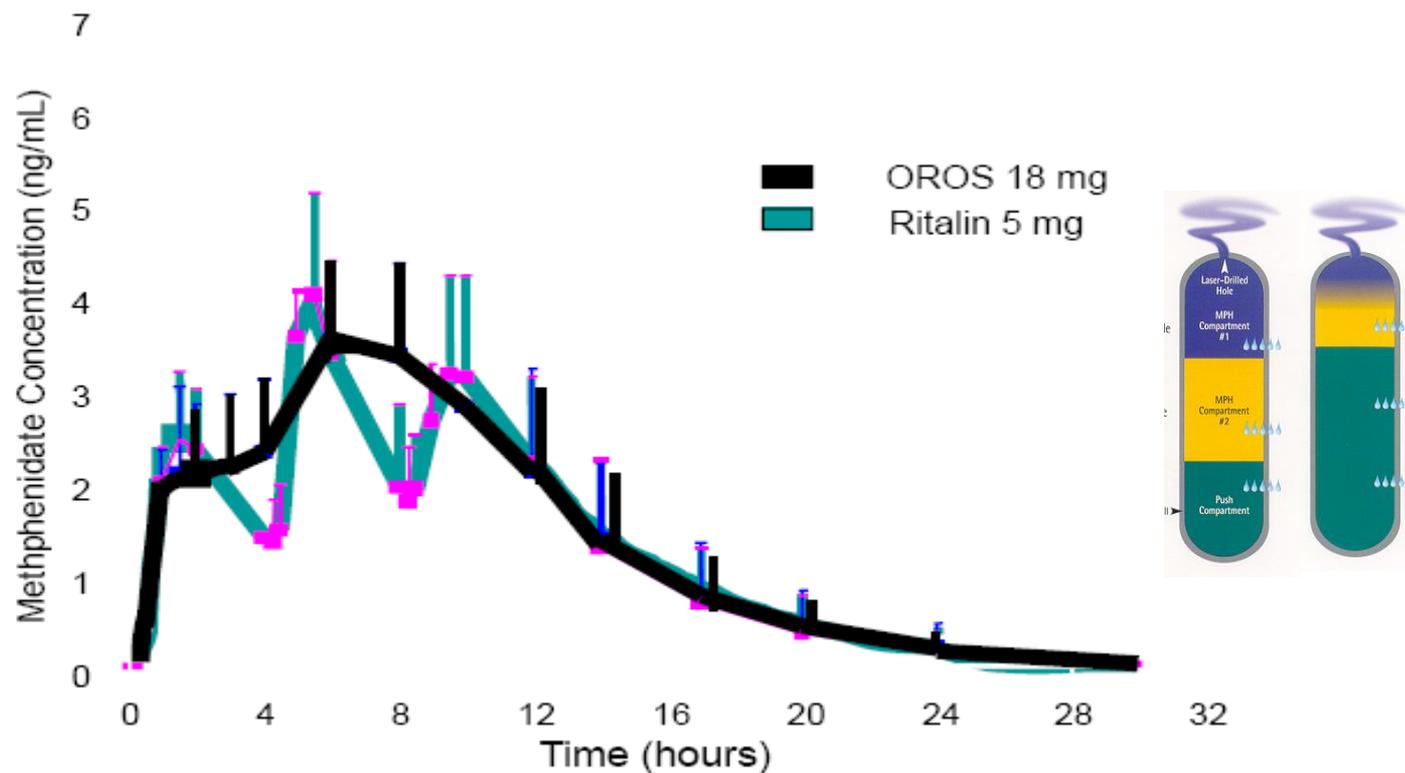
All comparisons adjusted for age and gender

Respuesta al tratamiento

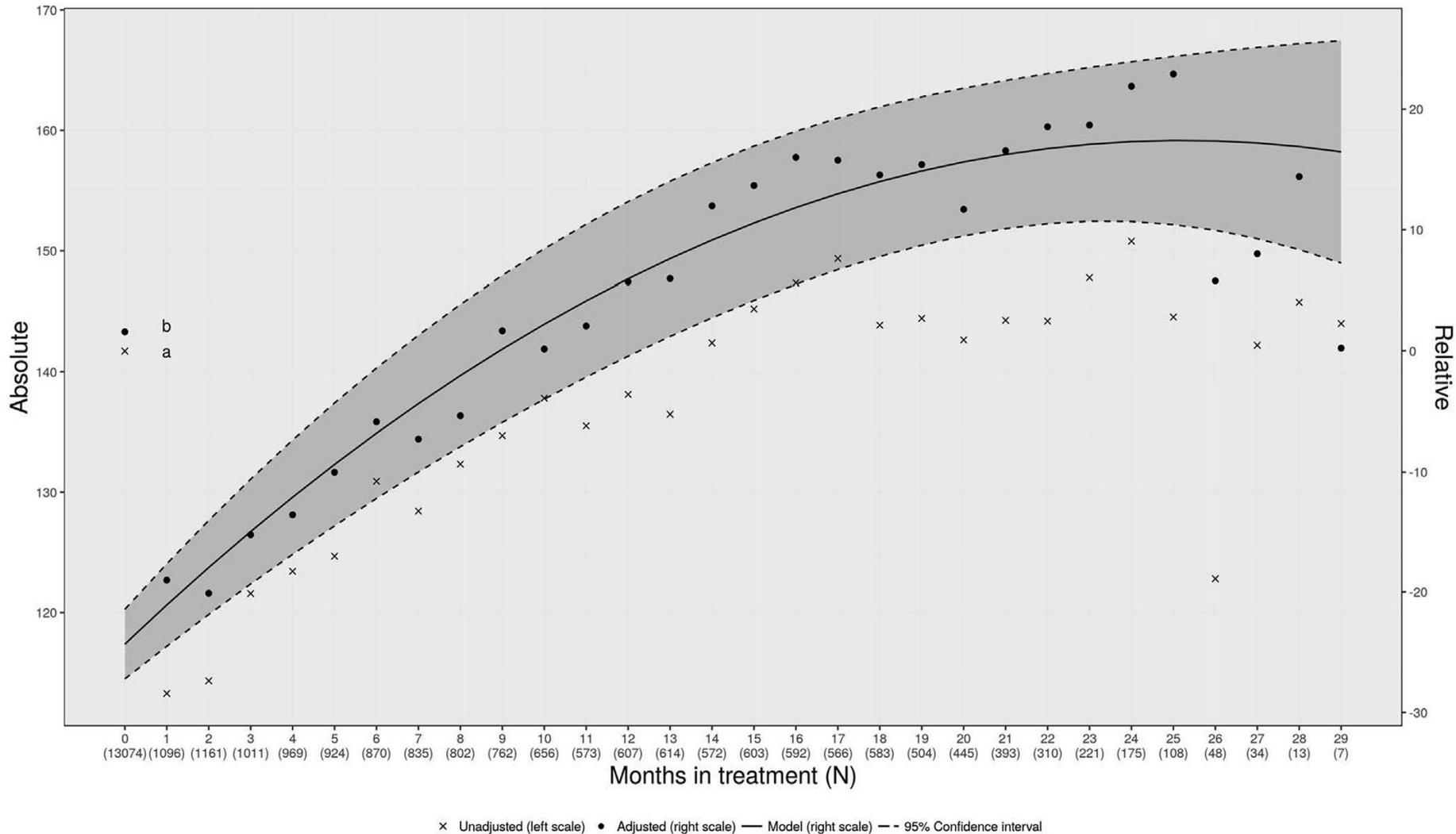


Turnbow JM et al. Poster. US Psychiatric and Mental Health Conference; 2005; Las Vegas, Nov.

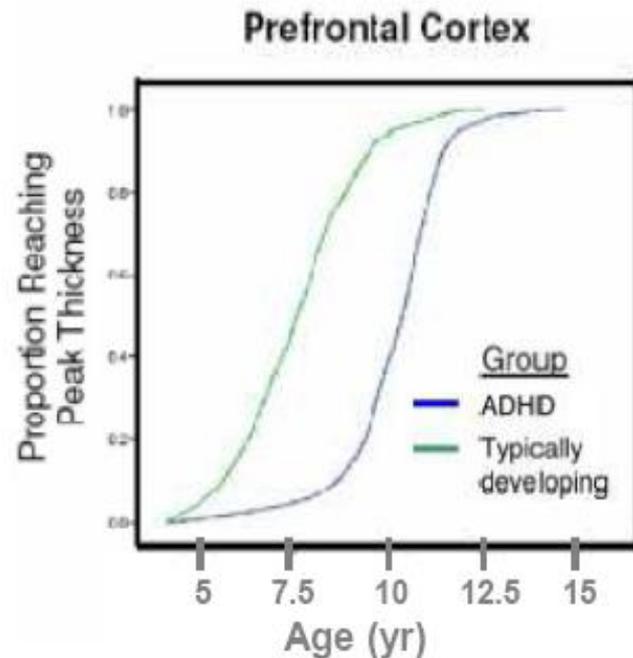
Concentración de Metilfenidato (MPH)- Ritalin vs OROS-MPH



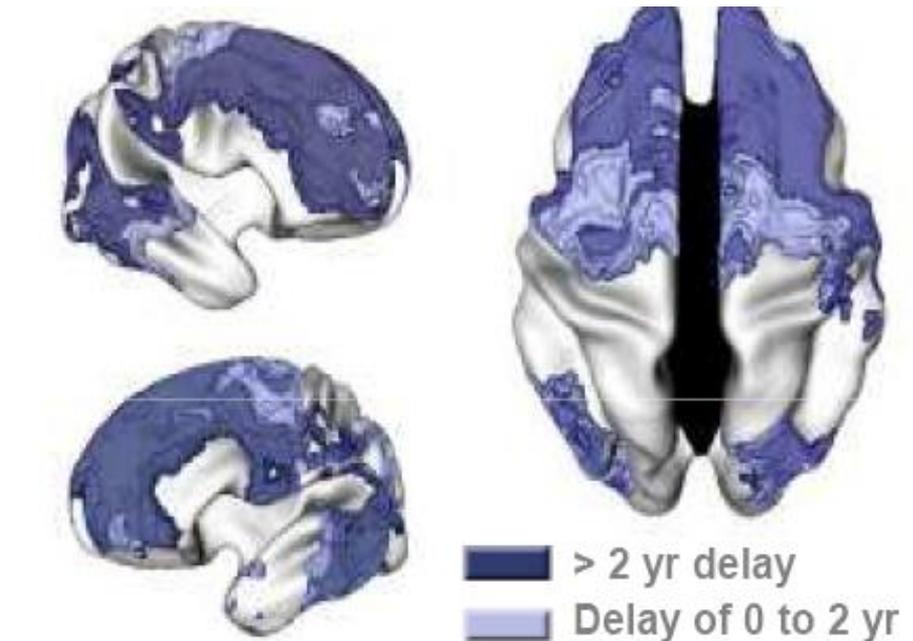
Grade Point Sum by Length of Treatment With Attention-Deficit/Hyperactivity Disorder (ADHD) Medication



Hallazgos en el desarrollo cerebral



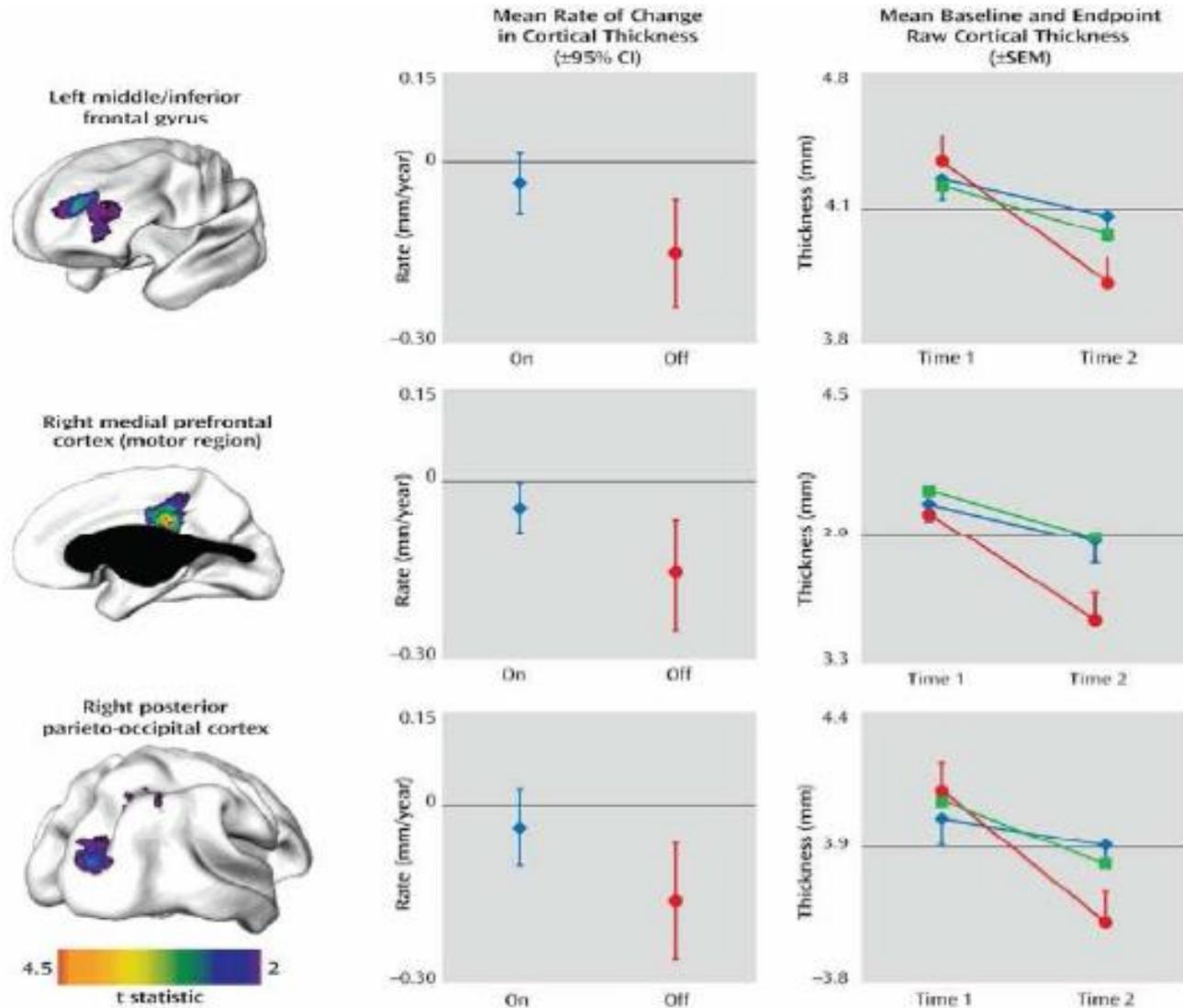
Kaplan-Meier curve showing fraction of cortical points that had reached peak thickness at each age



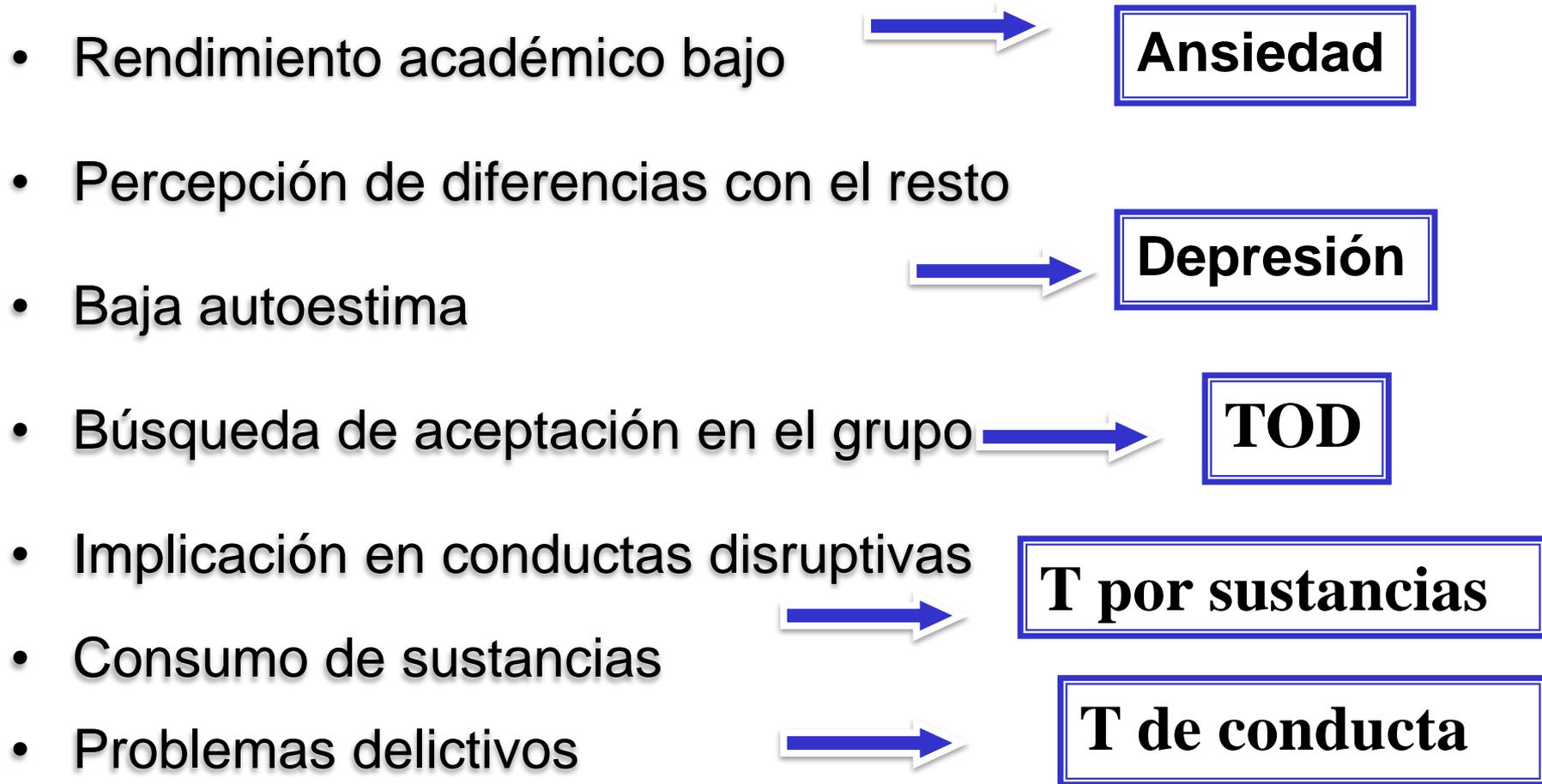
Regions where the ADHD group had delayed cortical maturation

Based on 824 MRI scans of 223 children with ADHD and 223 controls; longitudinal data; mean interval between scans 2.8 years

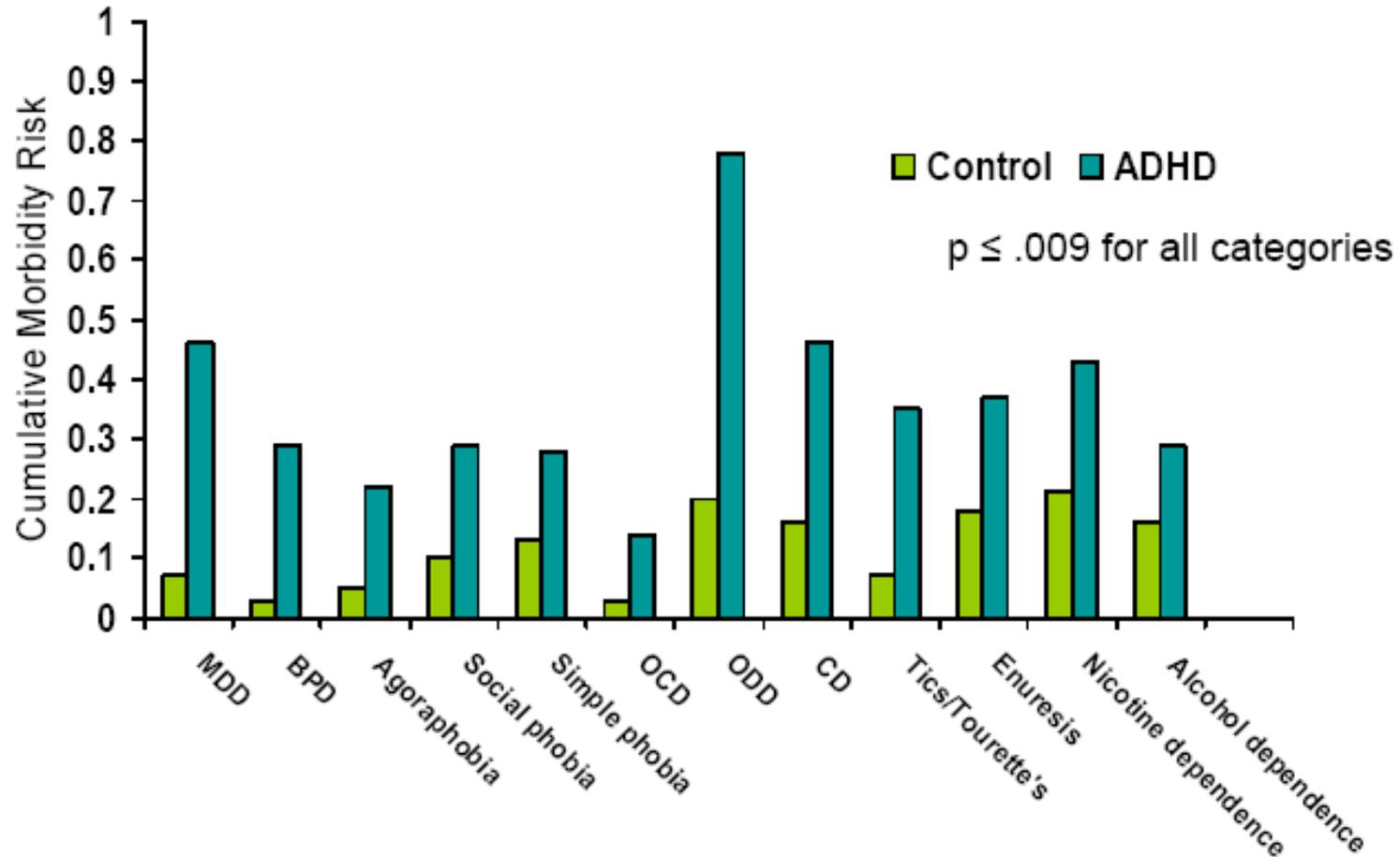
Razones para tratar el TDAH en el niño

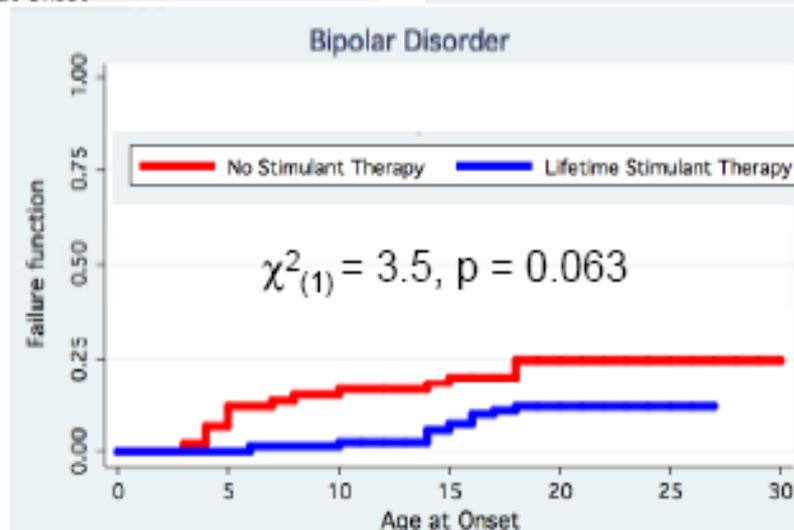
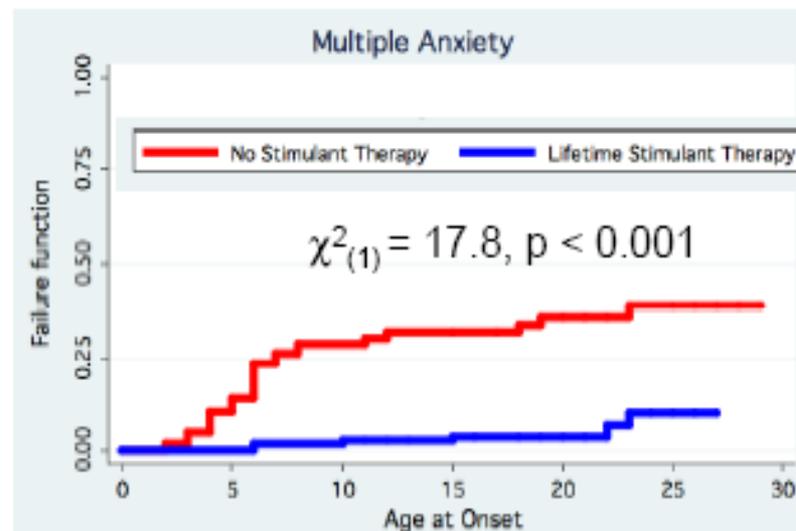
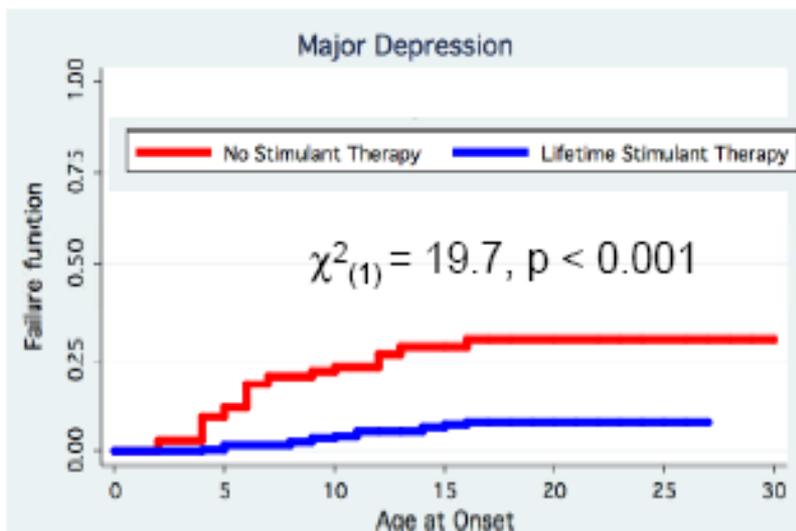


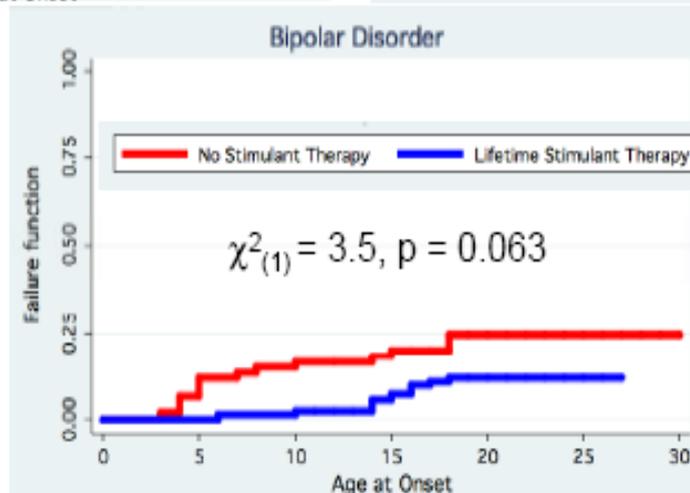
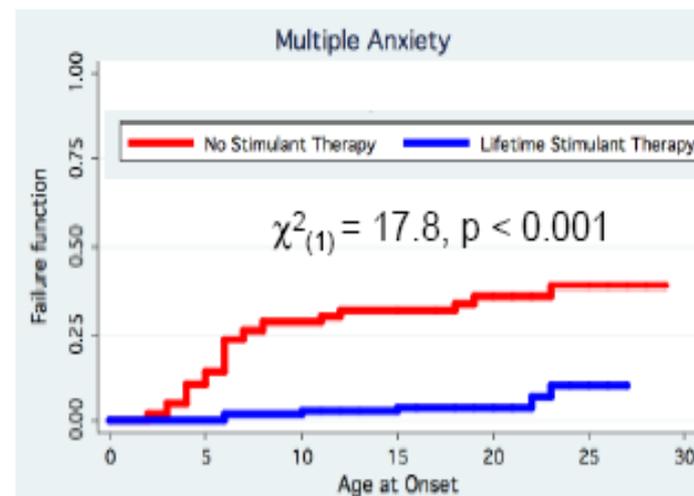
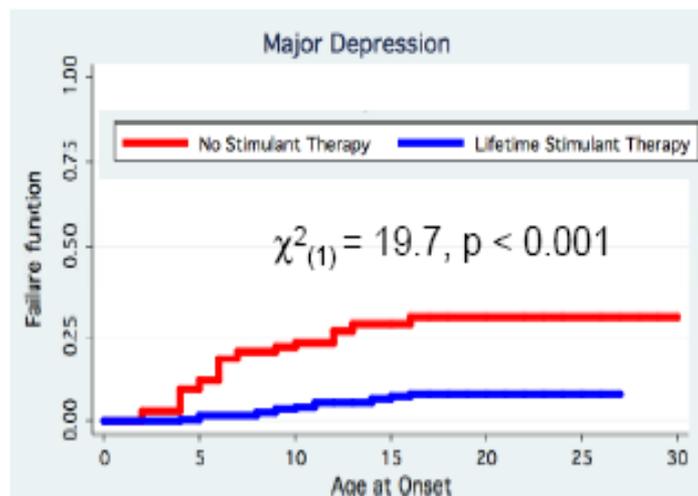
Factores de riesgo asociados al TDAH



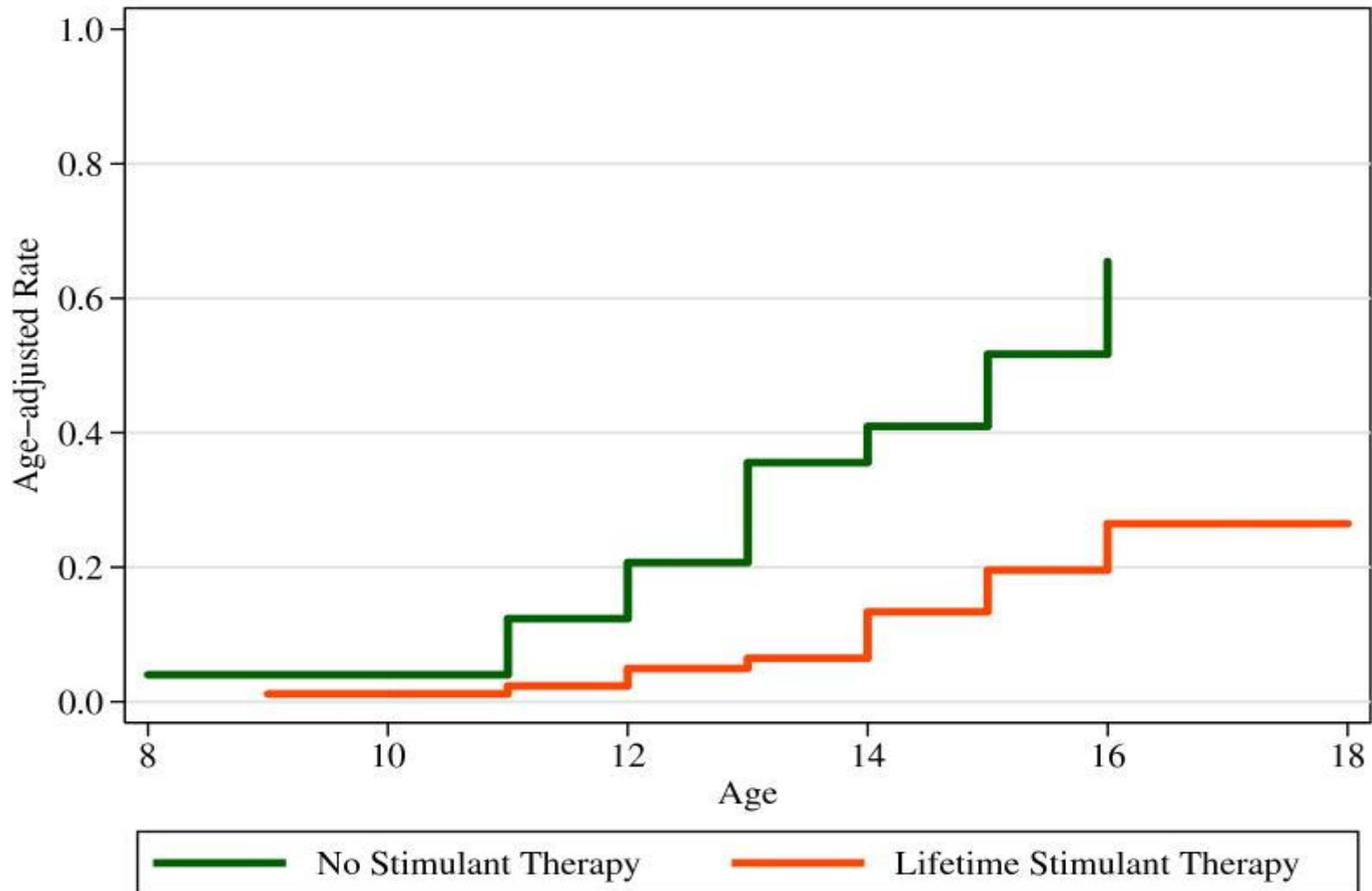
Razones para tratar el TDAH en el niño

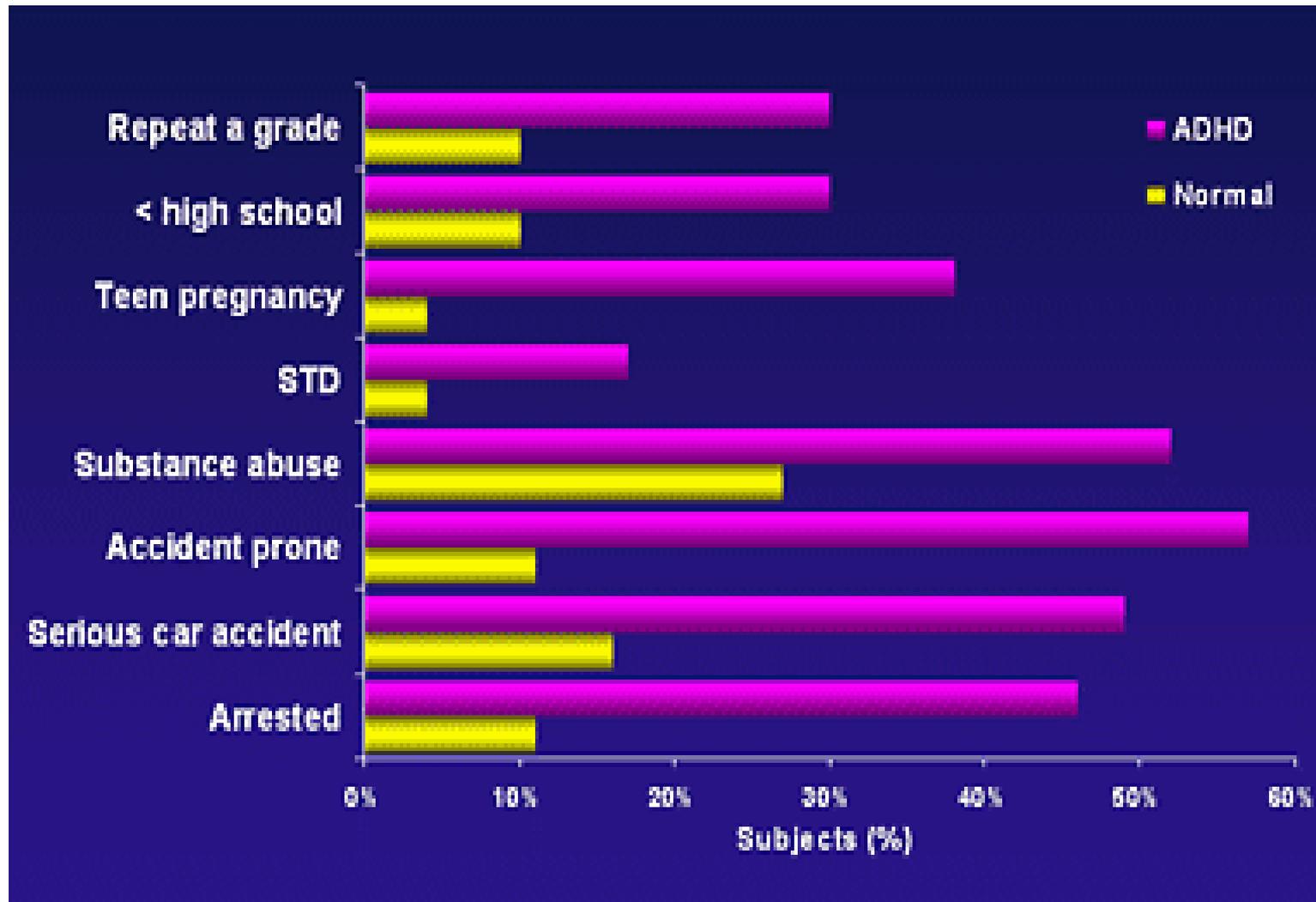






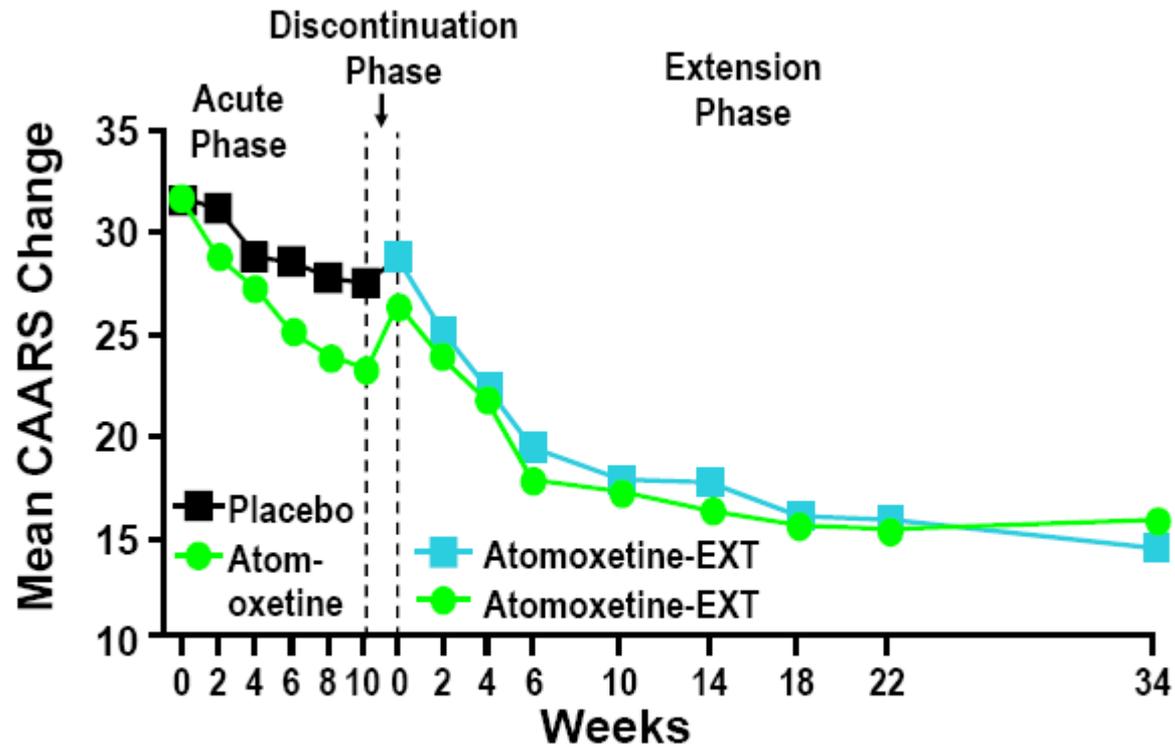
TDAH&SUD





Barkley RA. *Attention-Deficit Hyperactivity Disorder. A Handbook for Diagnosis and Treatment*, 1998. Barkley RA, et al. *JAACAP*. 1990;29:546-557. Biederman J, et al. *Arch Gen Psychiatry*. 1996;53:437-446. Weiss et al. *J Am Acad Child Psychiatry*. 1985;24:211-220. Satterfield, Schell. *JAACAP*. 1997;36:1726-1735. Biederman J, et al. *Am J Psychiatry*. 1995;152:1652-1658.

Respuesta al tratamiento



N = 384; Adler L et al. J Clin Psych. 2006 .

Willens et al.

Diferentes preparaciones farmacéuticas

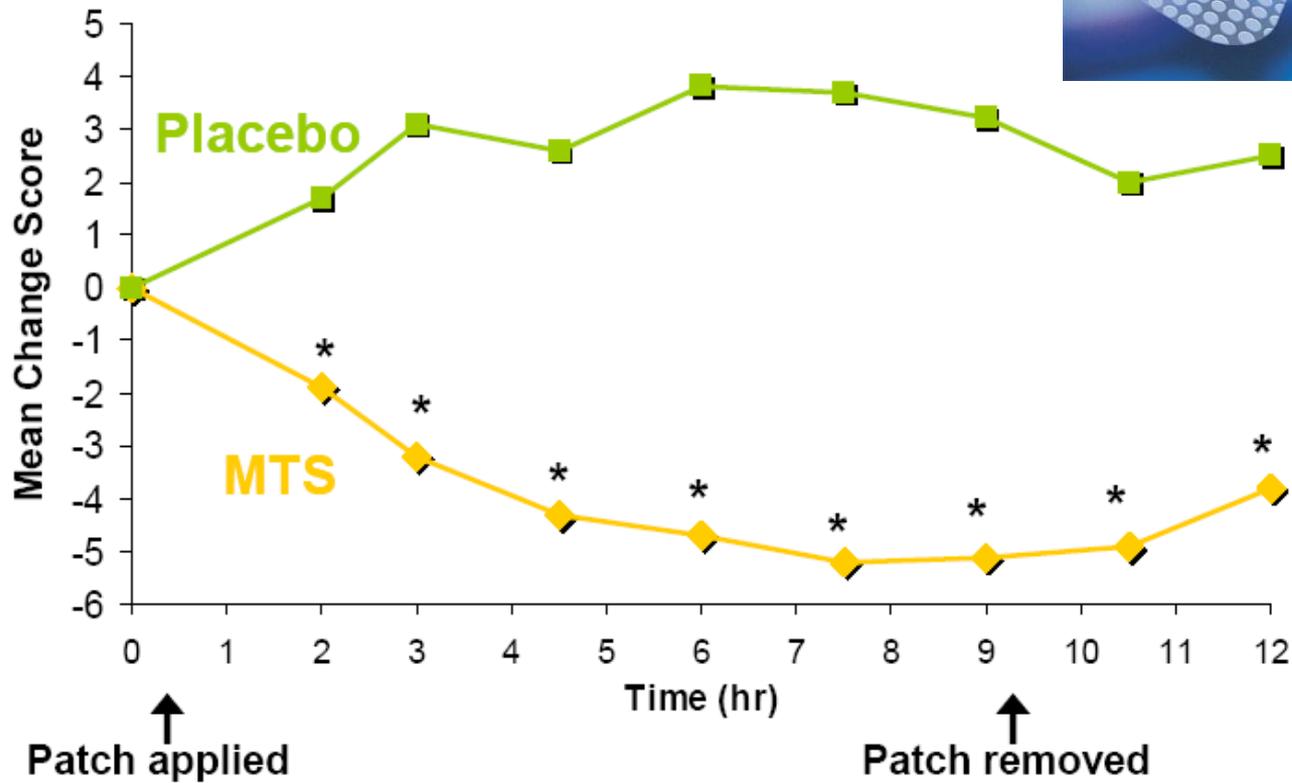
Equazym

LDX

Medikinet



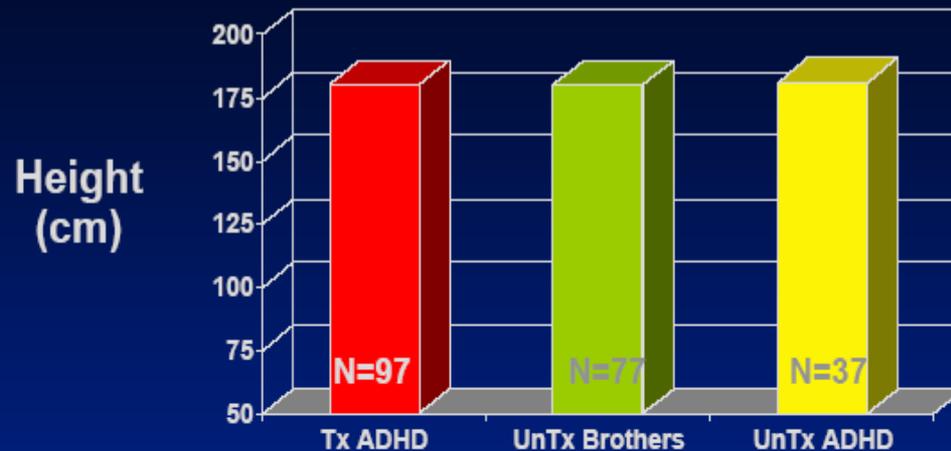
Nuevas preparaciones farmacéuticas



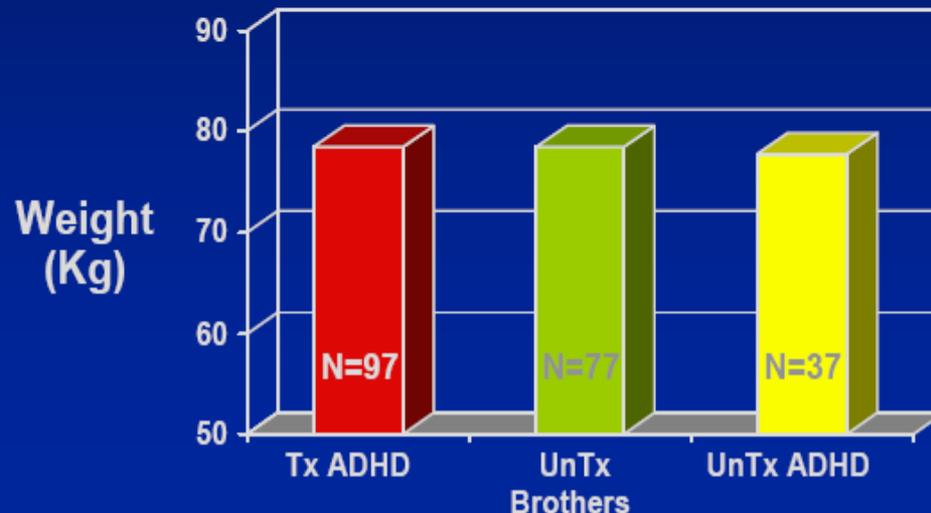
Medicación	Tamaño del efecto
Derivados de anfetaminas	0.92
Metilfenidato	0,80
Atomoxetina	0,73
Modafenilo	0.49
Bupropion	0,32

Faraone & Spencer , 2006

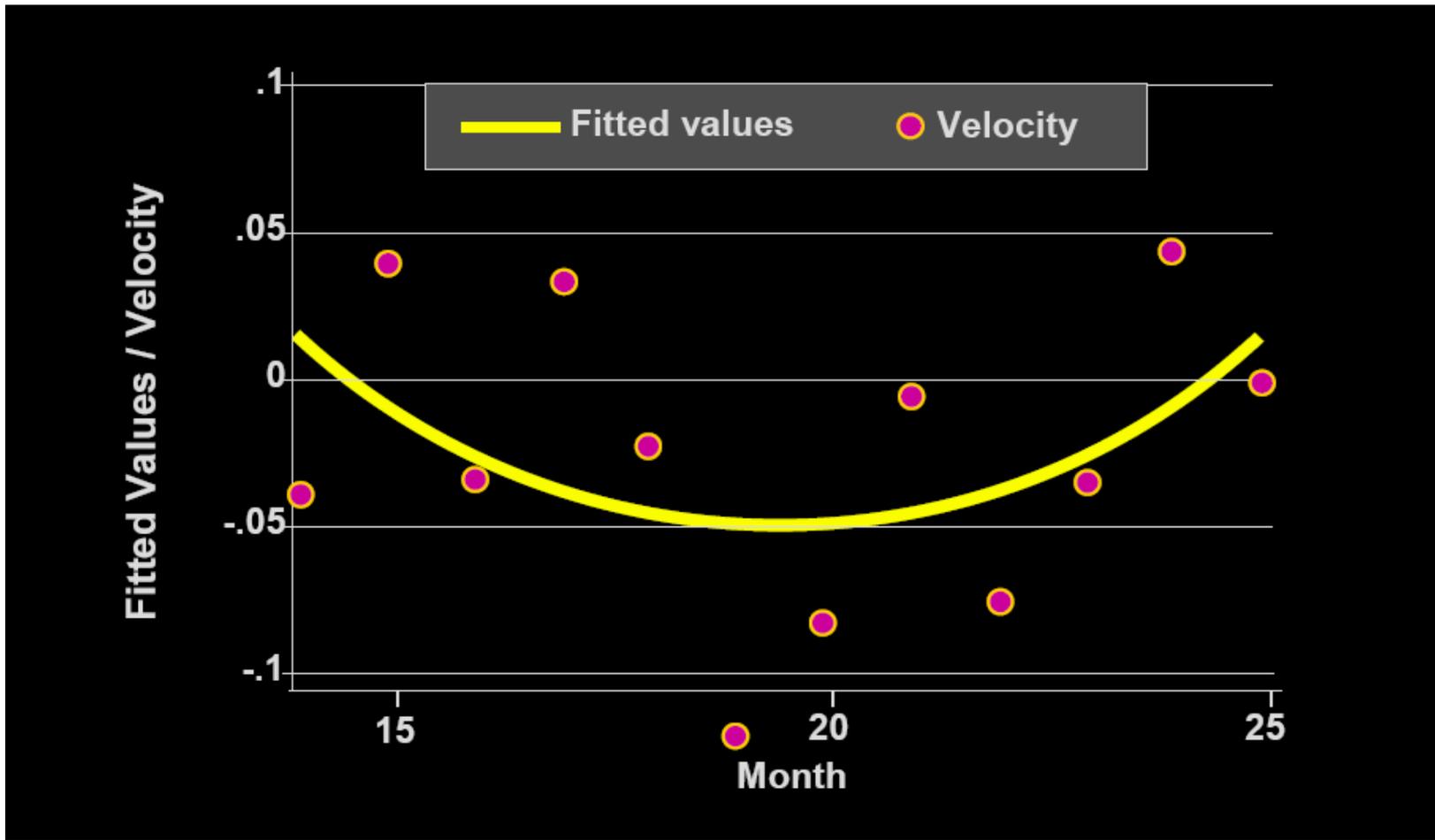
Tópicos acerca del tratamiento del TDAH



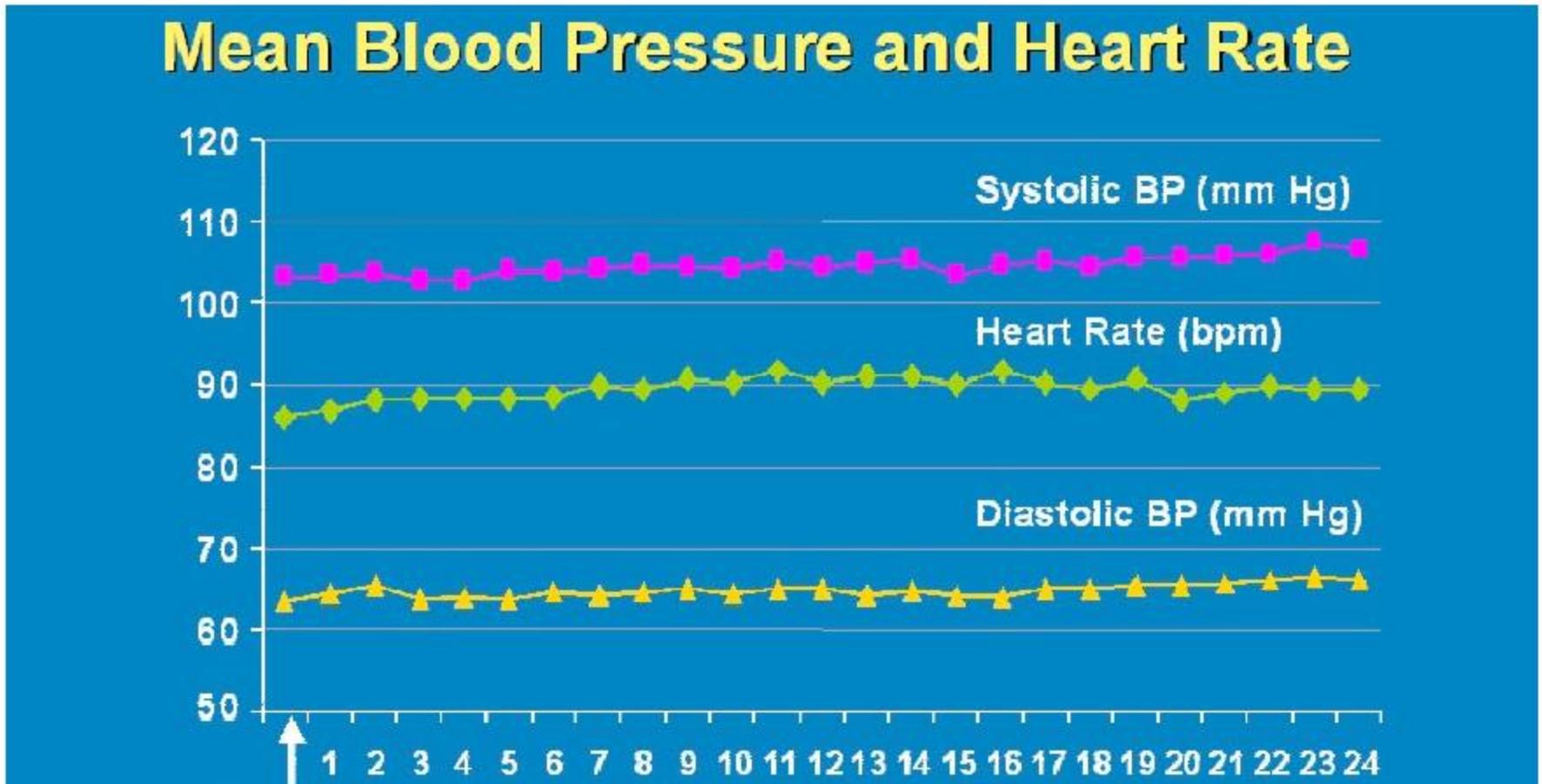
Youth aged 4 -12 yrs
MPH exposure = 36 mo
Reeval @ 21-23 years



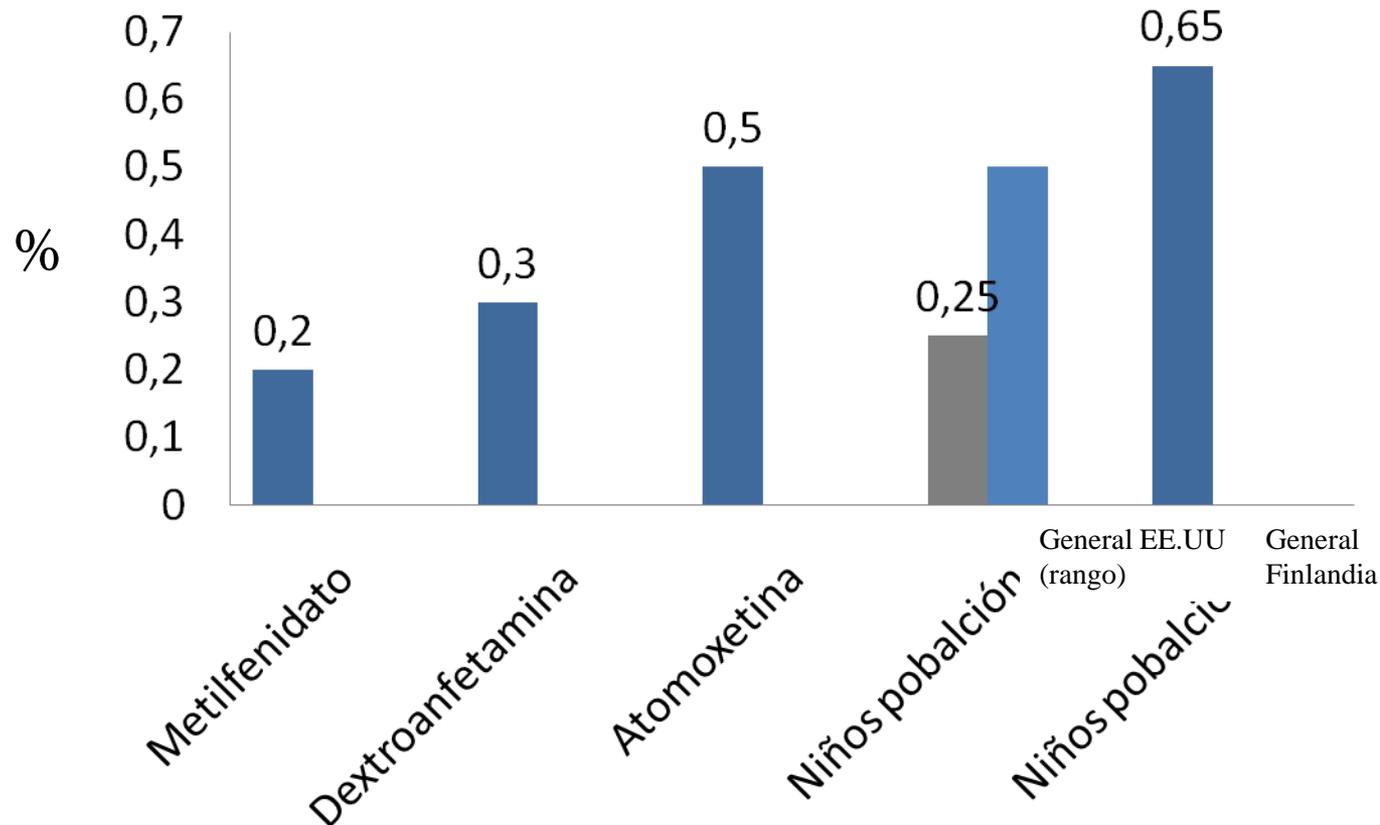
TDAH & Crecimiento



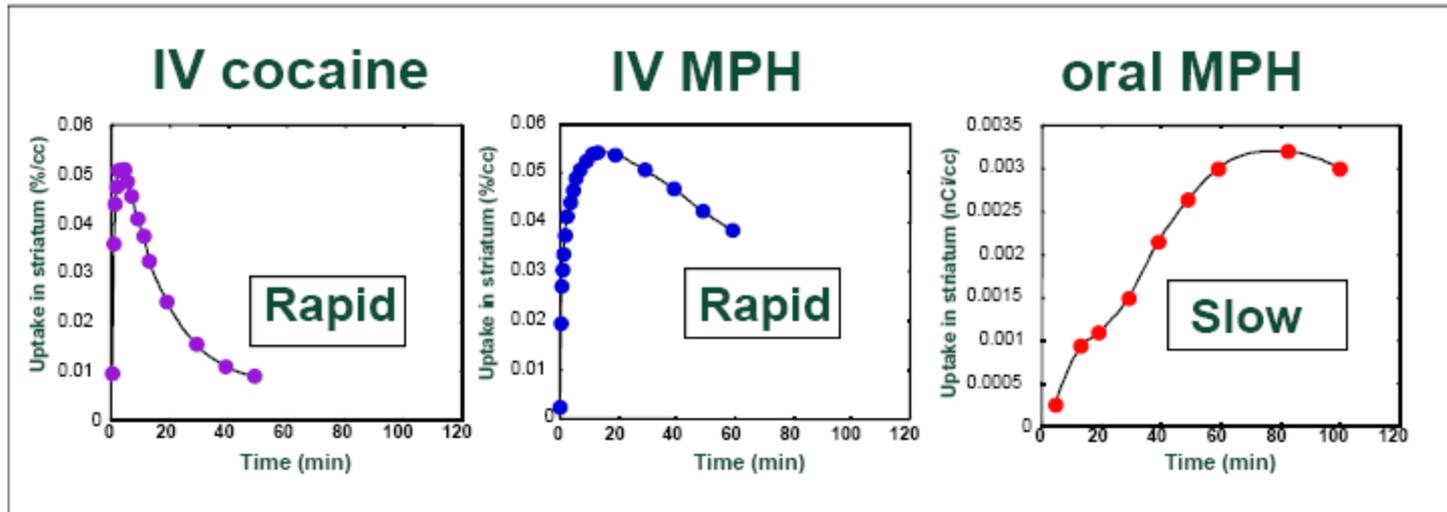
Control de efectos secundarios



Tasa de muerte súbita (x100.000niños/año) en la población general (EE.UU y Finlandia) y en los tratados con estimulantes/no estimulantes

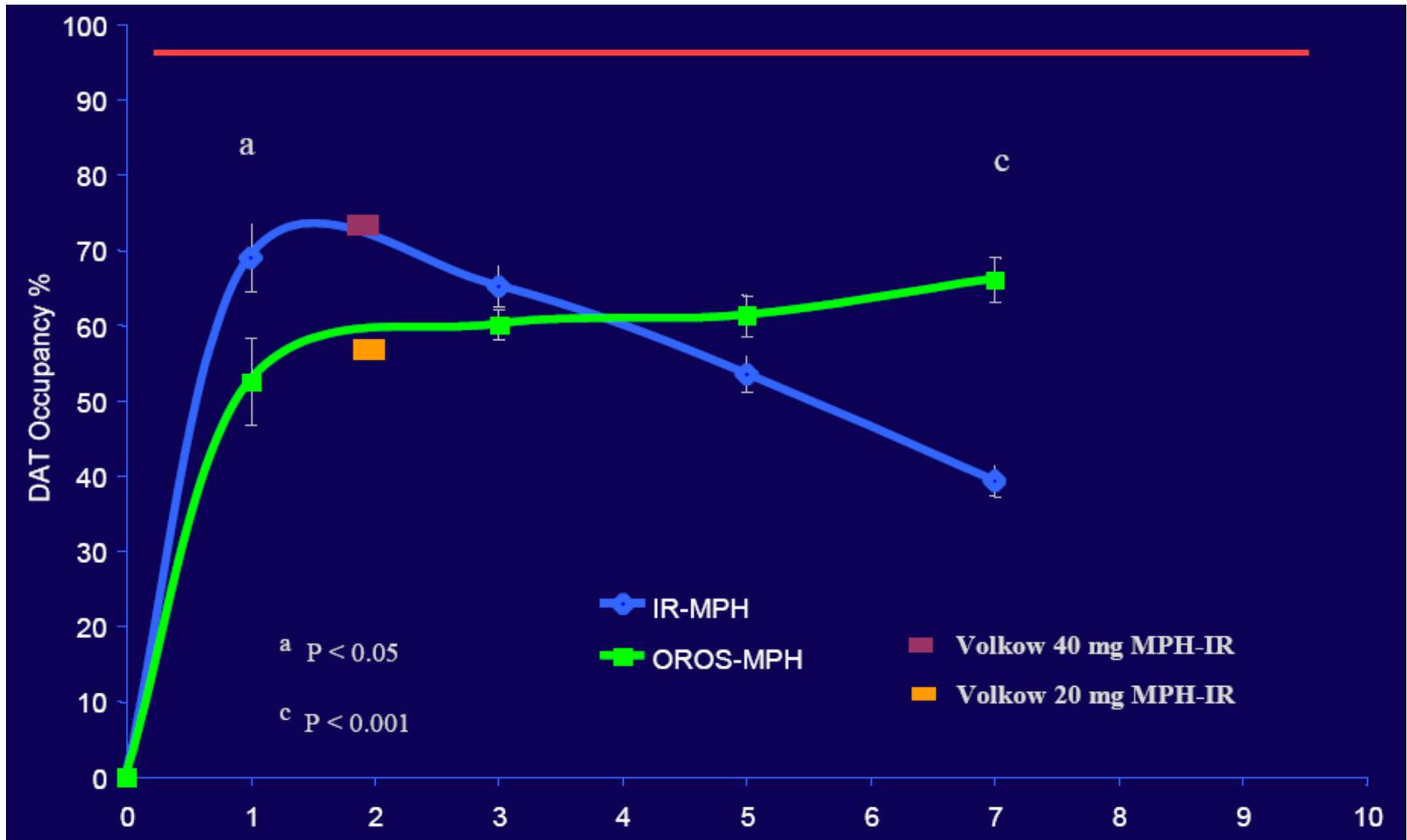


Tópicos acerca del tratamiento del TDAH

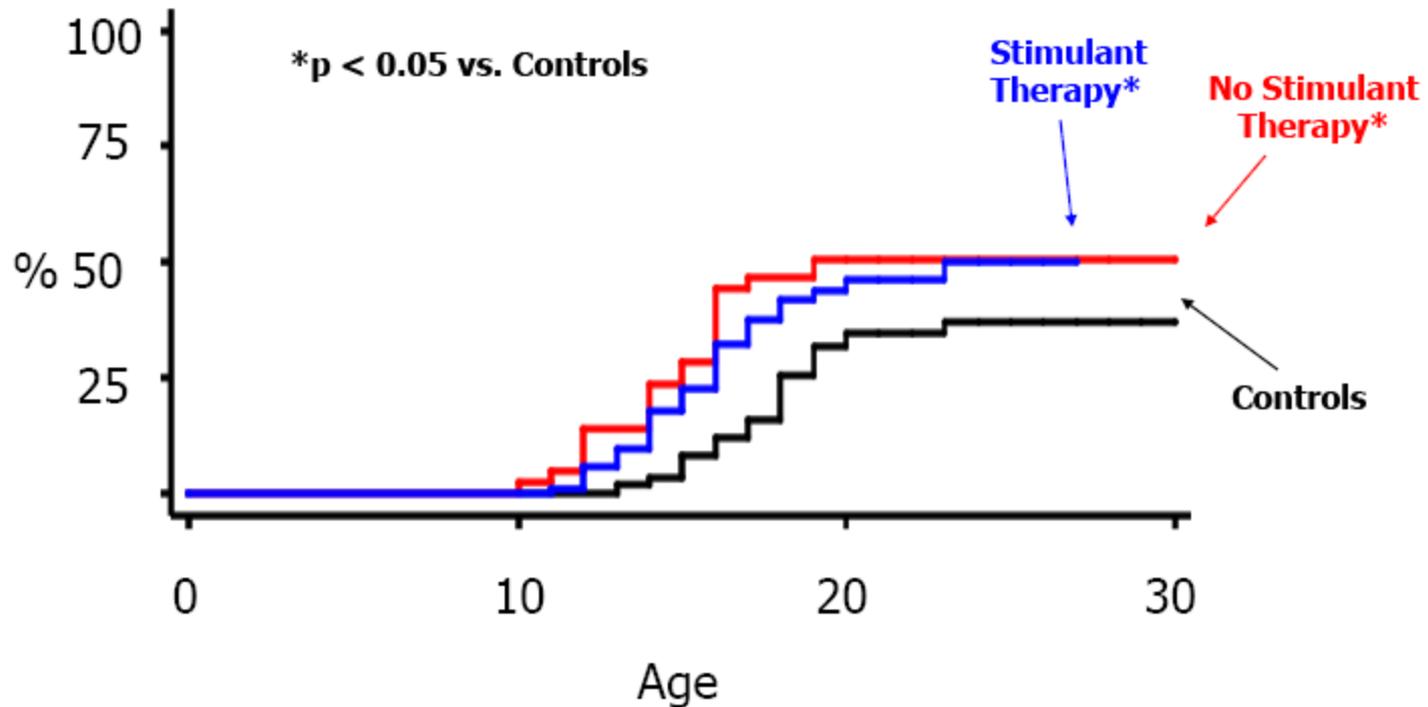


- Cocaine (IV) and methylphenidate (IV) produce a “high” but methylphenidate (oral) does not
- The slow brain uptake of oral methylphenidate permits effective treatment without a “high”

TDAH & Adicción



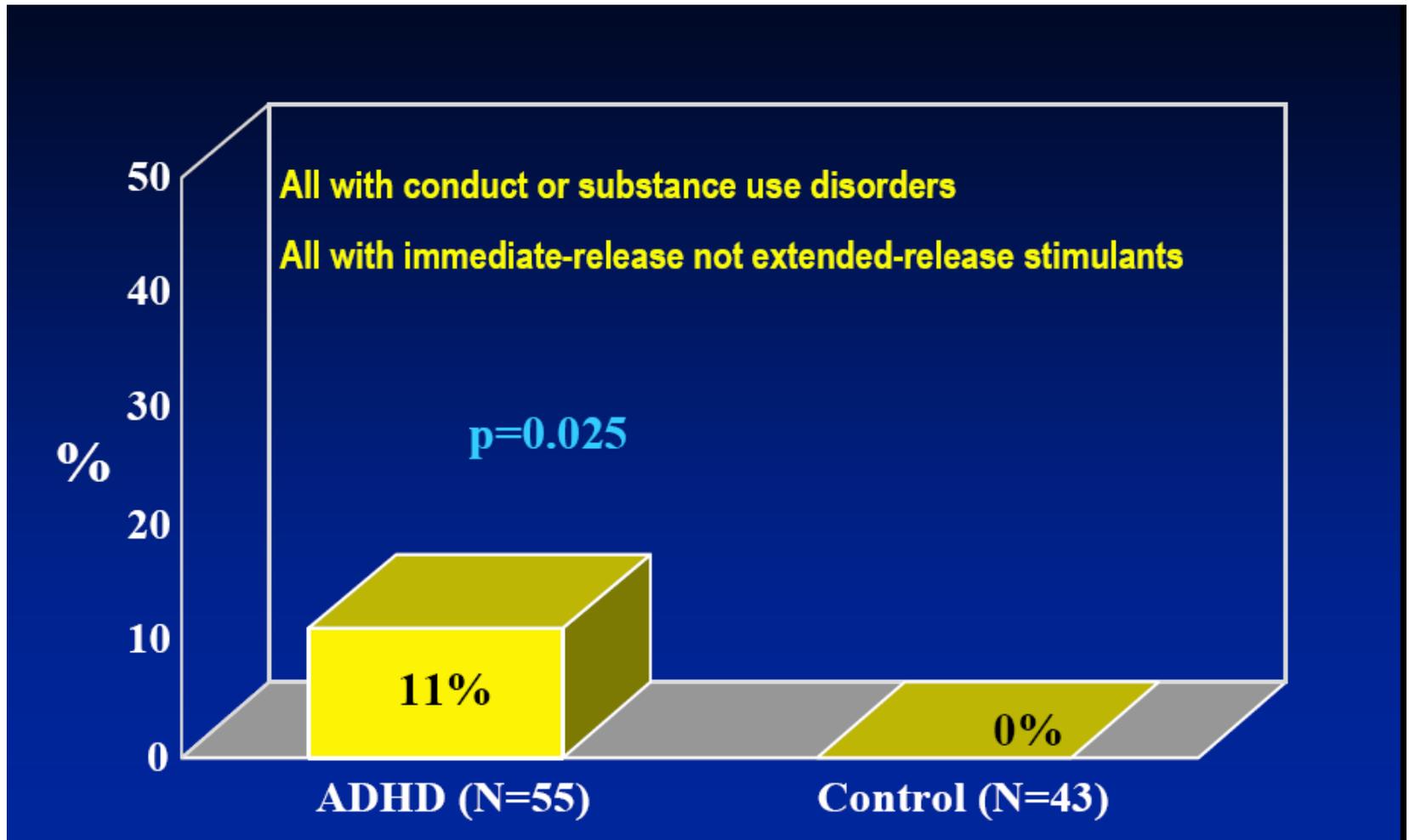
Tópicos acerca del tratamiento del TDAH



Biederman et al. Am J Psychiatry. 2008 Mar 3.

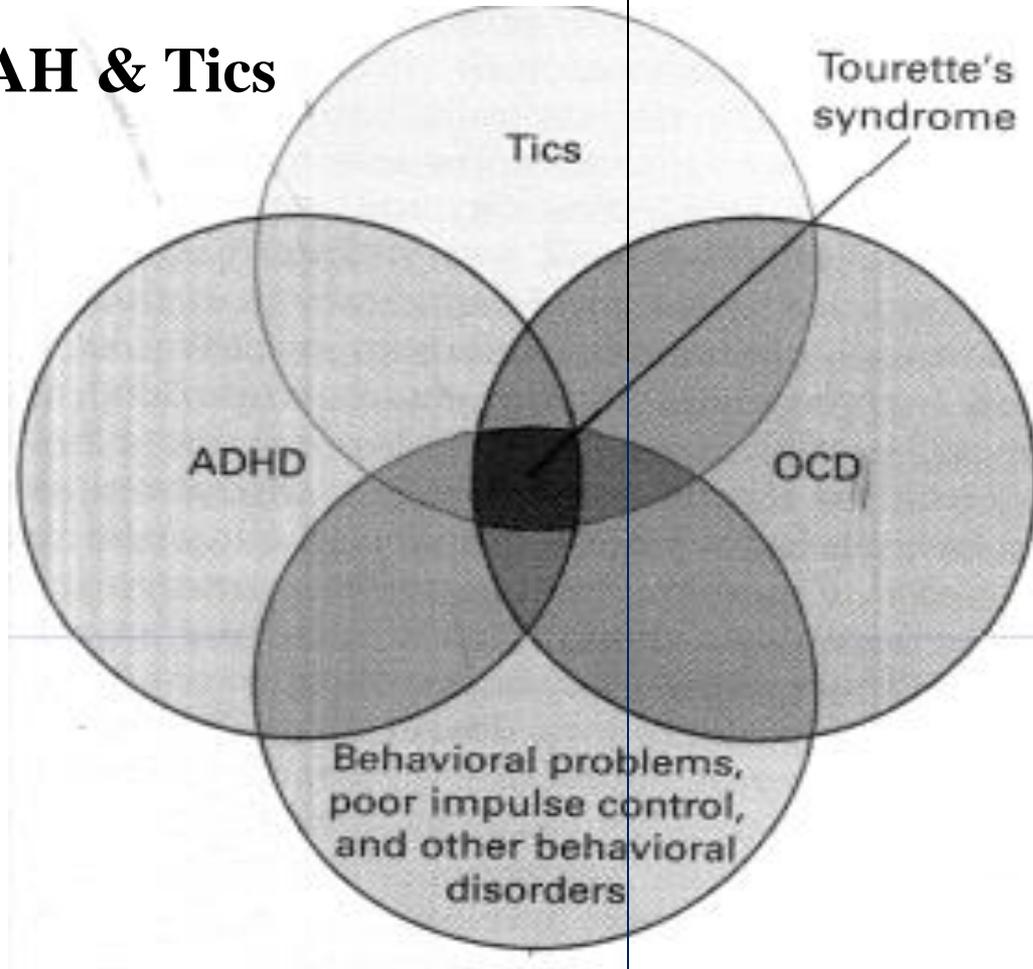
Faraone SV et al. Psychol Med. 2006;36:159-165

TDAH & Consumo de sustancias



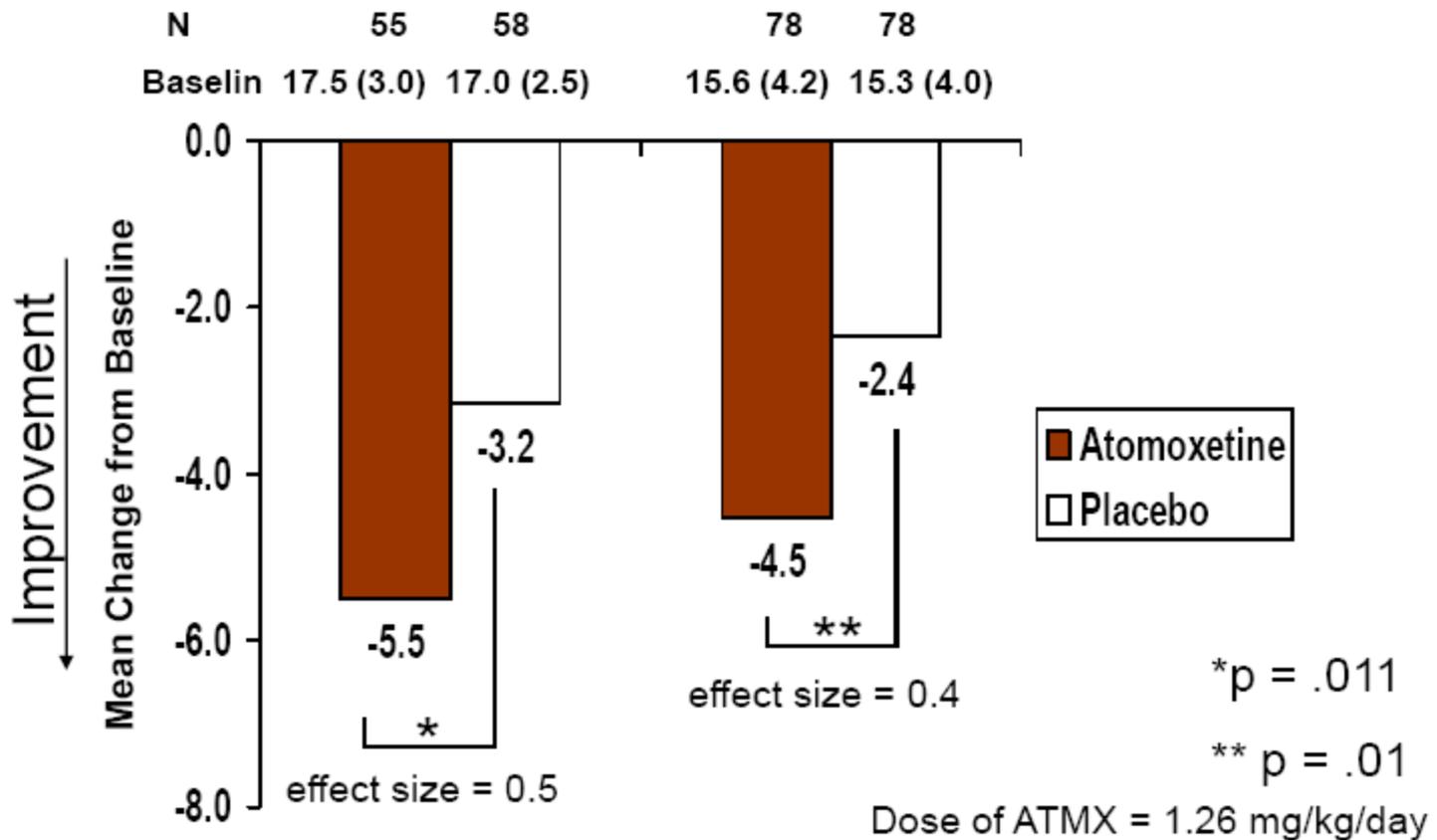
Comorbilidad (consideraciones especiales)

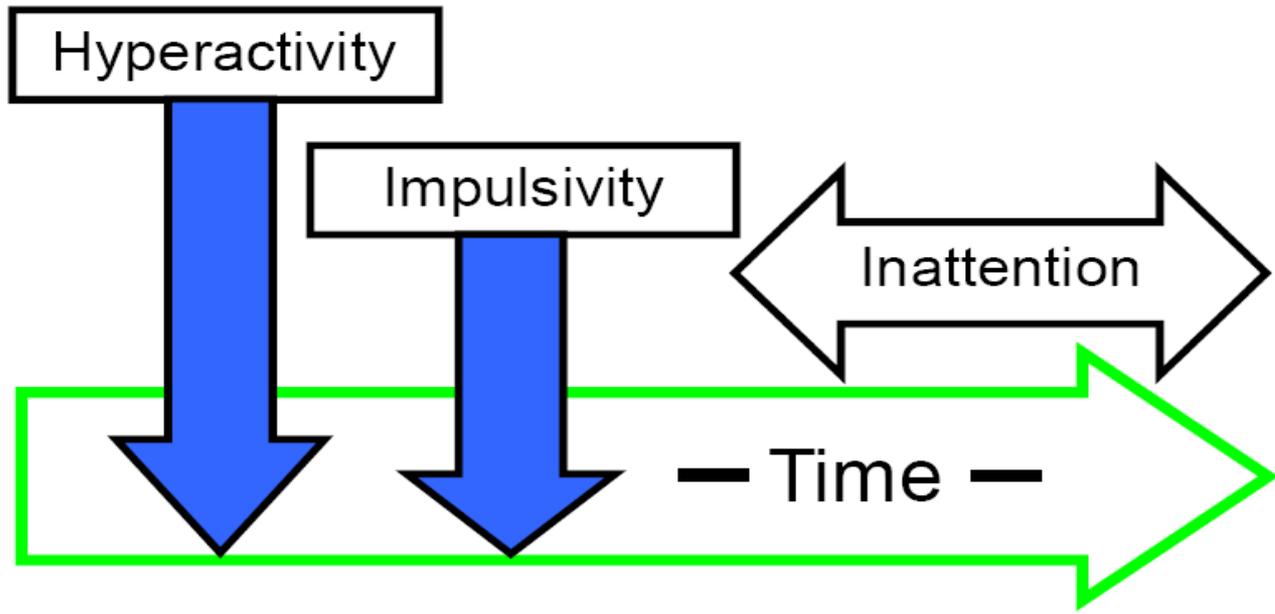
TDAH & Tics



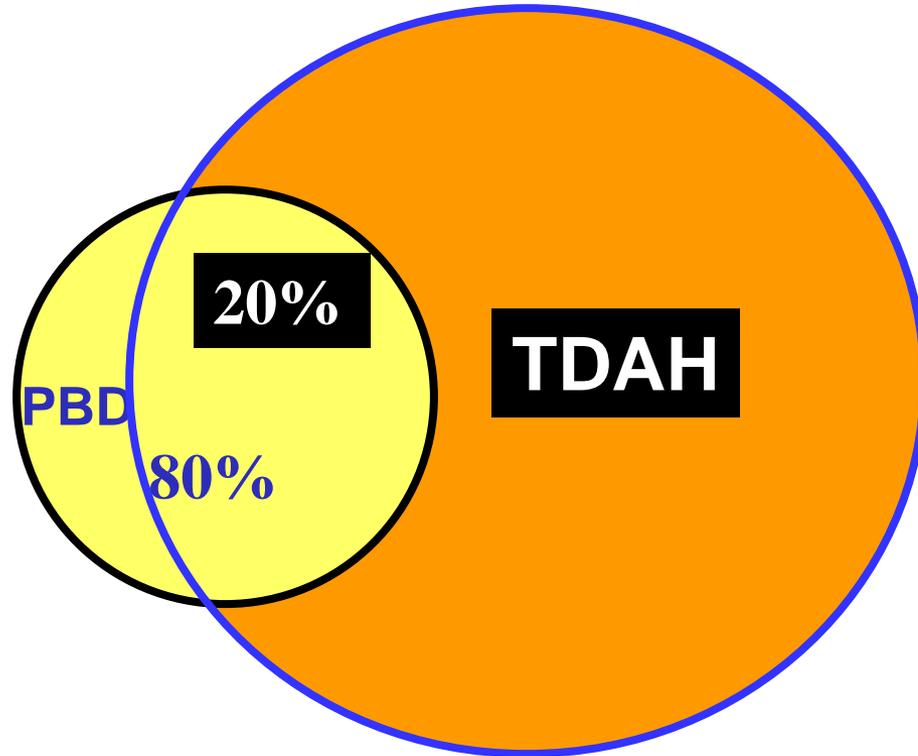
Comorbilidad (consideraciones especiales)

TDAH & Ansiedad





Comorbilidad (consideraciones especiales)



**Déficit funciones
ejecutivas**

Inatención

Olvidos frecuentes
Descuidos
Distraibilidad
Atención en reuniones dis.

Dificultad en la planificación y

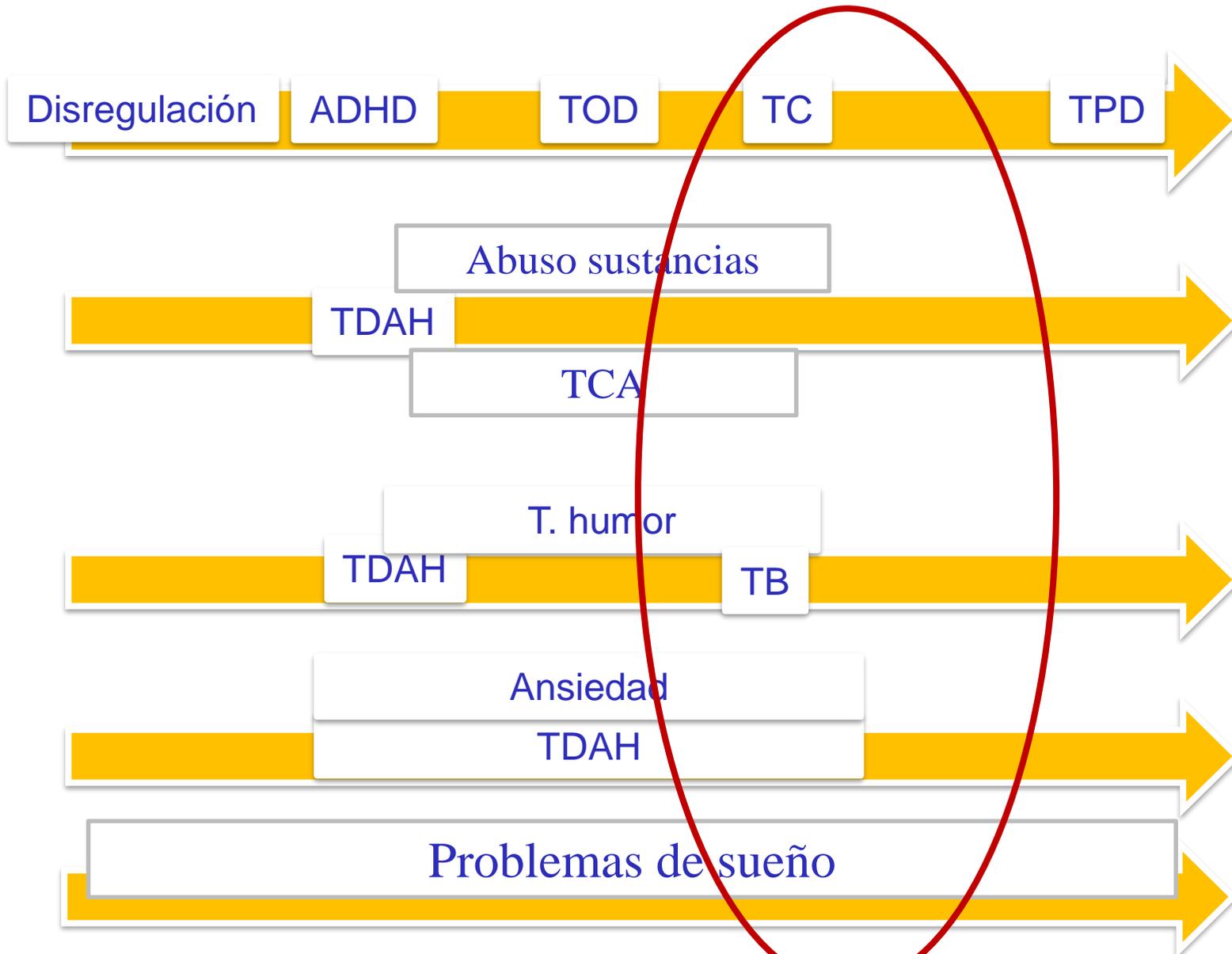
Impulsividad

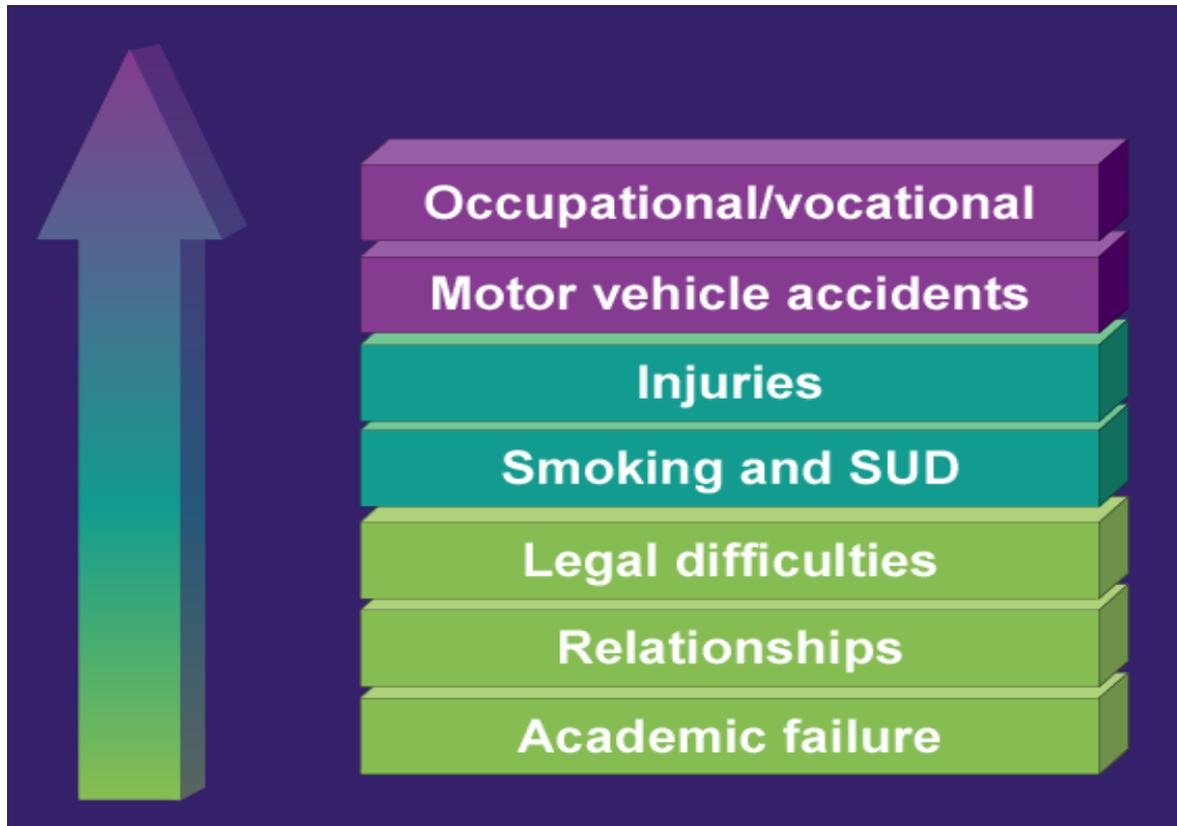
**Organización/
vida diaria**

DESR

- ✓ **Baja tolerancia a la frustración**
- ✓ **Irritabilidad reactiva
moderada**
- ✓ **Labilidad emocional**

Etiopatogenía de la Comorbilidad





- Tratamiento de primera elección
- Recomendable combinar (psicopedagógico/psicoterap.)
 - Elección del fármaco
- Circunstancias personales del paciente
- Comorbilidad
 - Control de peso secundarios:
- Peso, talla, HTA, FC,
 - Duración del tratamiento:
- Etapa de desarrollo
- Impacto funcional



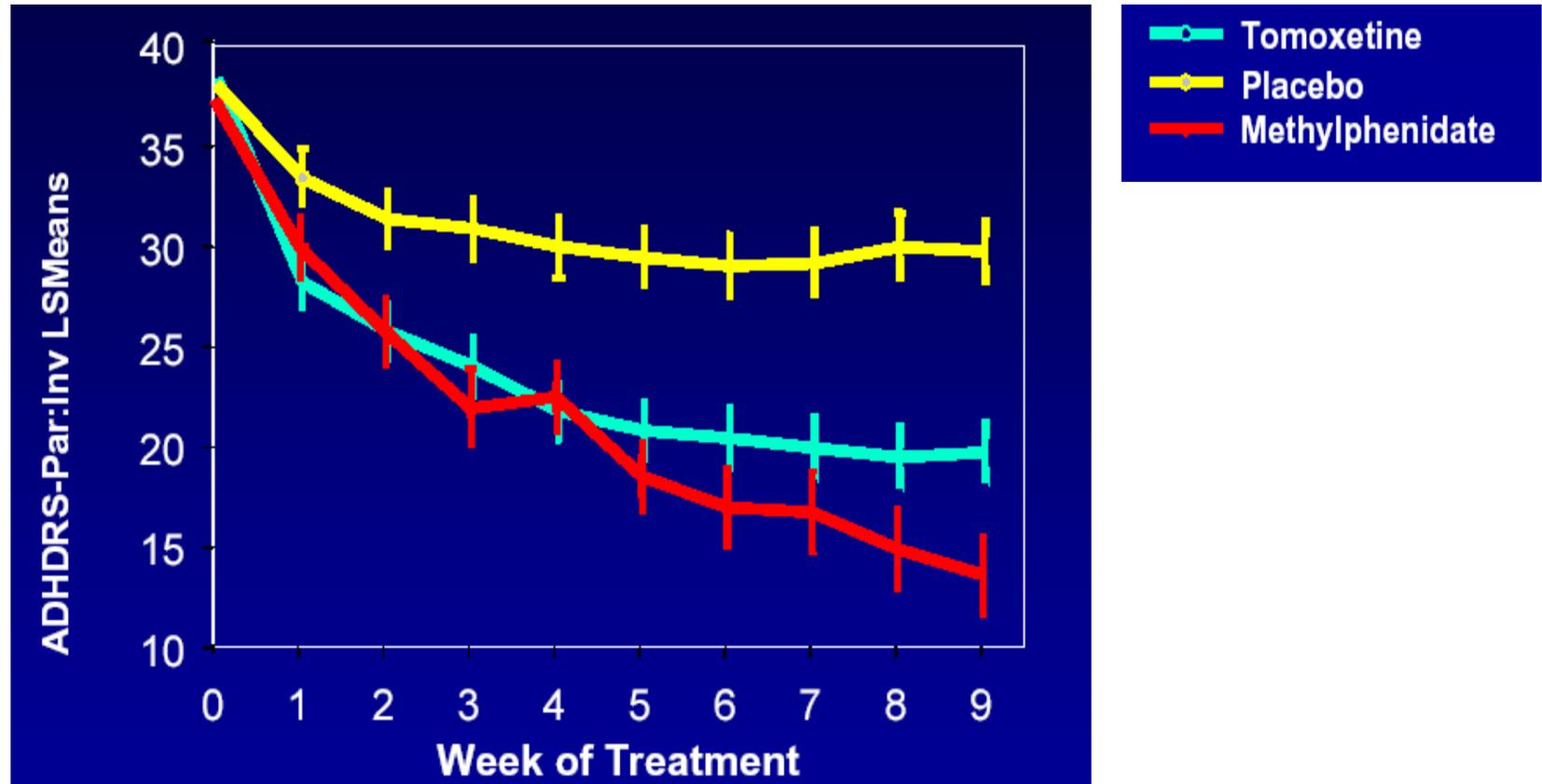
Porque **creemos** en la genialidad de cada niño

Trastorno por Déficit de Atención e Hiperactividad *¿Es seguro el tratamiento?*

*"Empieza por hacer lo necesario,
luego haz lo posible
y, de pronto, estarás haciendo lo imposible"*

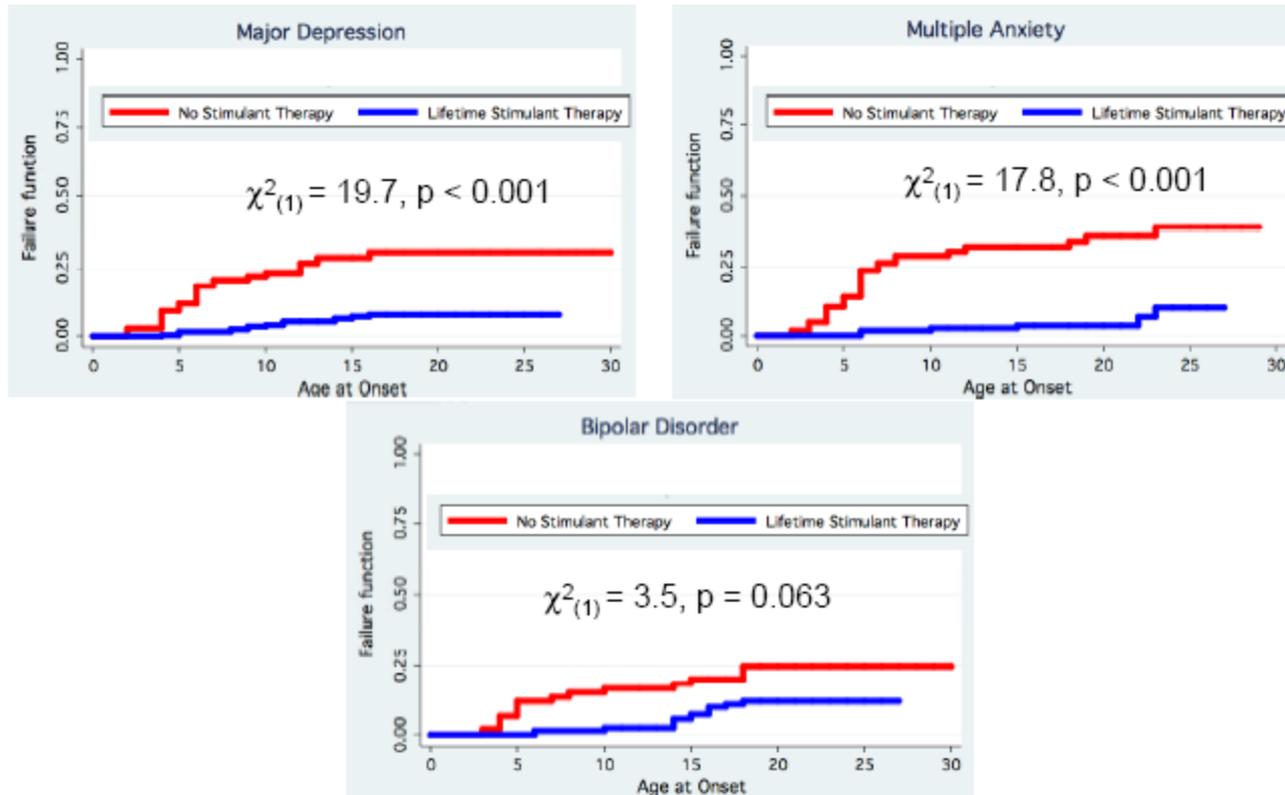


Respuesta al tratamiento

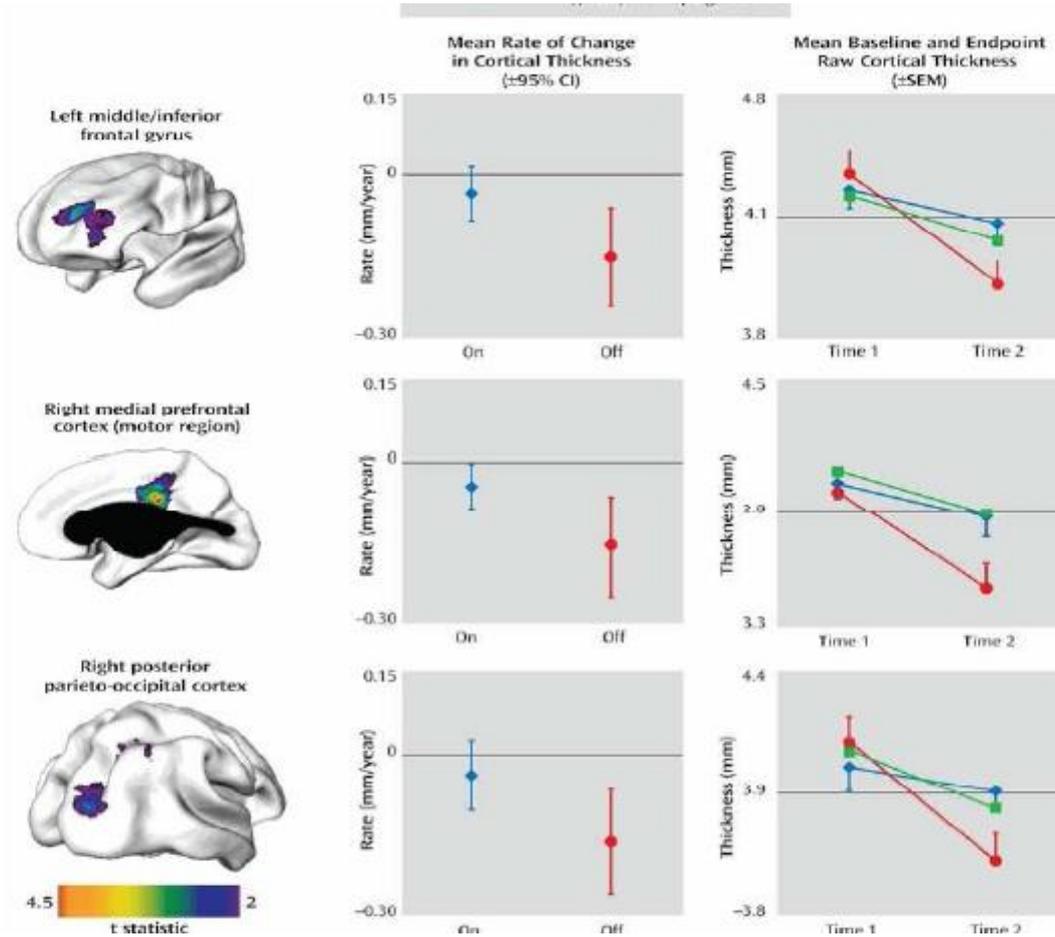


$p < .05$ for TMX vs PBO Weeks 1 through 9
 $p < .05$ for MPH vs PBO Weeks 3 through 9
TMX vs MPH not statistically significantly different at any visit

Tópicos acerca del tratamiento del TDAH



TDAH & “Mal uso del tratamiento”



Shaw et al 200

TDAH: Comorbilidad

Tics

N=136 niños TDAH&ADHD

✓ MPH & MPH + clonidina mejor que placebo

✓ Valorar ansiedad como precipitante

(Tourette's Syndrome Study Group, Neurology, 2002; 8(4):527-536)

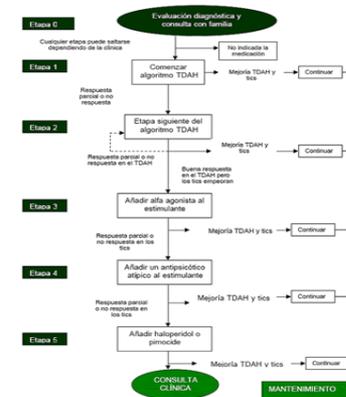
✓ Valorar Atomoxetina, 1ª opción

(Spencer et al., J Atten Dis 2008; 11(4):470-481)

Ansiedad

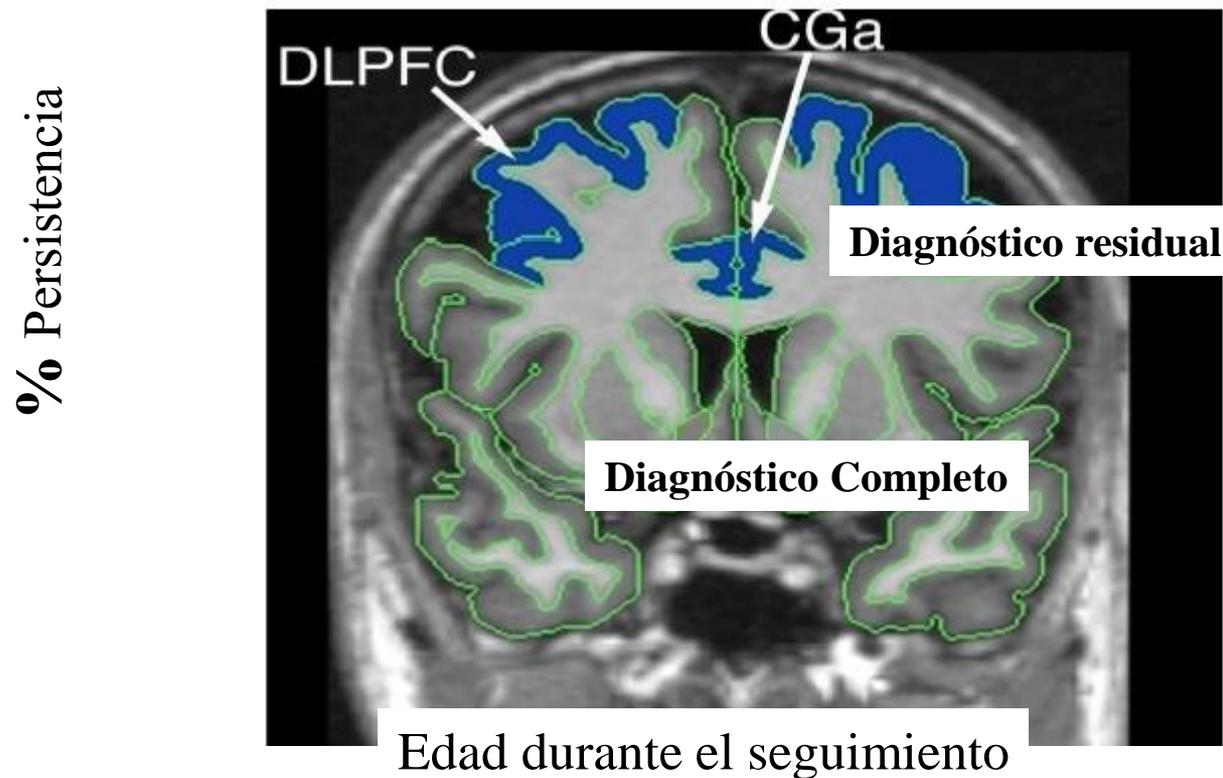
✓ Valora Atomoxetina, 1ª opción

Geller et al., J Am Acad Child Adolesc Psychiatry 2007; 46(9):1119-1127

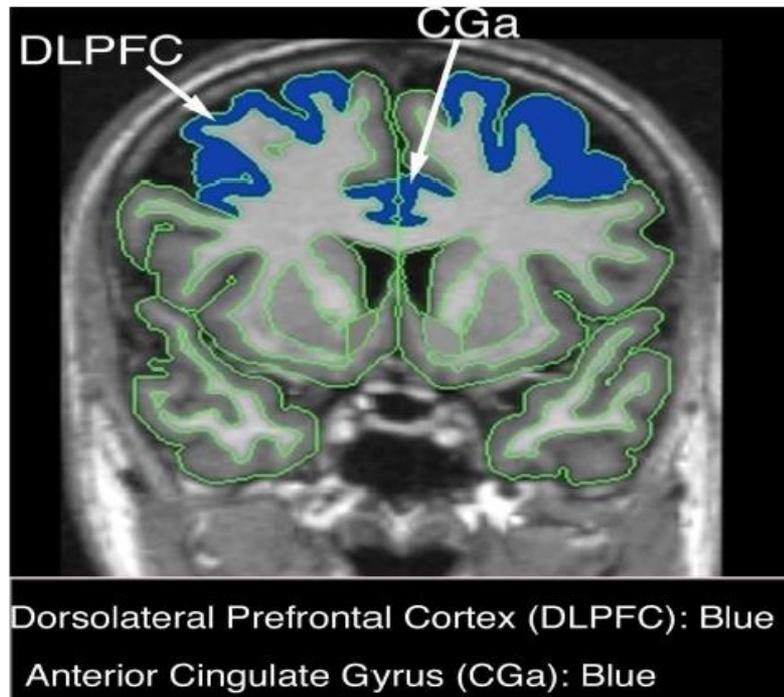


Curso clínico

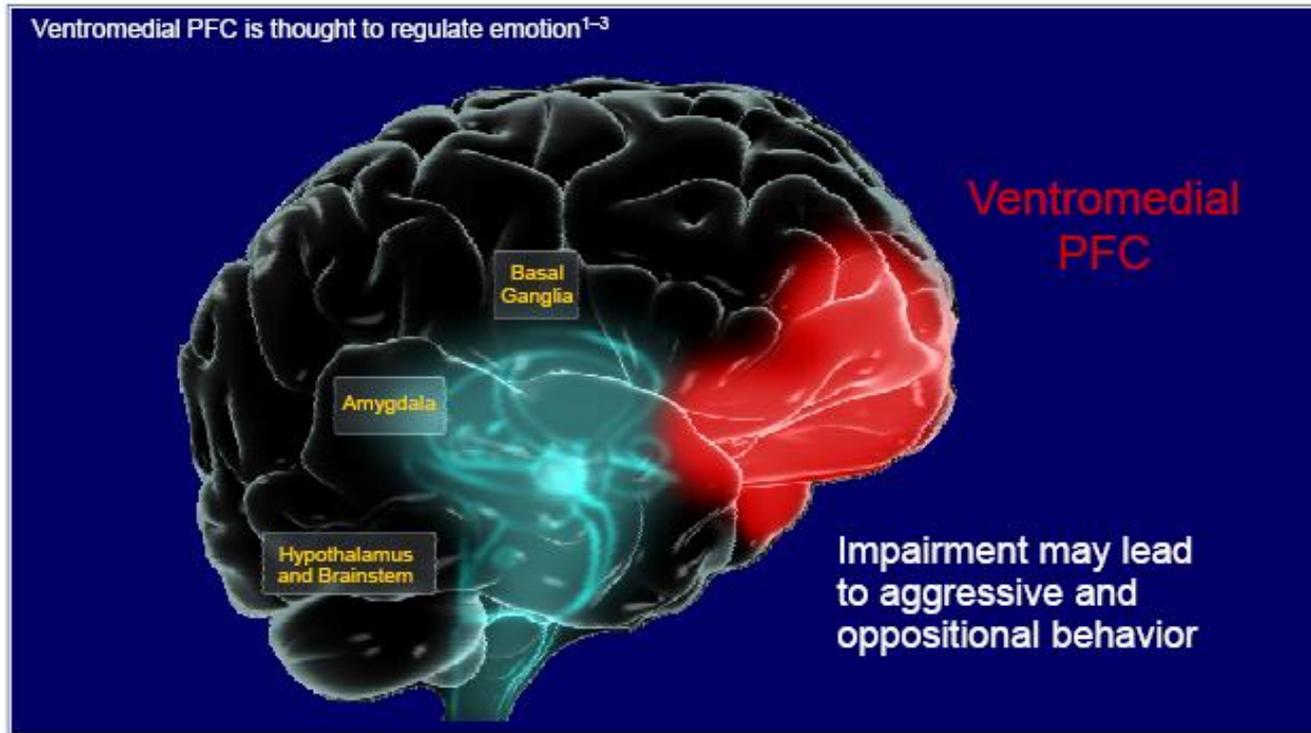
Persistencia de todos los criterios diagnósticos (completo) o sólo de algunos (residual) pero se mantiene la disfunción.



Curso clínico



TDAH & Regulación emocional



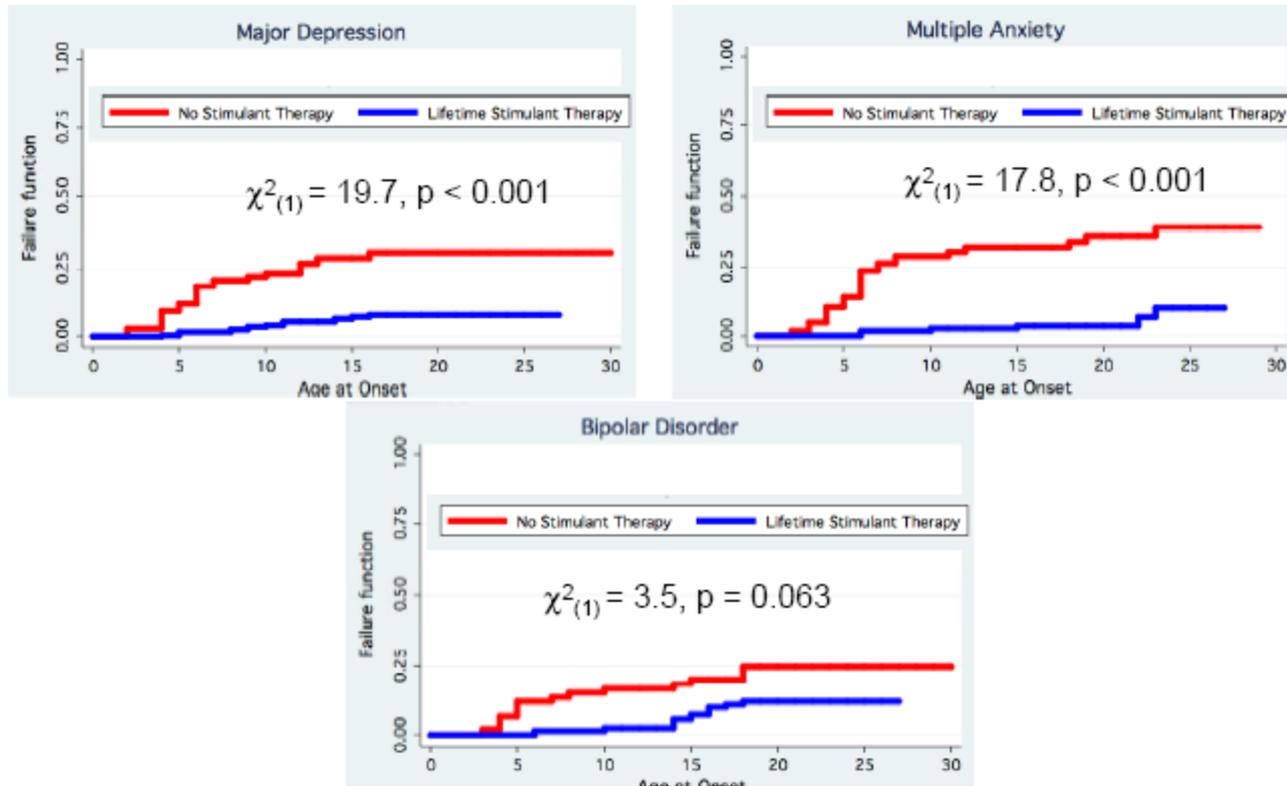
¹Anderson SW et al. Nat Neurosci. 1999;2:1032-1037.

²Arnsten AFT et al. J Child Adolesc Psychopharmacol. 2007;17:393-406.

³Price JL et al. Prog Brain Res. 1996;107:523-536.

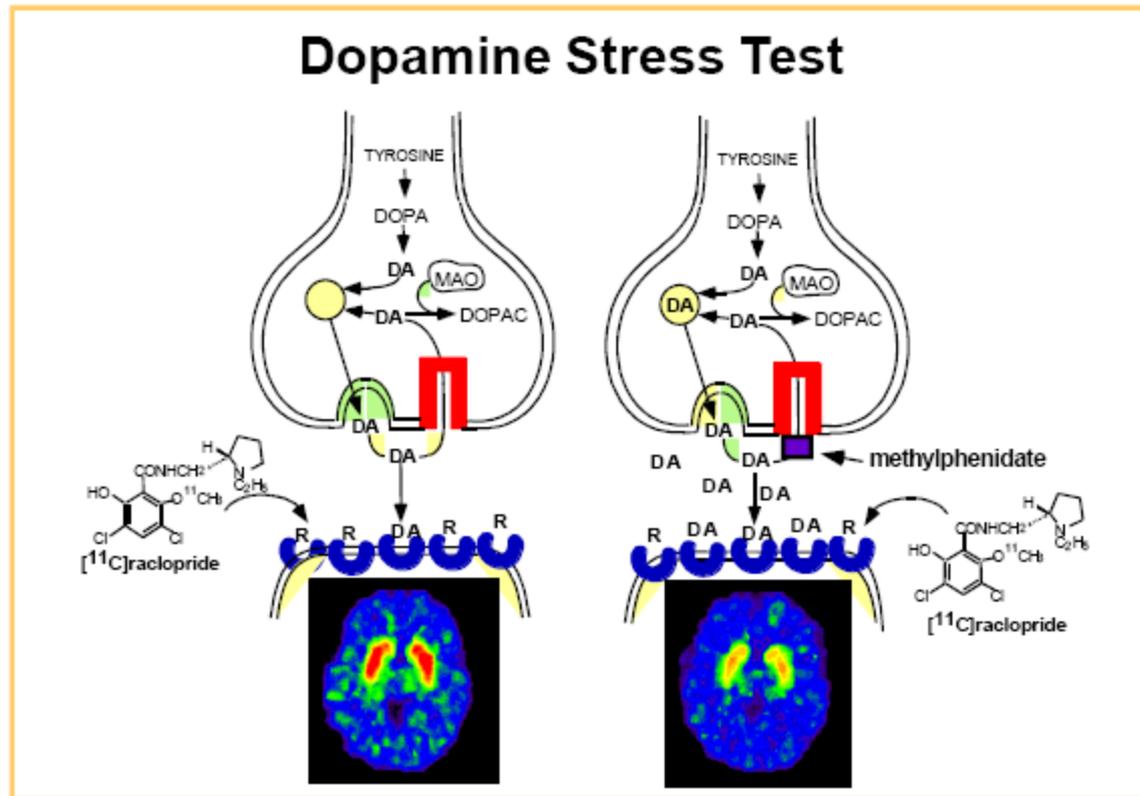


Tópicos acerca del tratamiento del TDAH



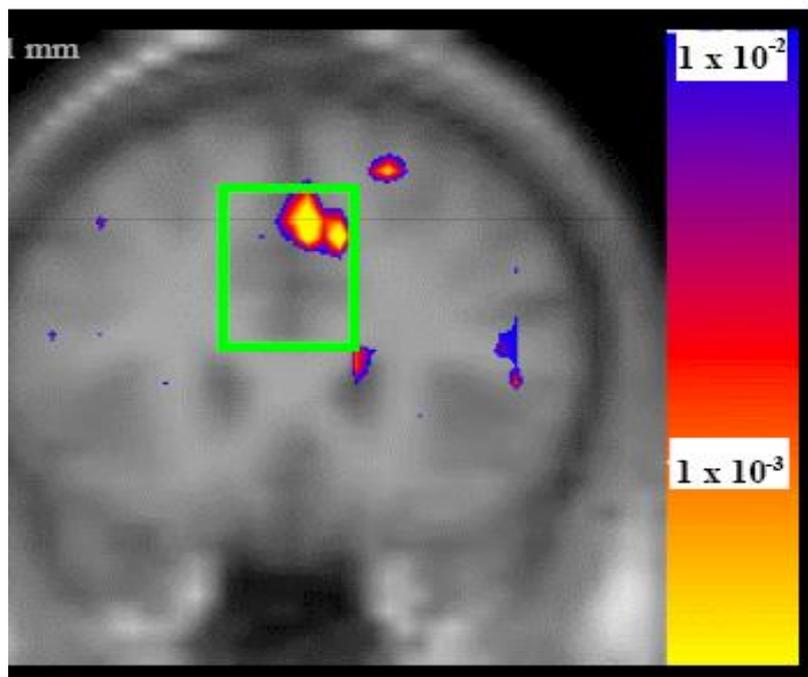
Hallazgos neuroquímicos

measuring changes in Dopamine



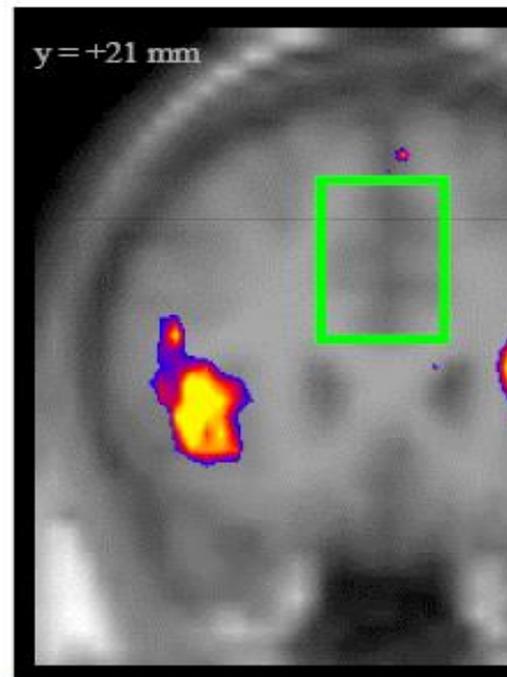
Hallazgos funcionales

Normal Controls



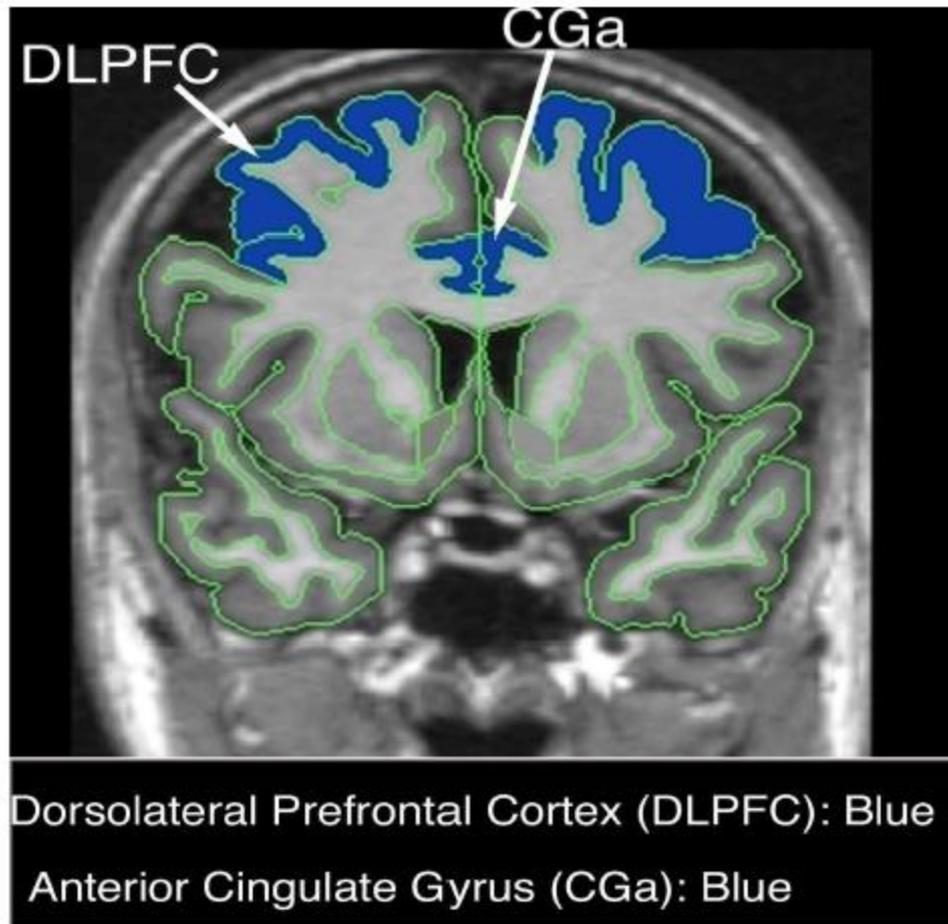
MGH-NMR Center & Harvard-MIT CITP

ADHD

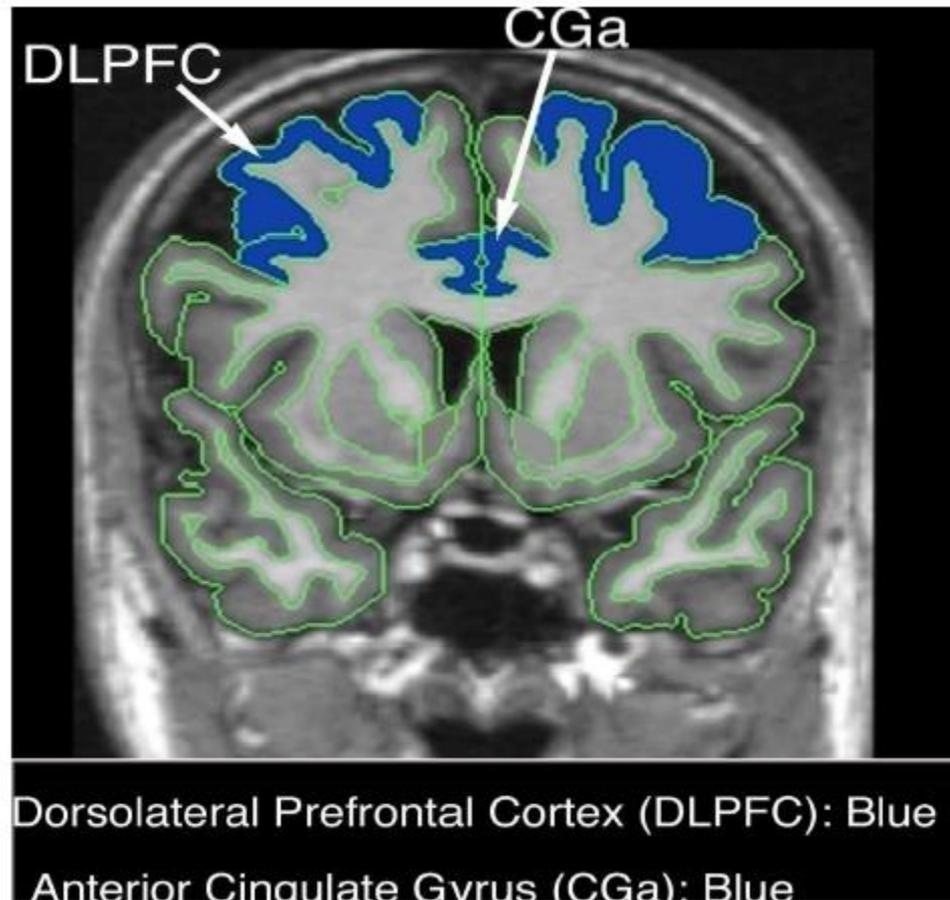


Bush et al. Biological Psych

Hallazgos estructurales

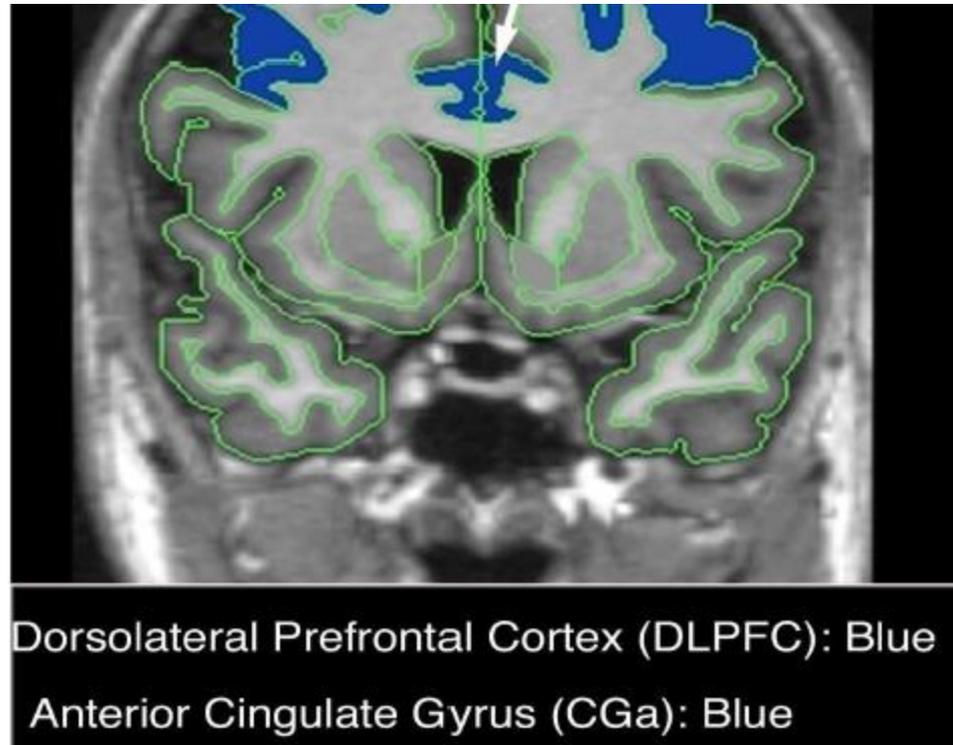


Hallazgos estructurales

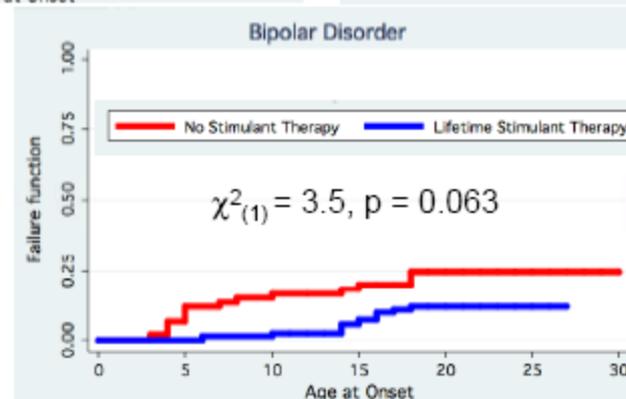
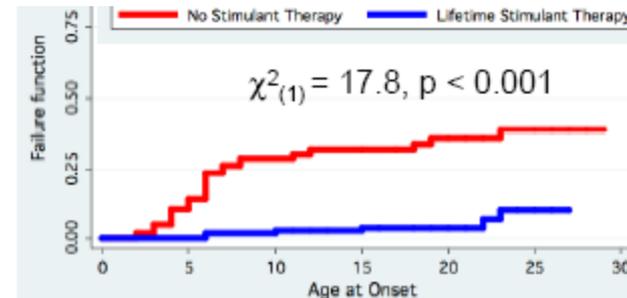
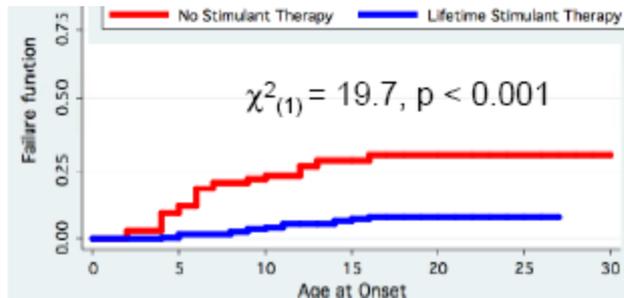


Hallazgos estructurales

Volumen cerebral en niños y adolescentes diagnosticados de TDAH y medicados vs no medicados



Tópicos acerca del tratamiento del TDAH

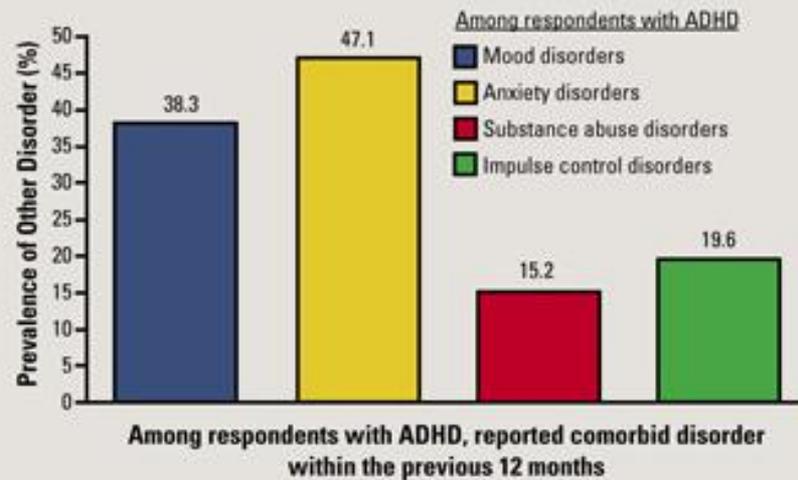


Riederman et al. Pediatrics. 2009; in press

SLIDE 1

Comorbidity of Other DSM-IV Disorders with ADHD³

National Comorbidity Survey Replication (N=3199)



DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; ADHD=attention-deficit/hyperactivity disorder.

Patterns of comorbidity between children and adults with ADHD are similar.⁴ Developme:

Developmental Relationship Between ADHD & Substance Abuse

Adolescent

- ADHD treatment may protect against cigarette and SUD
- Exposure to parental SUD increases SUD in ADHD



Gestational

- Family-genetic factors link ADHD and SUD risk
- Alcohol and nicotine in utero exposure increase ADHD risk

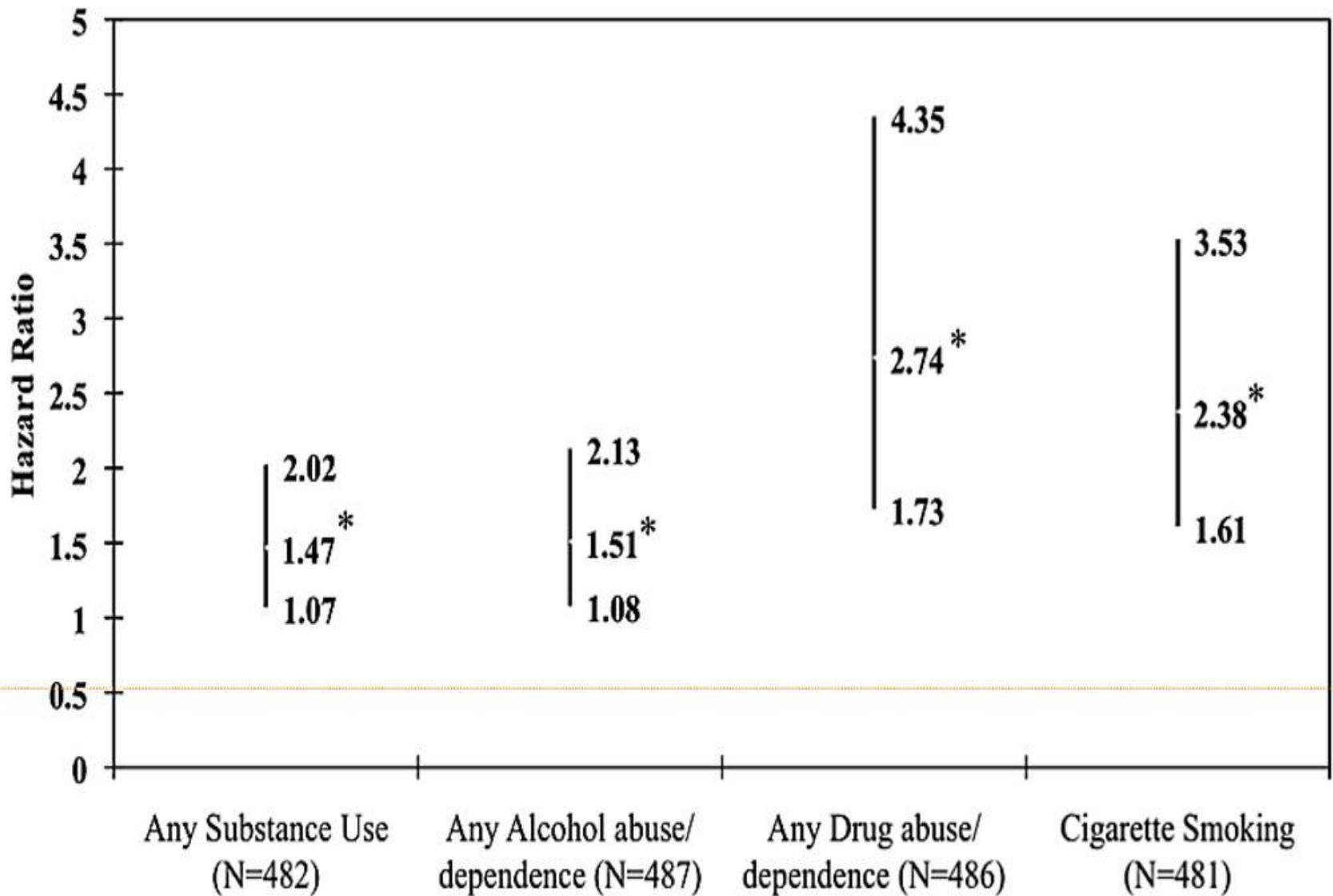


Child

- Comorbid ADHD linked to early-onset cigarette smoking and SUD

Adult

- ADHD linked to more cigarette smoking and SUD
- ADHD linked to more severe and chronic SUD
- ADHD linked to less remission from cigarette smoking and SUD
- ADHD treatment does not increase SUD



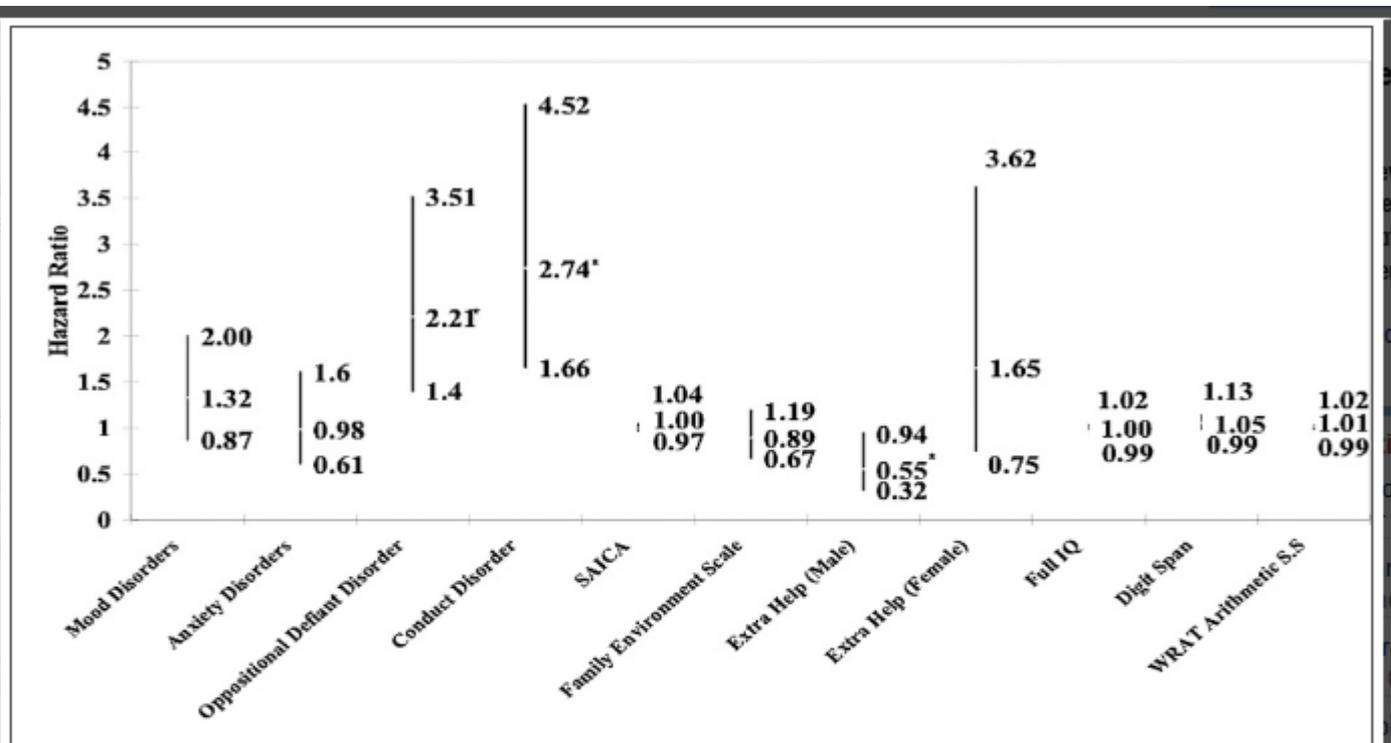


Figure 2

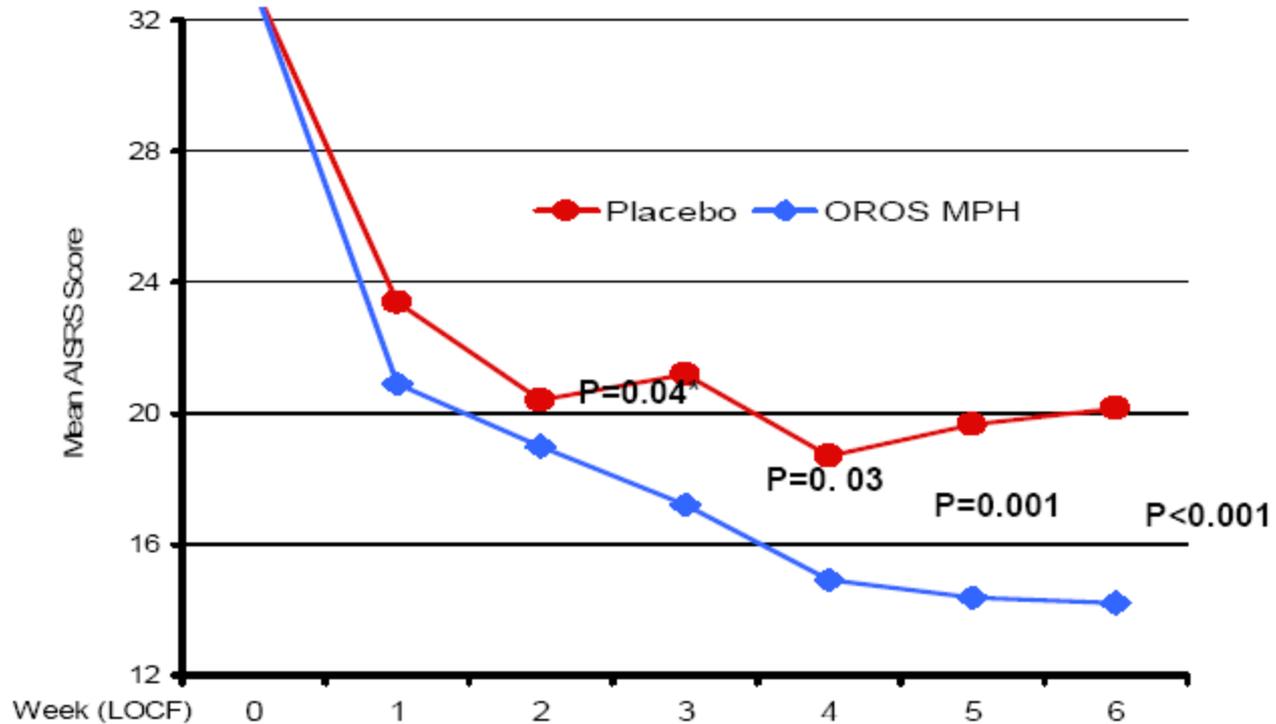
Predictors of Substance Use Disorders (SUD) Among Young Adults with Attention-Deficit/Hyperactivity Disorder (ADHD) (N=257). Note: Comorbid oppositional defiant disorder and conduct disorder were significant predictors of any SUD while adjusting for sex and parental history of SUD ($p < 0.01$; $p < 0.01$, respectively). Sex predisposed subjects to a different risk profile for extra help ($z = -2.19$, $p = 0.03$; all other p values > 0.05); extra help for boys was shown to be *protective* against the development of any SUD ($p = 0.03$). SAICA = Social Adjustment Inventory for Children and Adolescents; WRAT Arithmetic S.S. = Wide Range Achievement Test Arithmetic Scaled Score. *= $p < 0.05$

[Does ADHD Predict Substance Use Disorders? A 10-year Follow-up Study of Young Adults With ADHD](#)

J Am Acad Child Adolesc Psychiatry. 2011 June;50(6):543-553.

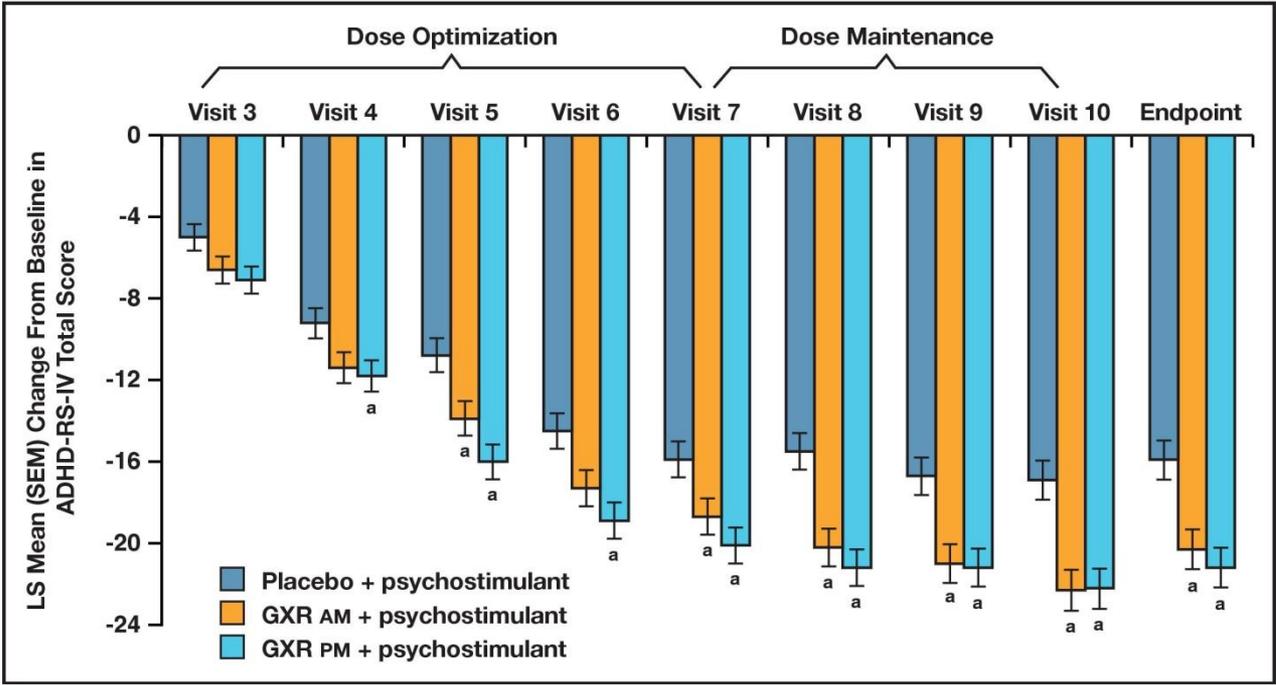
Resistencia al tratamiento/Remisión parcial

Week	1	2	3	4	5	6
OROS-MPH mg/day	36.0	58.7±17.8	72.6±26.5	77.9±29.6	81.3±31.0	80.9±31.8
Placebo mg/day	36.0	66.3±12.8	82.2±22.4	92.2±23.8	94.9±25.5	96.8±25.9

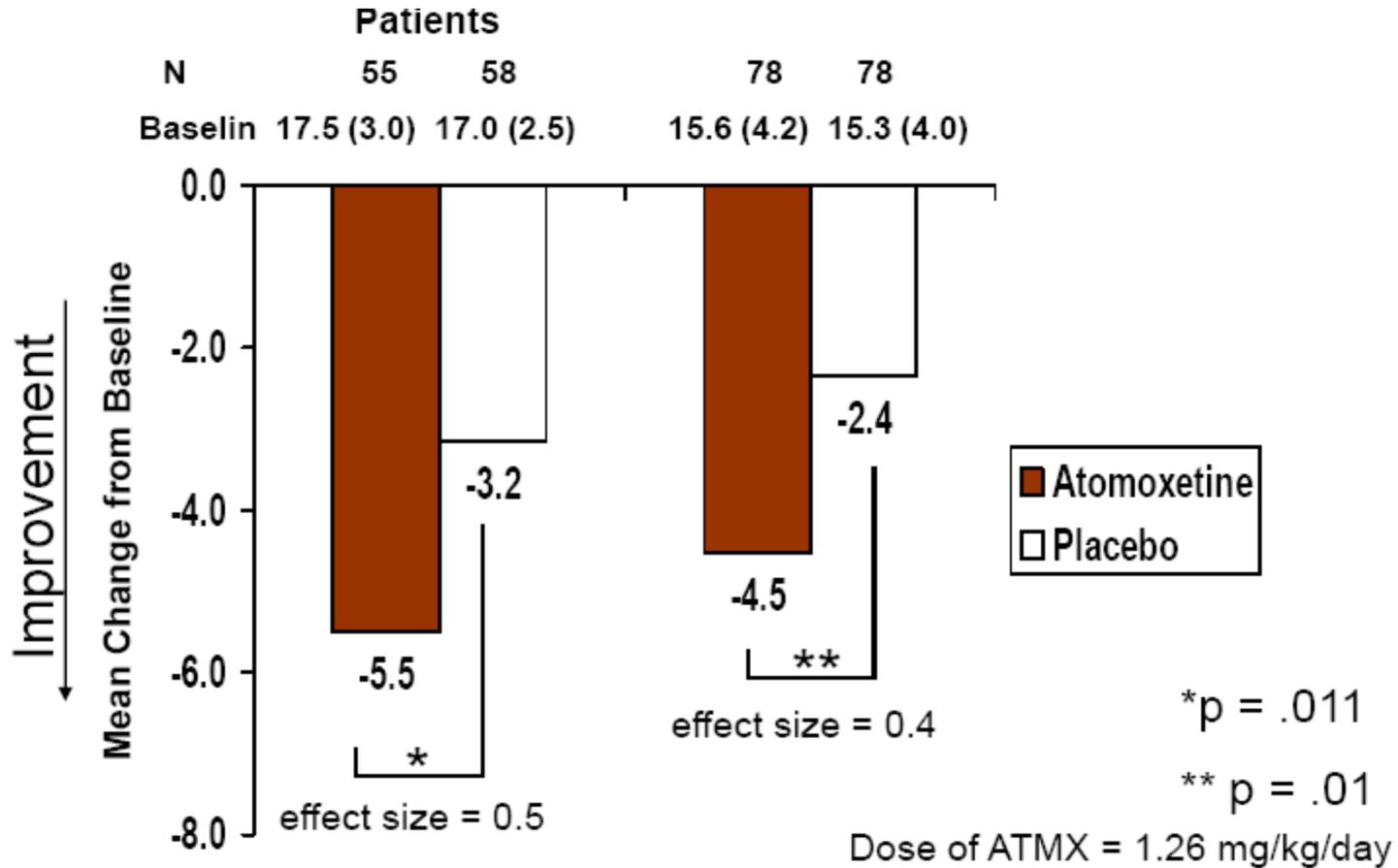


LS Mean (SEM) Change From Baseline in
ADHD-RS-IV Inattention Subscale Score

LS Mean (SEM) Change From Baseline in
ADHD-RS-IV Hyperactivity/Impulsivity Subscale Score

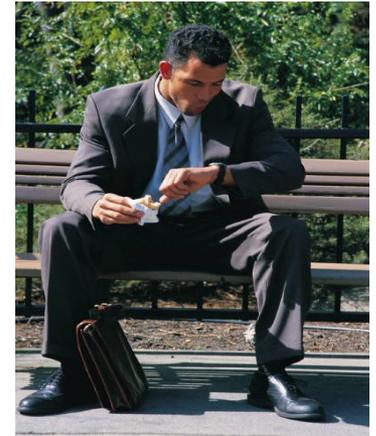
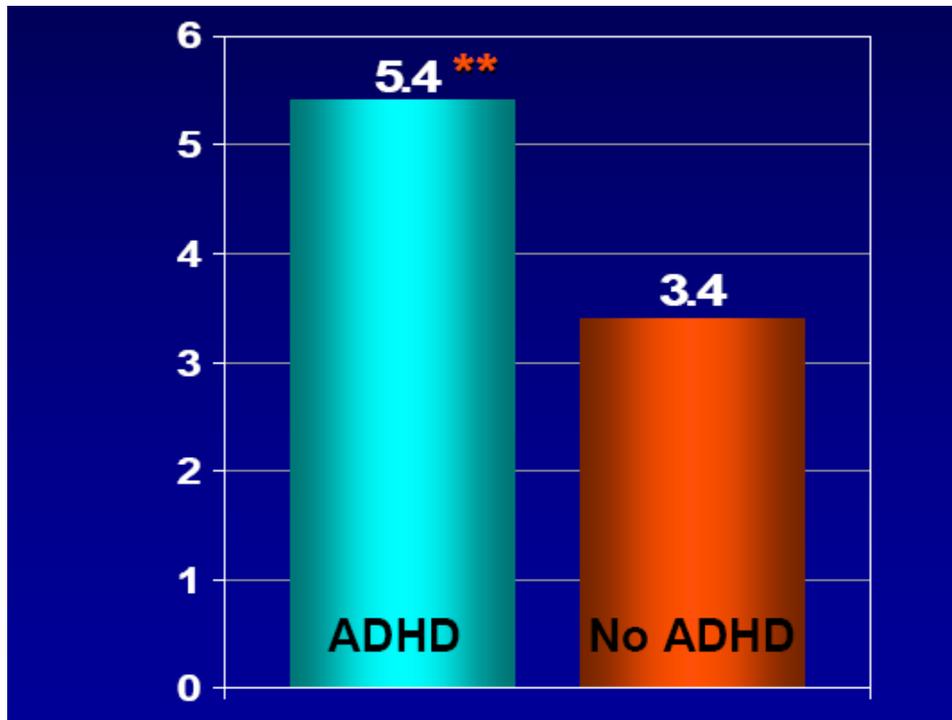


Resistencia al tratamiento/Remisión parcial



Impacto del TDAH en la vida laboral

Número de trabajos en los últimos 10 años



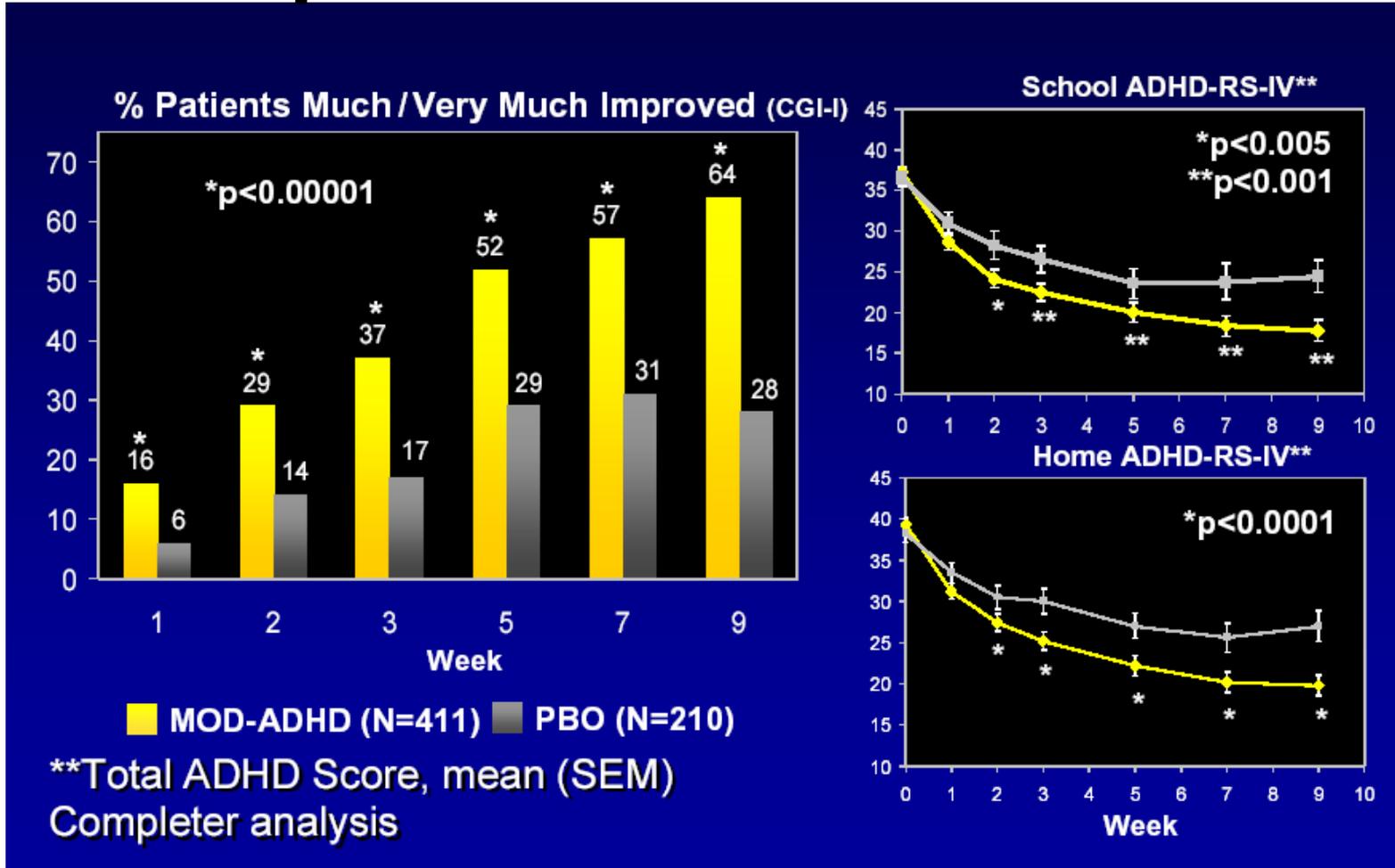
43% abandonó 1/+ trabajos en los últimos 10 años por los síntomas de TDAH

Exploración y pruebas diagnósticas

- **Imprescindible**
 - Entrevista y evaluación clínica
- **Recomendable**
 - Diferencia entre C.I. Verbal y manipulativo
 - Evaluación pedagógica y pruebas de aprendizaje
 - Test de atención
 - Analítica general
- **Necesario si sospecha de otro problema**
 - Electroencefalograma (EEG)
 - Resonancia Magnética Cerebral
 - Análisis genético

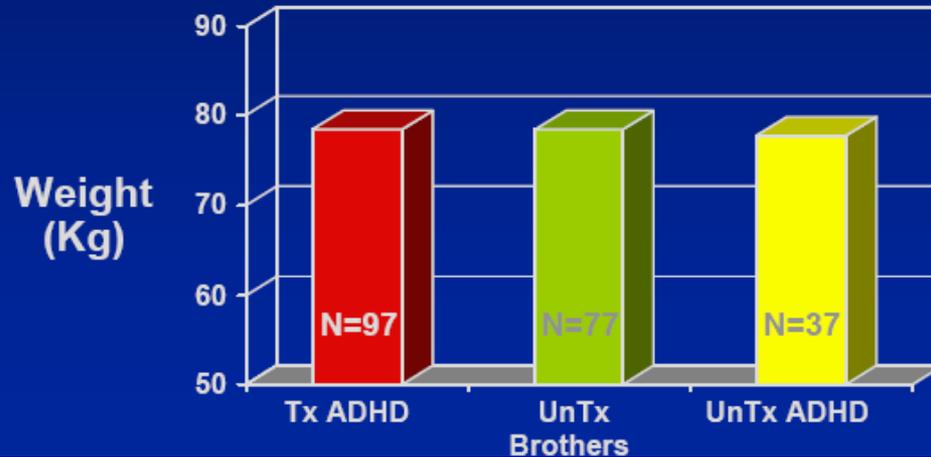
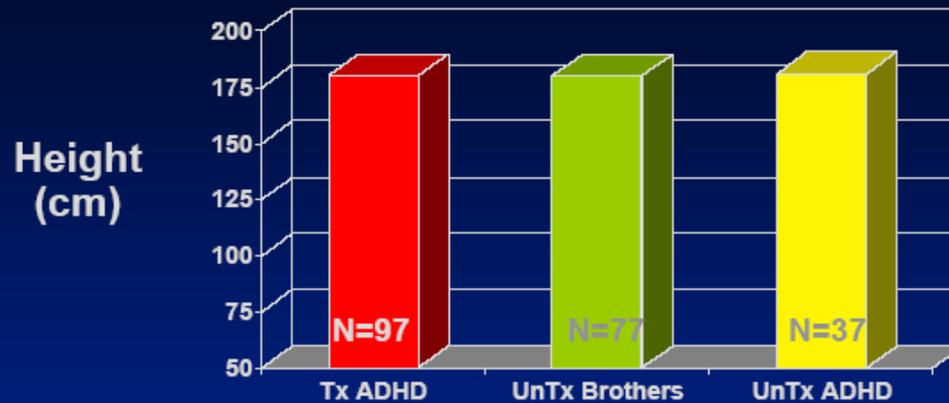


Respuesta al tratamiento



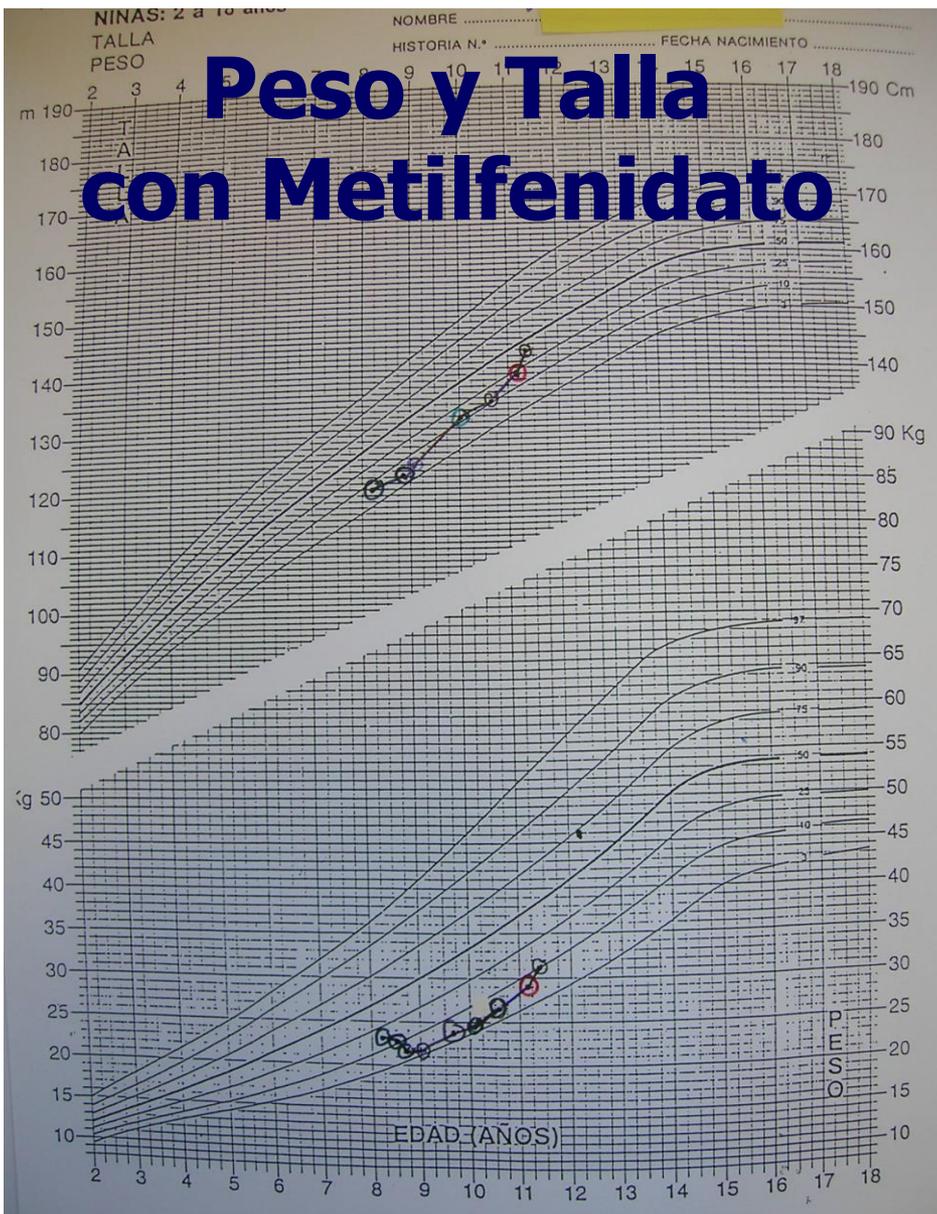
TDAH & Peso y crecimiento

Kramer, et al. *J Am Acad Child Adolesc Psychiatry.* 2000;39:517-524.



Youth aged 4 -12 yrs
MPH exposure = 36 mo
Reeval @ 21-23 years

Peso y Talla con Metilfenidato



TDAH & Bipolar

(Scheffer, Kowatch, Carmody et al. Am J Psych:2005 162:58-64)

**Study of BPD Spectrum
youth**

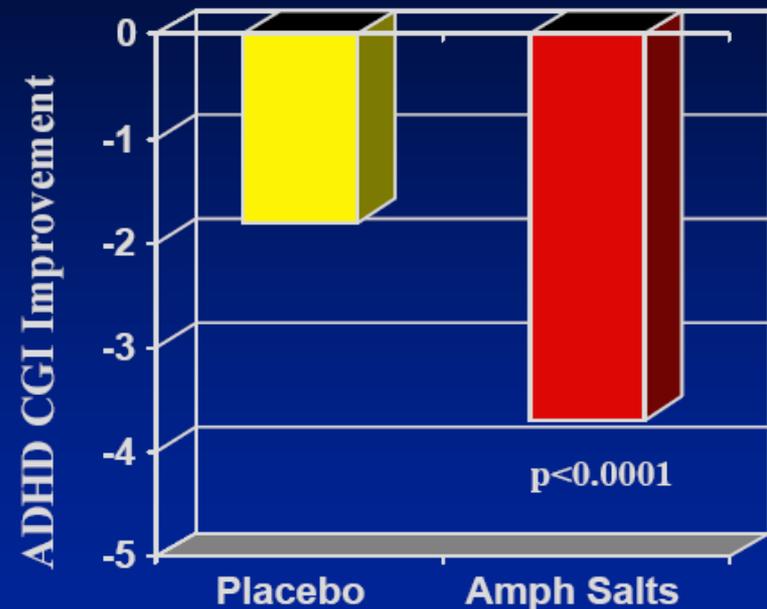
Age 6-17 years ($9 \pm 2.4y$)

Design:

8 Wk open (N=40) with DPK

4 Wk double blind (N=30)

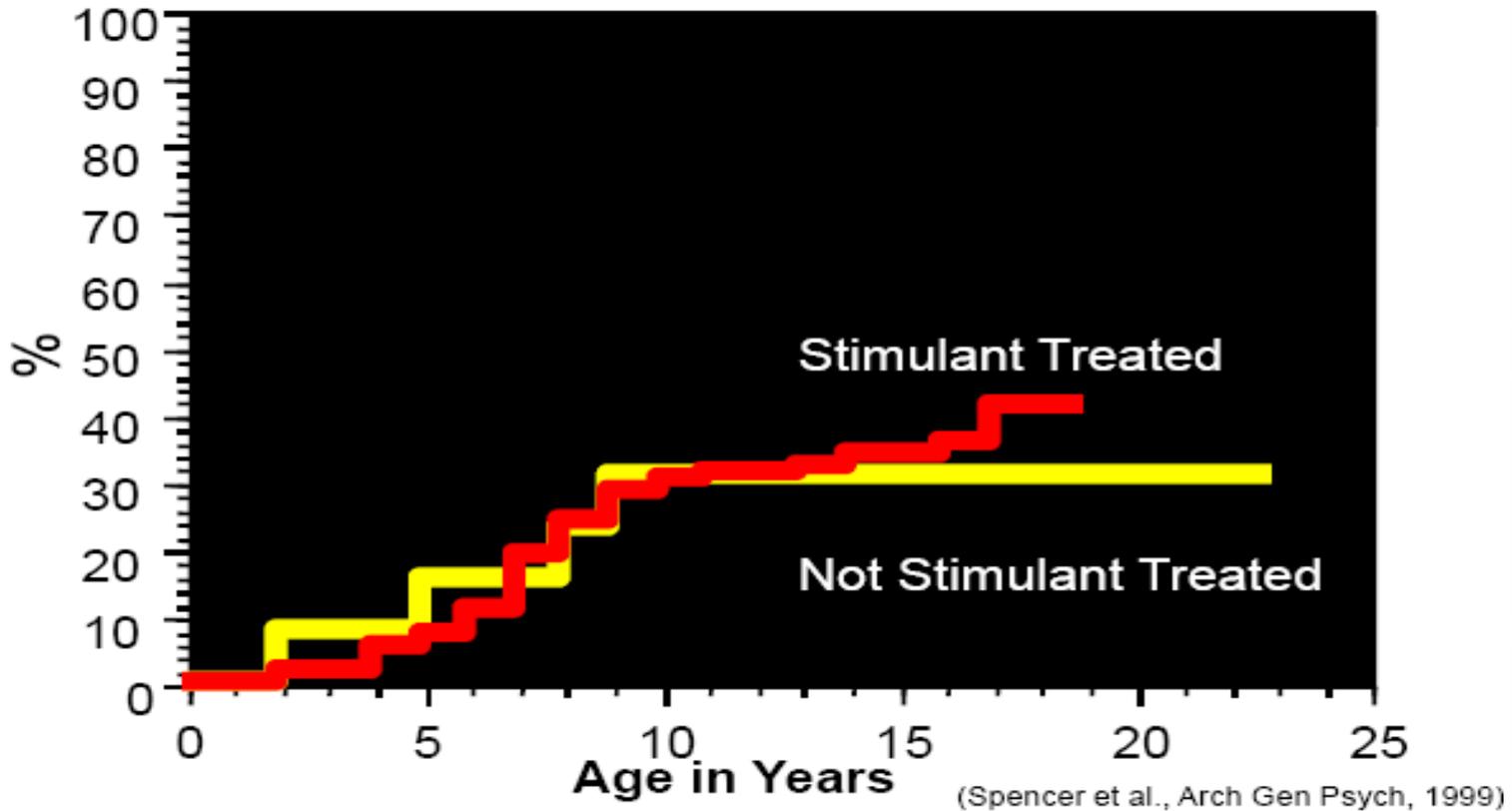
**DPK+Adderall (5mgBID)
or PBO**



**YMRS scores (endpoint):
PBO 5.9, Amph 7.1 (pNS)**

Comorbilidad (consideraciones especiales)

TDAH & Tics



Biederman, remisión de los hallazgos en función
De los síntomas

Déficit en el control de la respuesta emocional (*DESR*):

- 1. Comportamiento inapropiado ante emociones positivas y negativas**
- 2. Dificultad en redirigir la atención después de emociones fuertes**
- 3. Estado “hiperaureasal” inducido por la emoción**
- 4. Problemas en la organización de una estrategia posterior para lograr un objetivo.**

Déficit en el control de la respuesta emocional (*DESR*):

✓ Baja tolerancia a la frustración

✓ Irritabilidad reactiva moderada

✓ Labilidad emocional

60% ADHD adults vs 15 % controls (Barkley et al., 2008)

44% ADHD adolescentes vs 2% controles (Spencer et al., 2012)

60% ADHD adultos vs 30 % (Biederman et al., 2012)

Comorbilidad TDAH	Tratamiento
Tics	ATMX/MPH ± Antipsicóticos/Clonidina
TOC	ISRS + MPH/ATX
Ansiedad	ATX/MPH ± ISRS
Depresión	MPH/ATX ± ISRS/Bupropion
T. Bipolar	1° Antipsicóticos ± Antiepiléticos ± litio (estabilizadores) 2° MPH/ATX/Bupropion (sólo después de estabilizar humor)
Abuso sustancias	MPH-OROS(supervisión del uso)/ATX + tratamiento específico

Déficit en el control de la respuesta emocional (*DESR*):

✓ Indicador de severidad y peor pronóstico del TDAH

- Prevalencia/vida de trastornos comórbidos
- Ajuste social (SAS)
- Accidentes de coches
- Número de divorcios

✓ Independiente de la comorbilidad asociada con el TDAH

✓ Y del Déficit de las Funciones Ejecutivas (DEF)

(Spencer et al, 2012; Surgman et al, 2011)

Validación de formas atípicas de TDAH

(Wilens et al., ADHD: across the life span (course). Harvard, MGH. Boston, 2013)

✓ **Edad de inicio superior a 7 años** (Faraone et al, 2006)

✓ **Nº < de criterios DSM- TDAH + disfunción**
(Faraone et al, 2006)

✓ **CI bajo + criterios DSM- TDAH**

✓ **CI alto + criterios DSM- TDAH** (Faraone et al., 2007)

de la corona de Aragón por el rey Alfonso
que fue el primer Rey de las Coronas

↓ TE

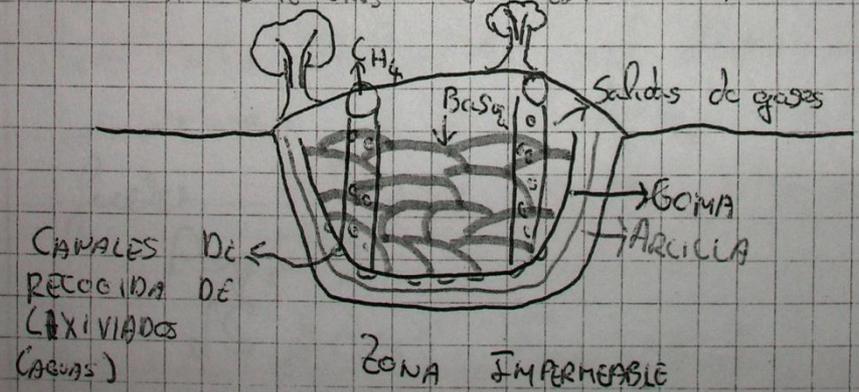
los reyes de la Corona de Aragón que
este lo expusieron por el matrimonio con
Pedro el grande y el que son el
y el nieto del rey Jaime por lo que
conquistara territorios Pedro IV y Alfonso
la Corona de Aragón se produjo de
su hijo Alfonso en 1282
los reyes de Aragón, Jaime I, Alfonso I
y Jaime II con la corona de Aragón

Respuesta al tratamiento

3.7.4. Metales Pesados

El agua disuelve muchas de estas sustancias fácilmente
por las raíces de las plantas e incorporadas a sus

3.2.5. VERTEDEROS DE RESIDUOS SÓLIDOS URBANOS



Caligrafía después
de Metilfenidato

Validación de formas atípicas de TDAH: recomendaciones

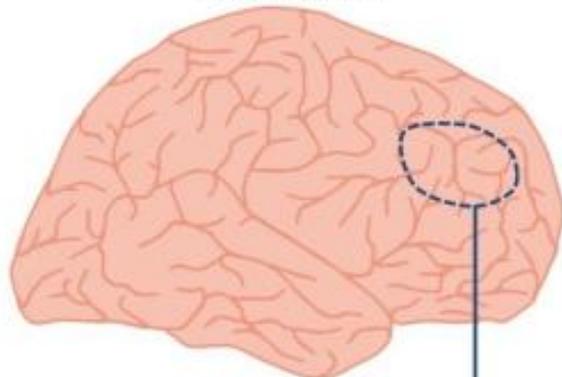
CI Bajo + Síntomas de TDAH

- Síntomas de TDAH (DSM-IV) excesivos para la edad mental (**y en niños con CI superior?**)
- Disfunción asociada a los síntomas de TDAH

CI Alto + Síntomas de TDAH

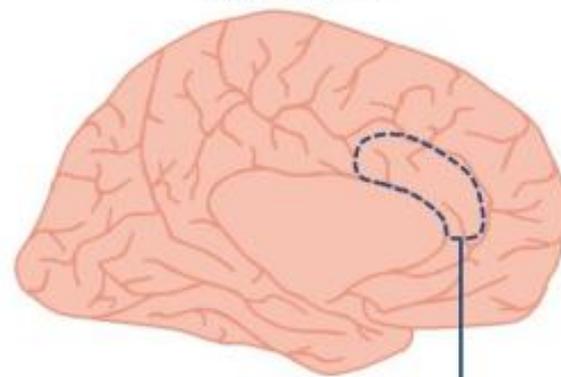
- Evaluación de estrategias y recursos de compensación
- “gap” entre rendimiento (*por debajo de lo esperado*) y capacidad

Vista externa

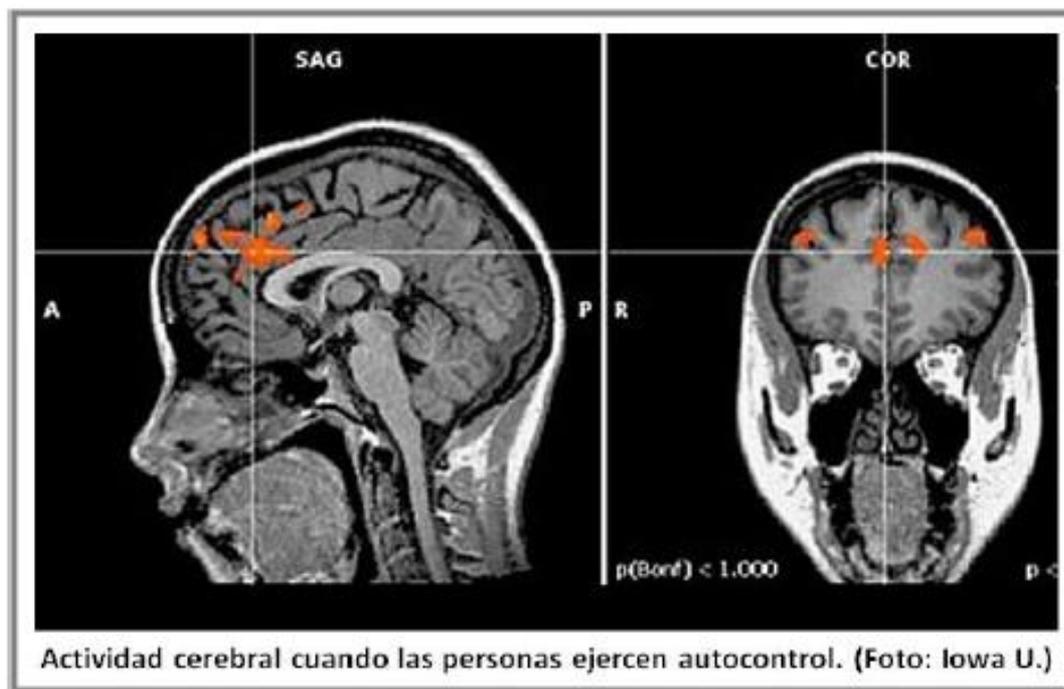


Corteza dorsolateral

Vista interna



Corteza cingular anterior





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LA EDUCACIÓN

El logo.pdf - Adobe Reader

Archivo Edición Ver Ventana Ayuda

1 / 1 107%

Adobe Reader interface showing the logo and text.

Correlates of alcohol use in adults with ADHD and comorbid alcohol use disorders: exploratory analysis of a placebo-controlled trial of atomoxetine.

[Wilens TE](#), [Adler LA](#), [Tanaka Y](#), [Xiao F](#), [D'Souza DN](#), [Gutkin SW](#), [Upadhyaya HP](#).

Massachusetts General Hospital, Boston, MA 02114, USA. twilens@partners.org

Abstract

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) and substance use disorder are often comorbid in adults. The effects of ADHD treatment on comorbid alcohol use disorder have not been extensively studied.

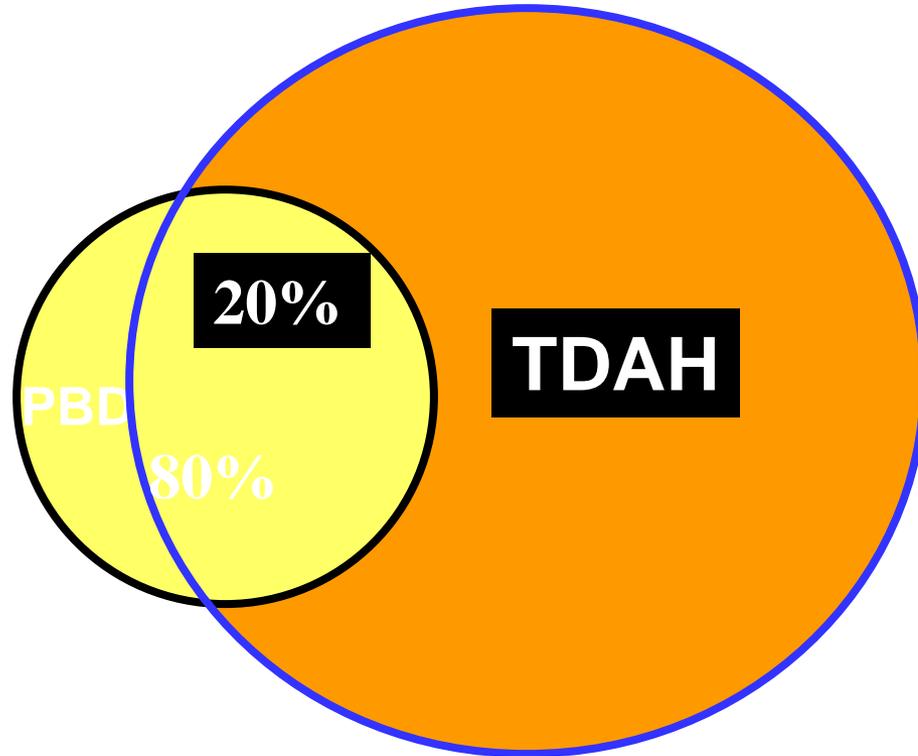
OBJECTIVE: To assess correlates of ADHD and alcohol use outcomes in ADHD with comorbid alcohol use disorders, via a post-hoc exploratory subgroup analysis of a previously conducted, randomized, double-blind, placebo-controlled study of recently abstinent adults.

METHODS: Adults who had ADHD and alcohol use disorders and were abstinent for 4-30 days were randomized to daily atomoxetine 25-100 mg (mean final dose = 89.9 mg) or placebo for 12 weeks. Changes in ADHD symptoms from baseline to endpoint were assessed using the ADHD Investigator Symptom Rating Scale (AISRS) total score, alcohol use by the timeline followback method, and alcohol cravings by the Obsessive Compulsive Drinking Scale.

RESULTS: Of 147 subjects receiving atomoxetine ($n = 72$) or placebo ($n = 75$) in the primary study, 80 (54%) completed 12 weeks ($n = 32$ atomoxetine; $n = 48$ placebo). Improvements in ADHD symptoms on the AISRS correlated significantly with decreases in alcohol cravings (Pearson's $r = 0.28$; 95% confidence interval [CI] = 0.11-0.43; $p = 0.002$), and the correlation was most notable with atomoxetine ($r = 0.29$; CI [0.04 - 0.51]; $p = 0.023$) rather than with placebo ($r = 0.24$; CI [0.00-0.46]; $p = 0.055$). On-treatment drinking levels correlated with AISRS scores ($r = 0.12$; CI [0.05 -0.19]; $p = 0.001$). Relapse to alcohol abuse significantly correlated with worse ADHD symptoms on 15 of 18 items of the AISRS in the placebo group ($p < 0.05$ for each).

CONCLUSIONS: No baseline predictor (other than degree of sobriety) of alcohol use or ADHD outcomes emerged. ADHD symptom improvements correlated significantly with reductions in alcohol cravings, and relapse to alcohol abuse correlated significantly with worsening of most ADHD symptoms in the placebo group, but not in the atomoxetine group. This post-hoc subgroup analysis is of a hypothesis-generating nature, and the generalizability of the findings may be limited by exclusion of adults with common ADHD comorbidities from the base study. Further, prospective clinical trials in larger and more heterogeneous patient populations are warranted to confirm or reject these preliminary associations. TRIAL REGISTRATION (BASE STUDY): ClinicalTrials.gov identifier: NCT00190957.

Resistencia al tratamiento/Remisión parcial



ABSTRACT

OBJECTIVE: According to studies of prevalence, up to 70% of adults with attention deficit/hyperactivity disorder have at least one psychiatric comorbidity, which leads to diagnostic and therapeutic difficulties as well as more severe functional impairment. There is a paucity of data on the comorbidity of attention deficit/hyperactivity disorder and eating disorders. The objective of this study was to review the literature regarding the attention deficit/hyperactivity disorder/eating disorders comorbidity, performing a critical analysis of relevant data.

METHOD: Articles in Medline, Lilacs, SciELO, ISI and PsycINFO databases from 1980 up to 2008, were searched. The references from the articles were used as additional sources of data.

RESULTS: Fourteen articles were found: five prevalence studies, four case reports, three case-control studies, one symptom-assessment study of attention deficit/hyperactivity disorder and eating disorders, and one article regarding possible causes of the association between attention deficit/hyperactivity disorder and eating disorders. These articles suggested that adult women with attention deficit/hyperactivity disorder are at higher risk of developing eating disorders, especially bulimia nervosa. Bulimia Nervosa rates found in attention deficit/hyperactivity disorder groups ranged from 1% to 12%, versus 0% to 2% in control groups.

CONCLUSIONS: Although there seems to be a relationship between attention deficit/hyperactivity disorder and eating disorders, the reduced number of studies available, with various methodologies, and small sample sizes limit the generalization of the findings.

Descriptors: Eating disorders; Bulimia nervosa; Attention deficit disorder with hyperactivity; Comorbidity; Impulsivity

Review of literature of attention-deficit/hyperactivity disorder with comorbid eating disorders

Revisão da literatura sobre a comorbidade do transtorno do déficit de atenção e hiperatividade com transtornos alimentares

Bruno Palazzo Nazar^{I,II,IV}; Camilla Moreira de Sousa Pinna^{I,III}; Gabriel Coutinho^{I,II}; Daniel Segenreich^{I,II}; Monica Duchesne^{II,IV}; José Carlos Appolinario^{II,IV,V}; Paulo Mattos^{I,V}

Borderline Personality Disorder, Bulimia Nervosa, Antisocial Personality Disorder, ADHD, Substance Use: Common Threads, Common Treatment Needs, and the Nature of Impulsivity

[Tamika C. B. Zapolski](#), [Regan E. Settles](#), [Melissa A. Cyders](#), and [Gregory T. Smith](#)

[Author information](#) ▶ [Copyright and License information](#) ▶

PubMed Central, Table 1: *Indep Pract.* 2010 WINTER; 30(1): 20–23. - Mozilla Firefox

www.ncbi.nlm.nih.gov/pmc/articles/PMC3022439/table/T1/

Accepted for publication in a peer reviewed journal

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From: [Indep Pract. Author manuscript, available in PMC 2011 January 18.](#)
Published in final edited form as:
Indep Pract. 2010 WINTER; 30(1): 20–23.

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Table 1

Suggested Interventions for the Five Dispositions to Rash Action

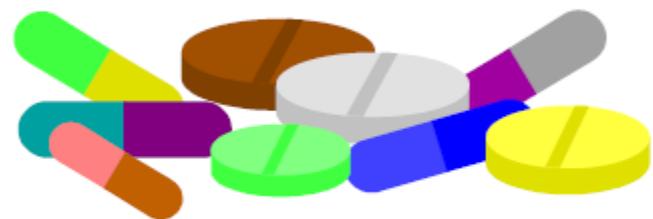
Trait	Interventions
Negative Urgency	Emotion regulation, distress tolerance, interpersonal effectiveness; adjust emotional reactions by considering the context, experience the emotions without acting, adjust reactions through relaxation, prayer, and other soothing activities, learn to effectively communicate feelings to others; SSRIs; identify precipitating events or triggers to emotional reactivity and learn adaptive alternatives similar to those provided in distress tolerance modules; learn to evaluate behavioral choices in terms of one's long-term goals.
Positive Urgency	Teach adaptive techniques for savoring success and positive mood; identify alternative, safer means of celebrating; learn to use cues indicating risk for maladaptive behavior; provide client with reminders or cues of the alternative behaviors identified.
Sensation Seeking	Highly stimulating media messages suggesting alternative, safe ways to pursue stimulation; development of a bank of safe, stimulating activities as behavioral options.
Lack of Planning	Cognitive mediation training; specifying all steps necessary to complete a task and the time necessary for each step; learn to anticipate the consequences of one's presence in situations and settings.
Lack of Perseverance	Stimulant medications plus cognitive-behavioral therapy; behavioral paradigms to reinforce task completion; learn to gauge attention span and distractibility delay, modify environment, learn techniques to reduce procrastination and increase follow-through.

NIH/PA Manuscripts

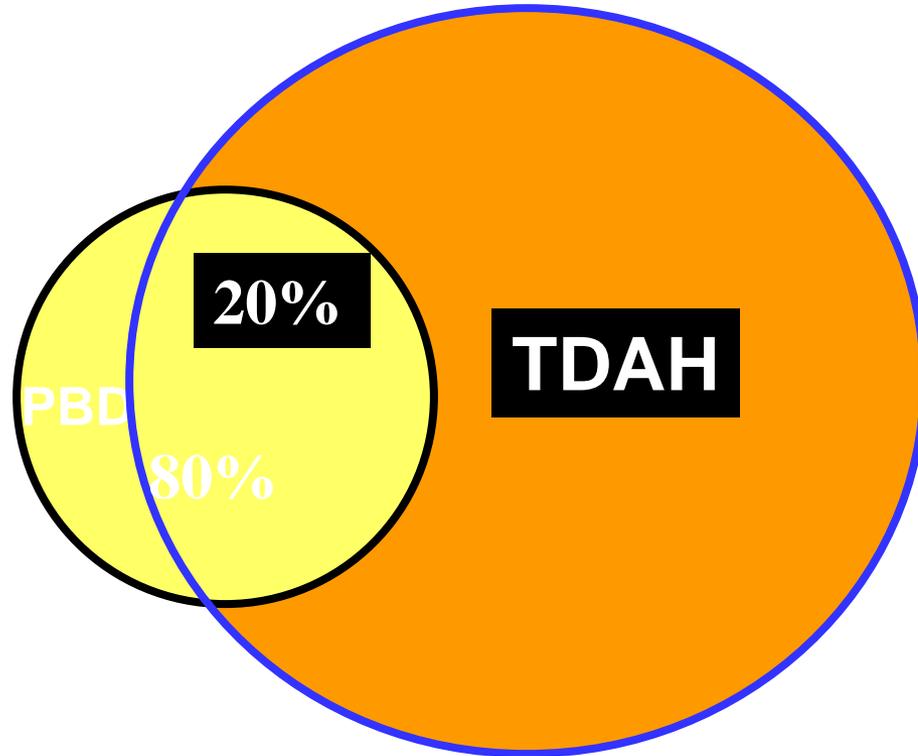
Medikinet

Equazym

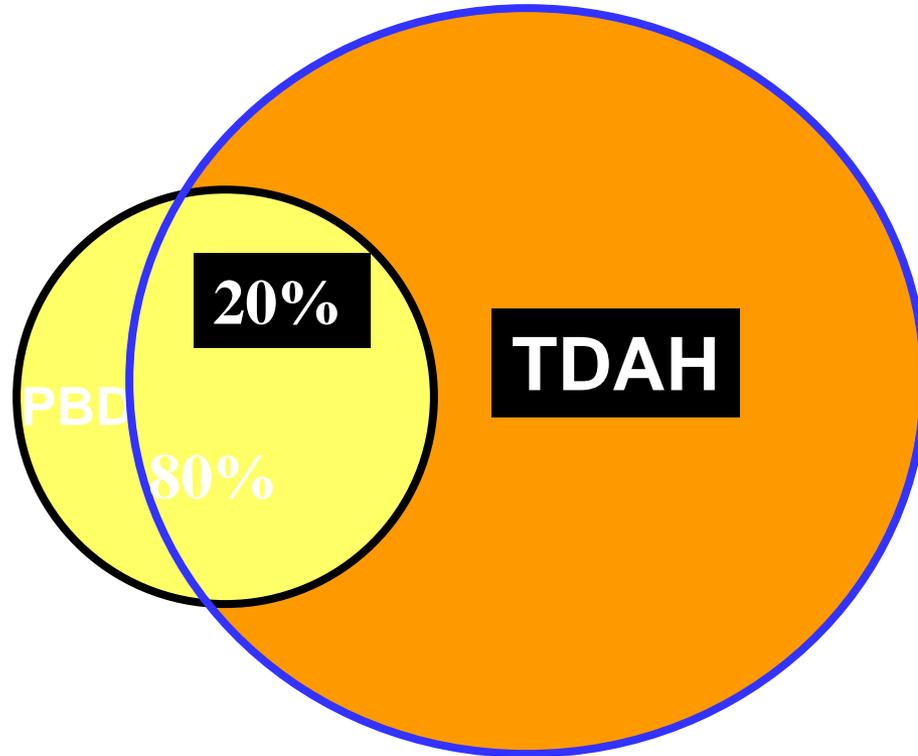
- Stimulants (FDA approved)
 - Methylphenidate
 - Amphetamine compounds
- Atomoxetine (FDA approved)
- Antihypertensives (FDA approved [guanfacine XR])
- Antidepressants
 - Bupropion
 - Tricyclics
- Modafinil
- Research
 - Natural agents
 - Combined
 - Cholinergic agents



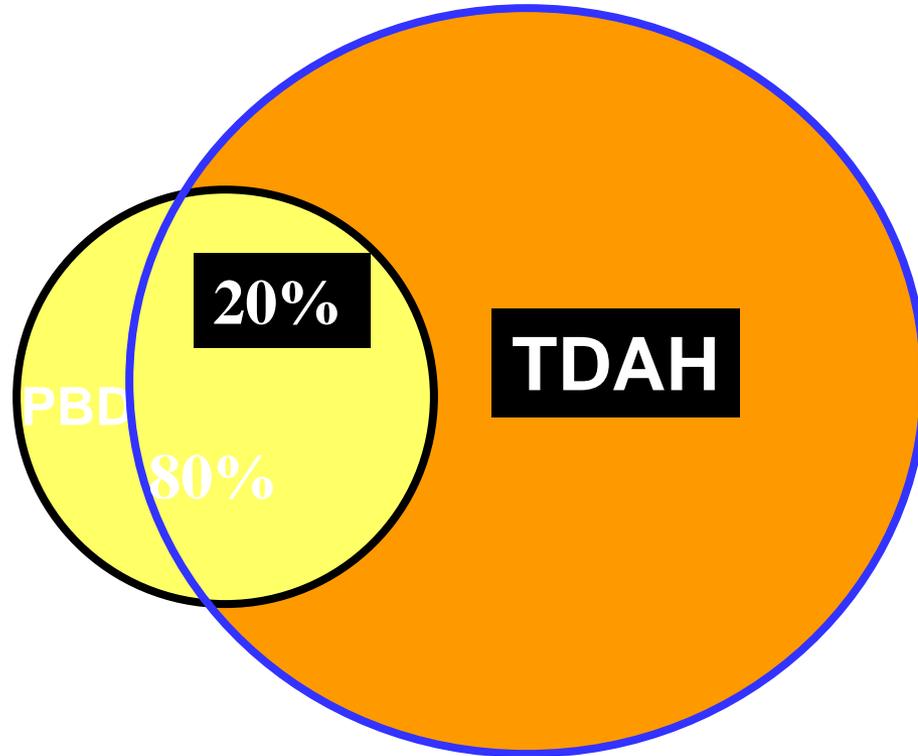
Resistencia al tratamiento/Remisión parcial

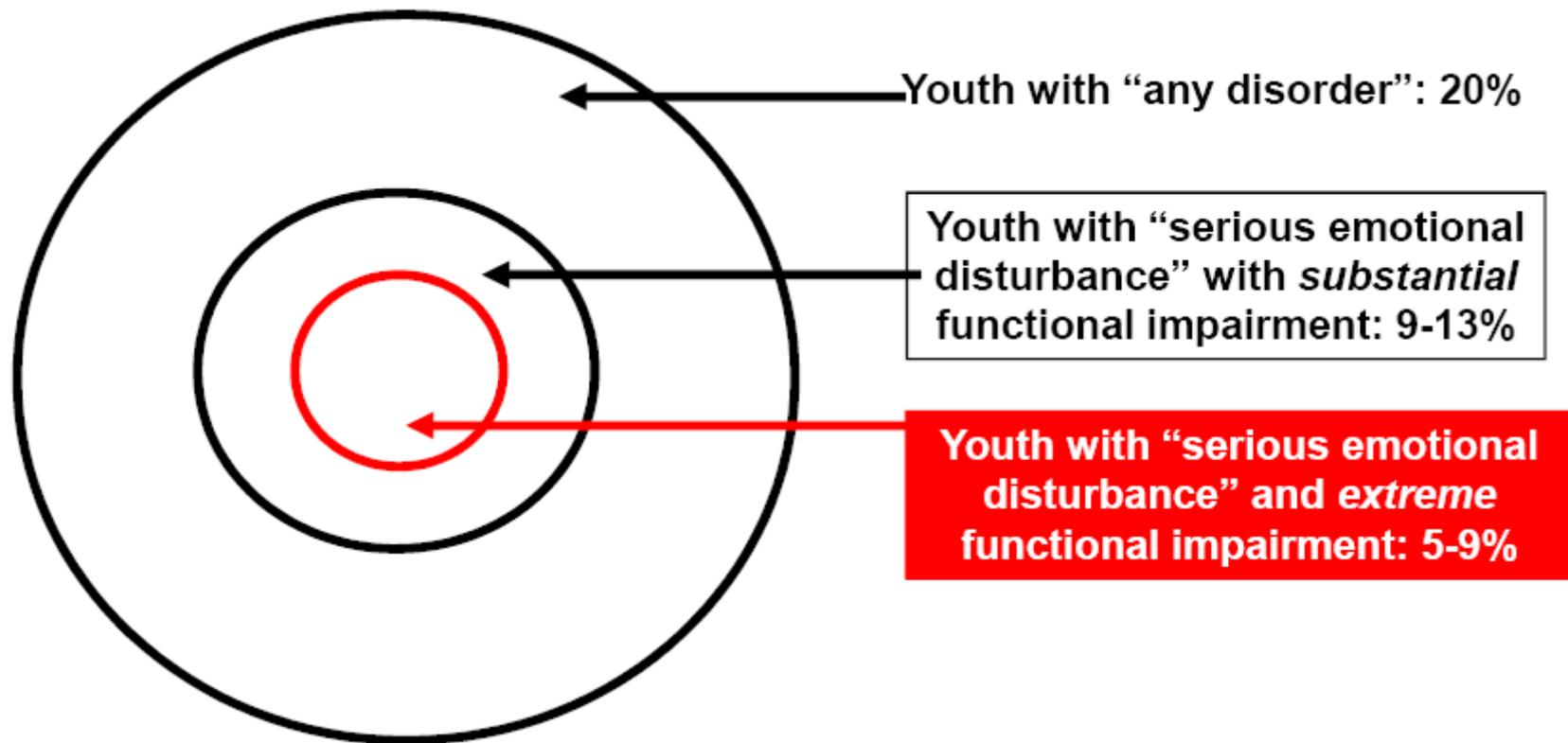


Resistencia al tratamiento/Remisión parcial

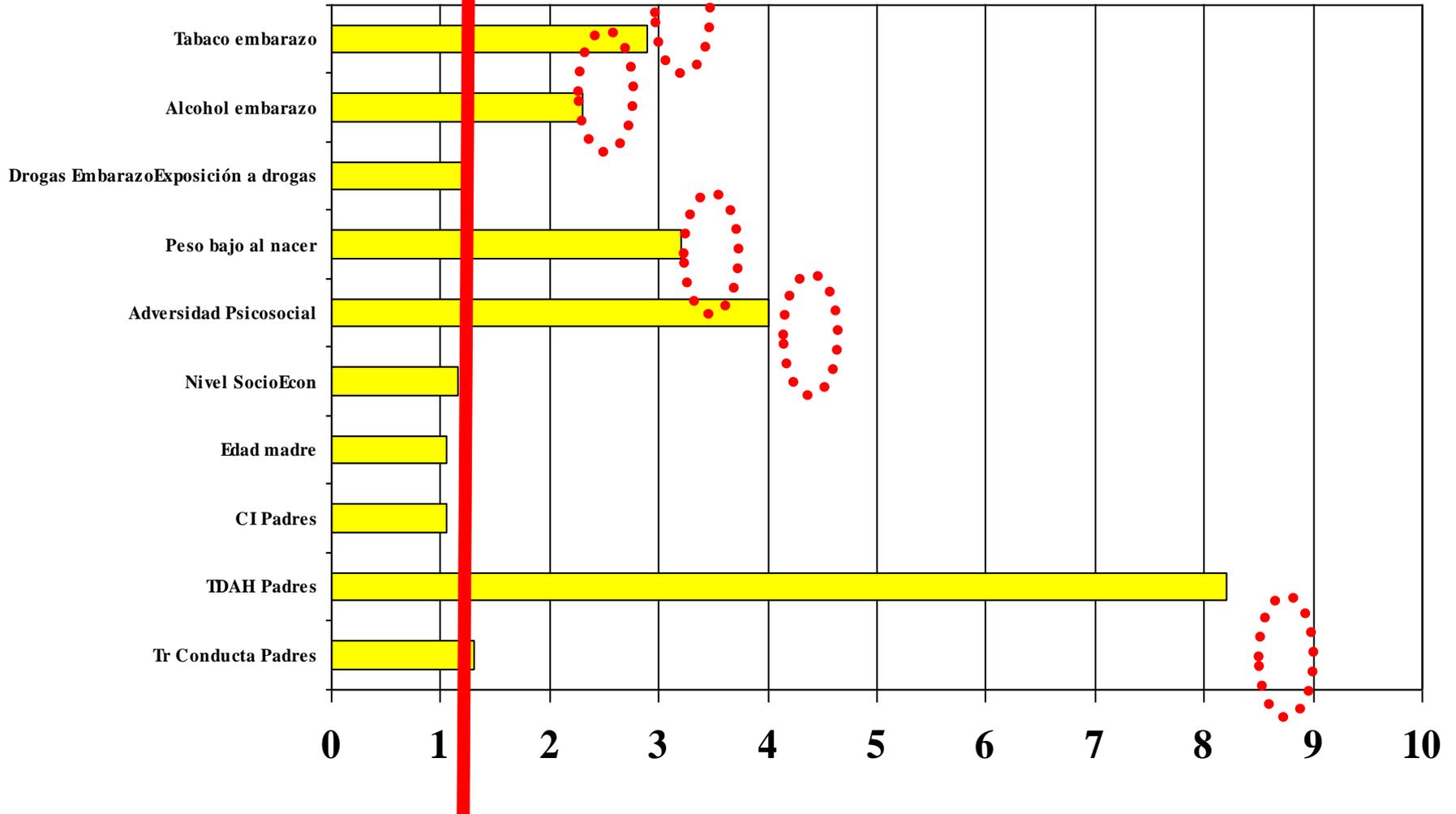


Resistencia al tratamiento/Remisión parcial





Hallazgos genéticos/impacto de factores externos



Síntomas

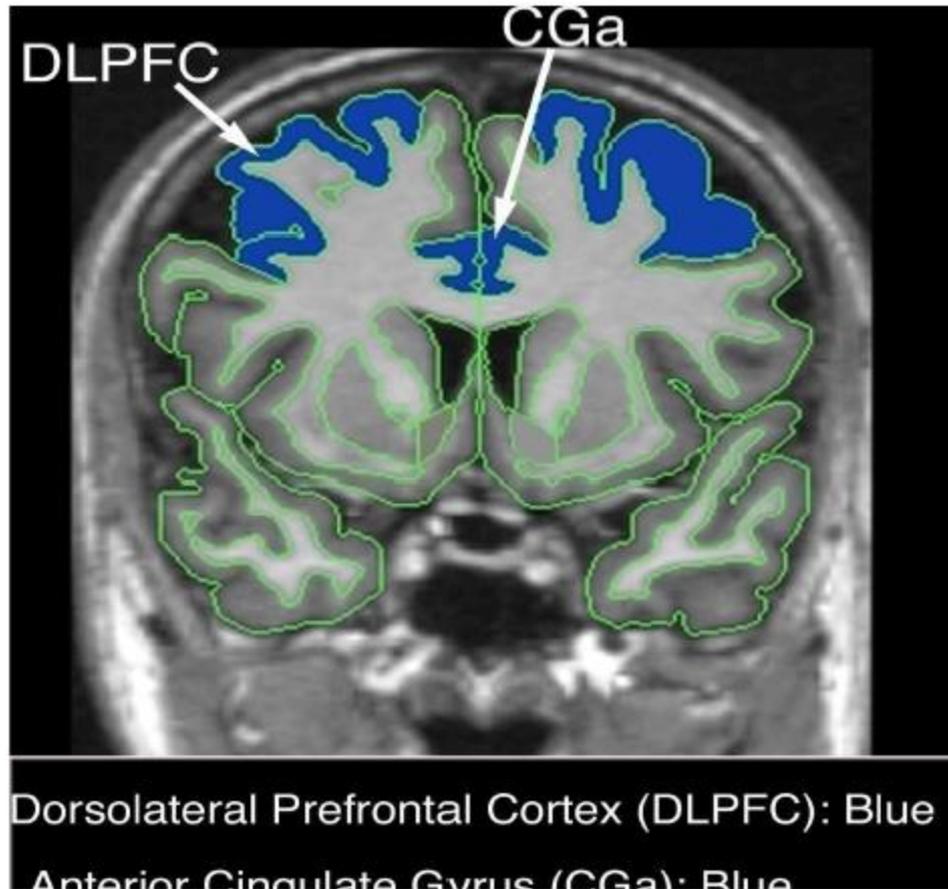


Fig. 1- Causa multifactorial de los problemas escolares

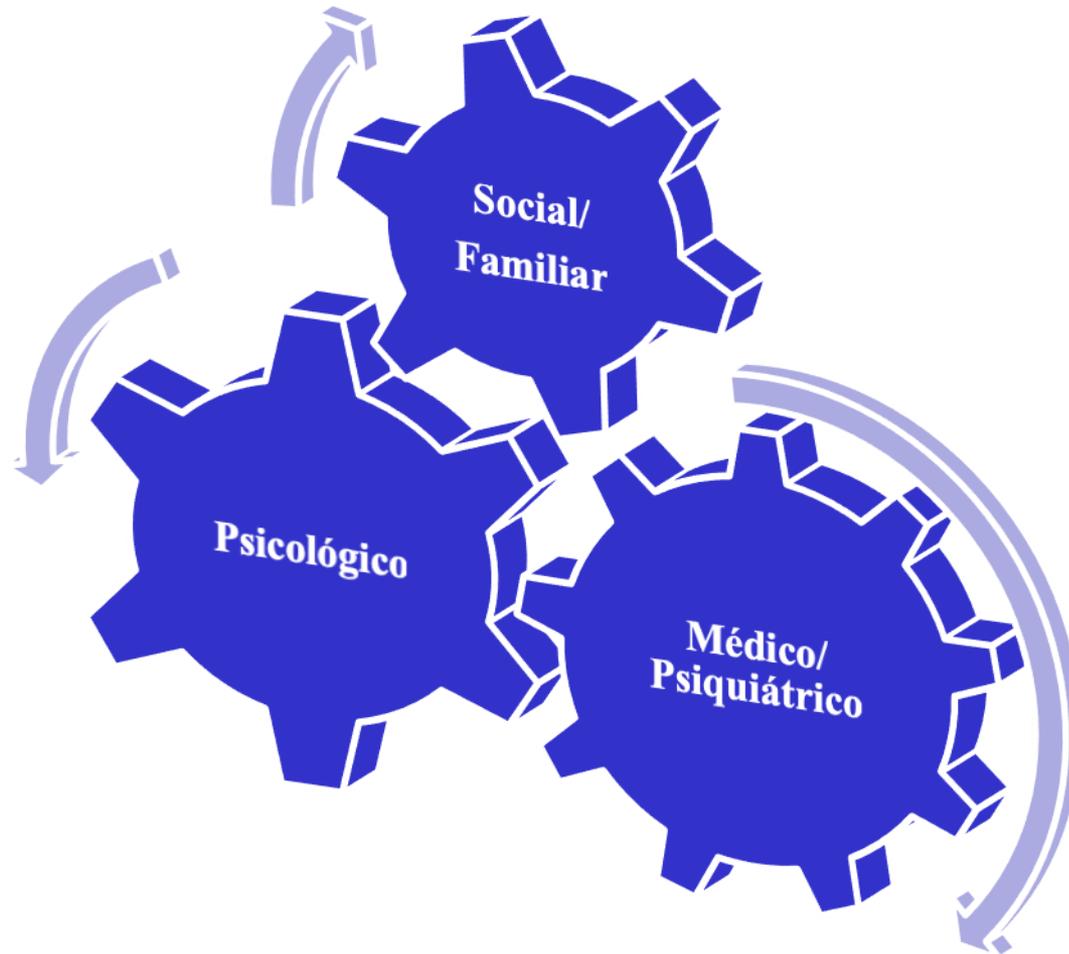


Fig. 2- Génesis de los conflictos graves en el entorno escolar

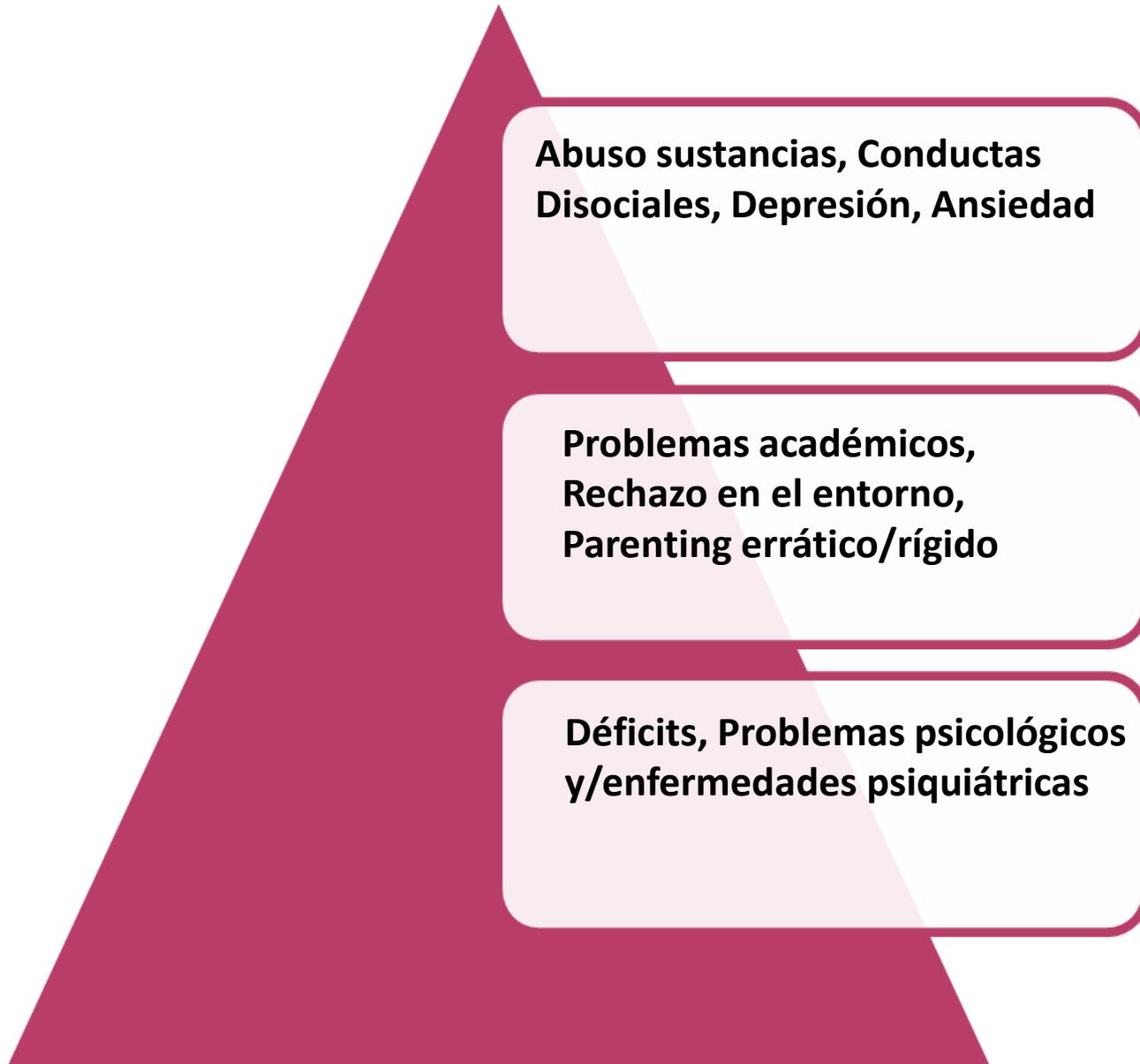


Fig. 3- Interrelación entre los diferentes factores implicados en los problemas de conducta

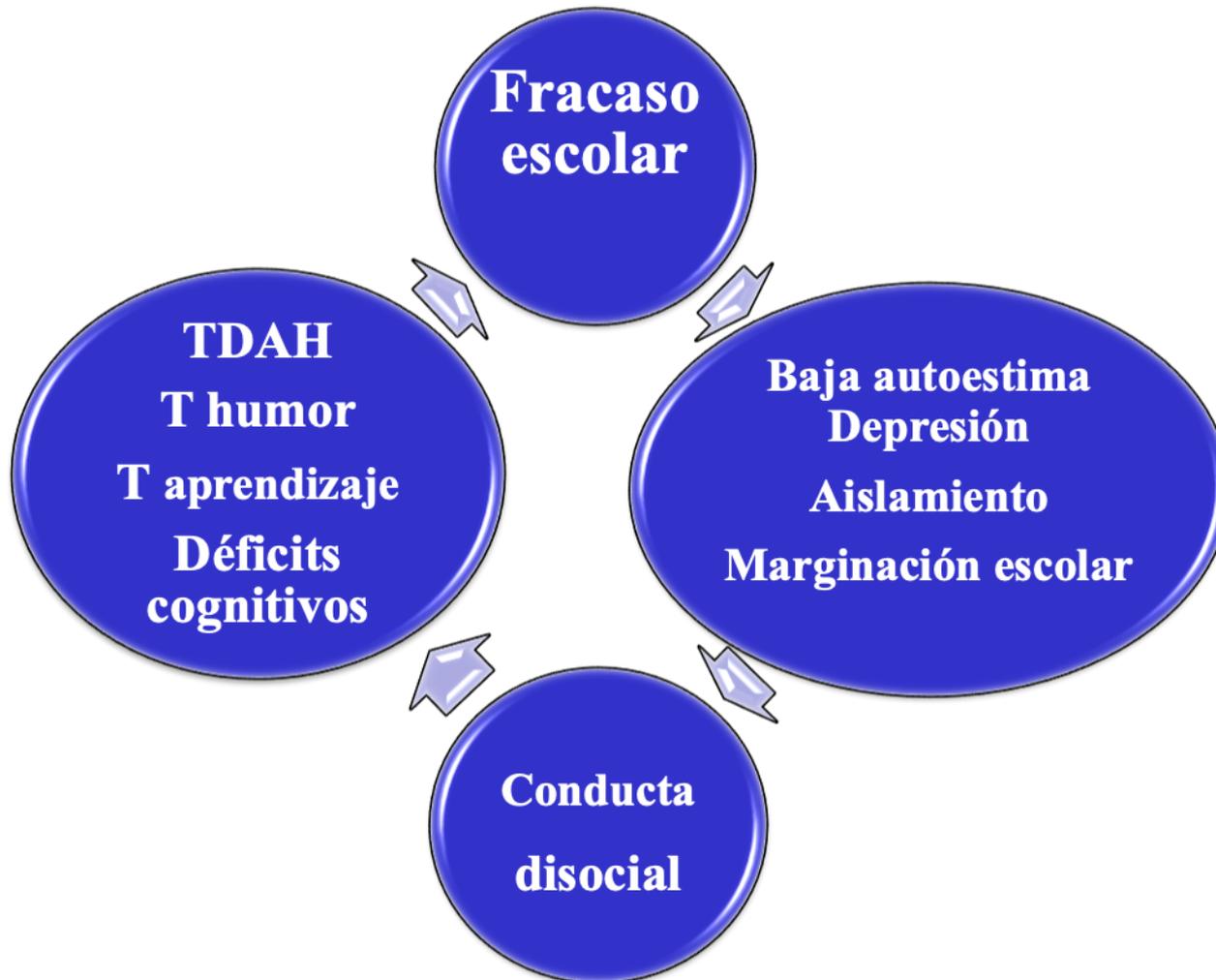
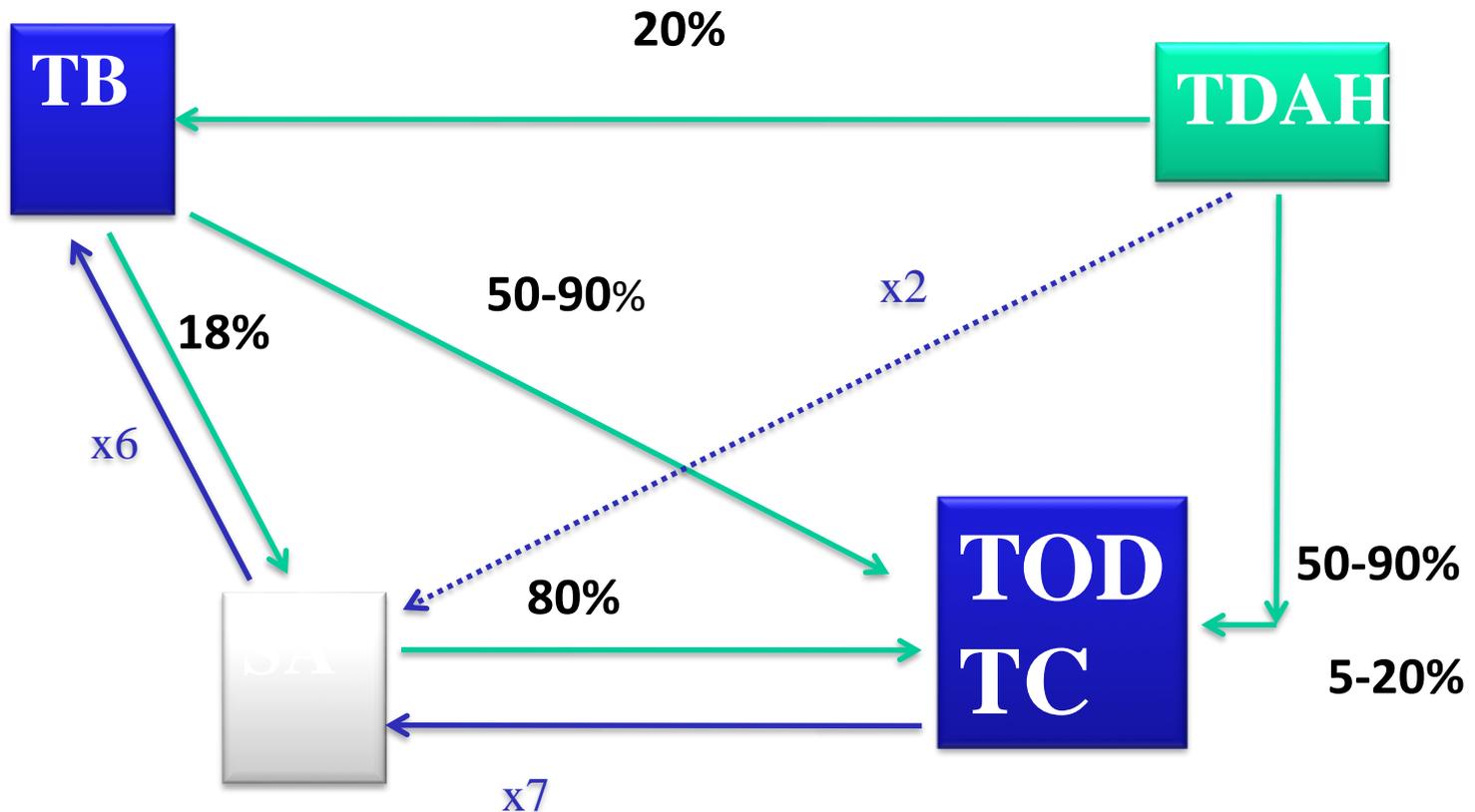
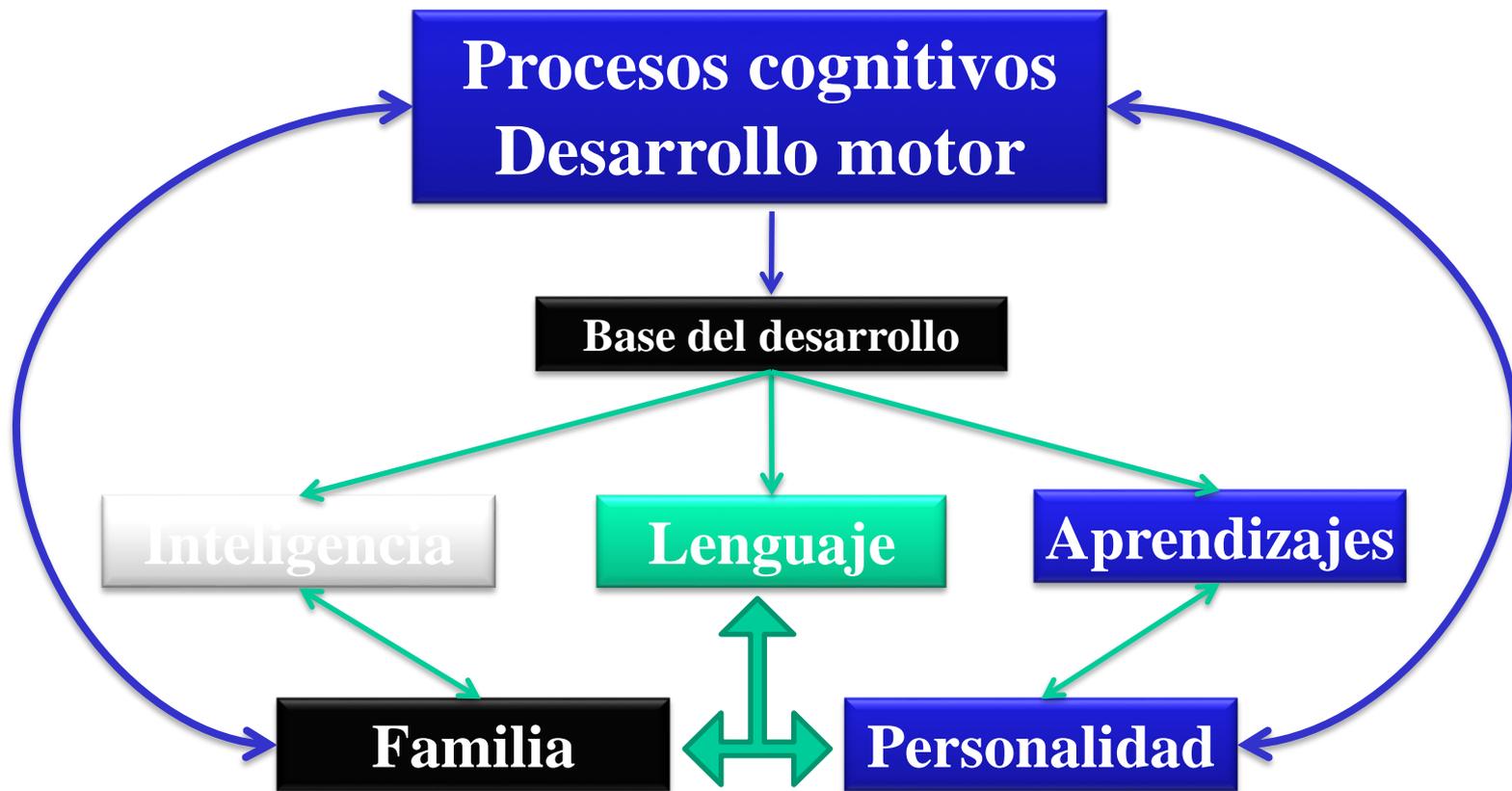


Fig. 4- Interrelación de los problemas de conducta con otros problemas psiquiátricos



TB, trastorno Bipolar; TDAH, Trastorno por Déficit de Atención e Hiperactividad; SA, abuso de sustancias; TOD/TC, Trastorno Oposicional y Desafiante/ Trastorno de Condcuta

Fig. 5- Interrelación de las distintas áreas del diagnóstico en educación.



Nota. Dentro de los procesos cognitivos se encuentran la percepción, atención, memoria, funciones ejecutivas, lenguaje y emociones.

**Dificultades escolares
(Comportamiento/Rendimiento)**

Equipo de orientación

Evaluación:

- 1. Entrevista con los padres y profesores**
- 2. Evaluación de la capacidad intelectual del niño**
- 3. Test de Screening de TDAH**

Informe final

Inicio del plan de intervención

Derivación al especialista

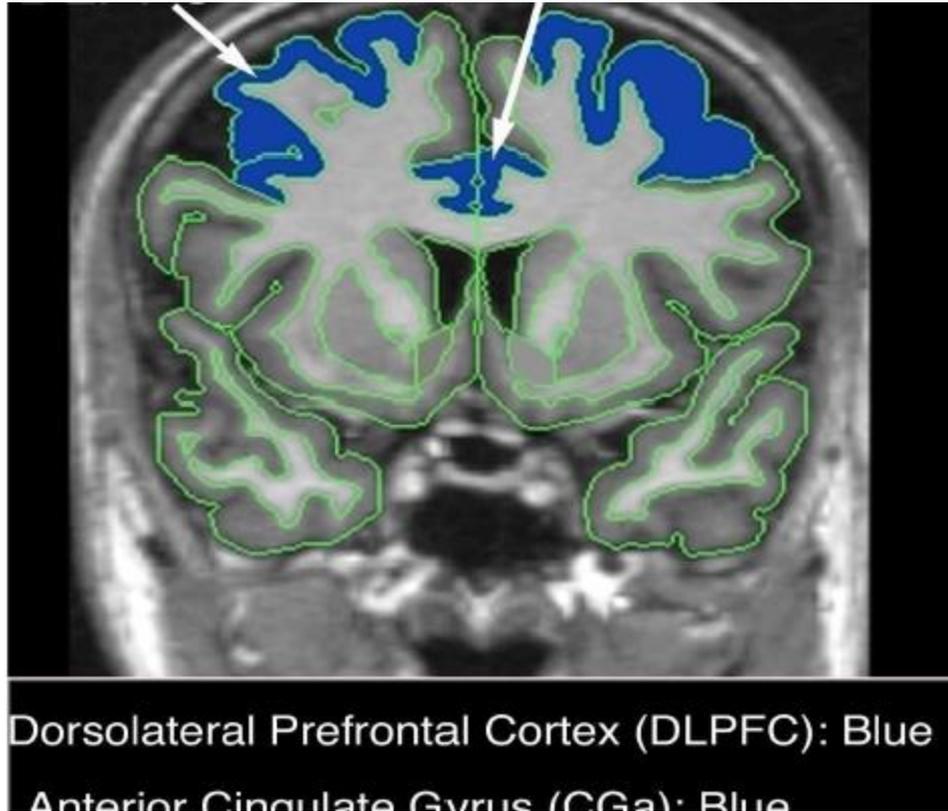
**Evaluación 3/6 meses
(feec-back profesor y padres)**

Mejoría

**Sin cambios
significativos**

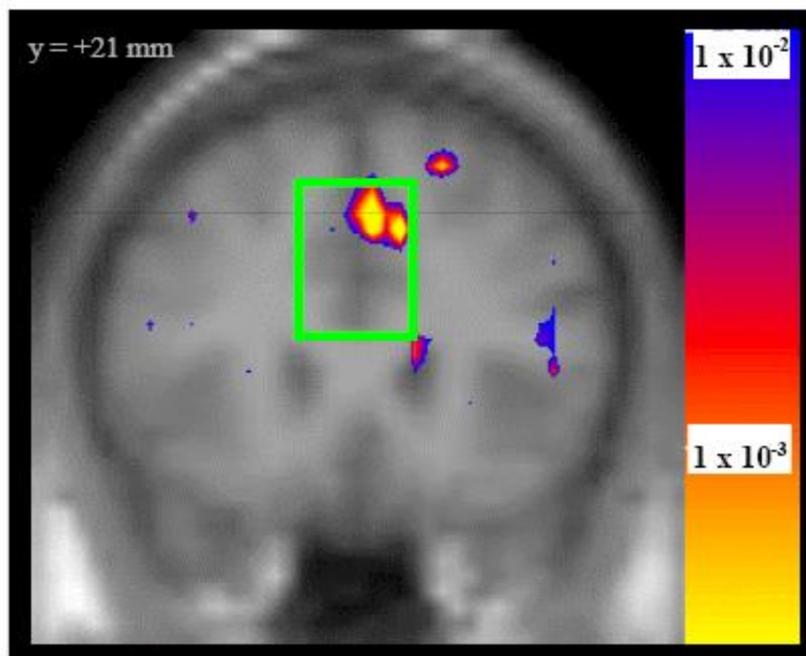
Fig. 5- Procedimiento de evaluación diagnóstica e inicio de intervención multidisciplinaria en el niño con dificultades en el entorno escolar

Etiología



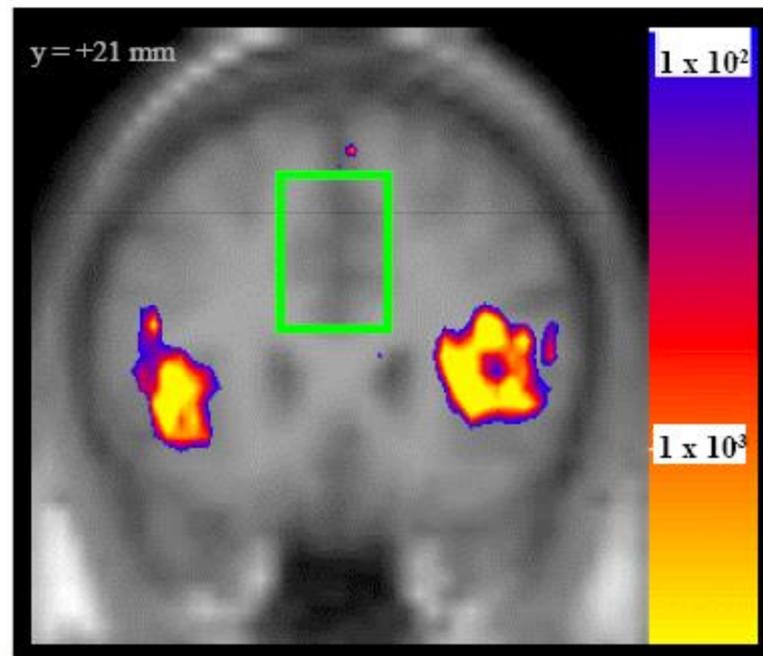
Hallazgos estructurales

Normal Controls



MGH-NMR Center & Harvard-MIT CITP

ADHD



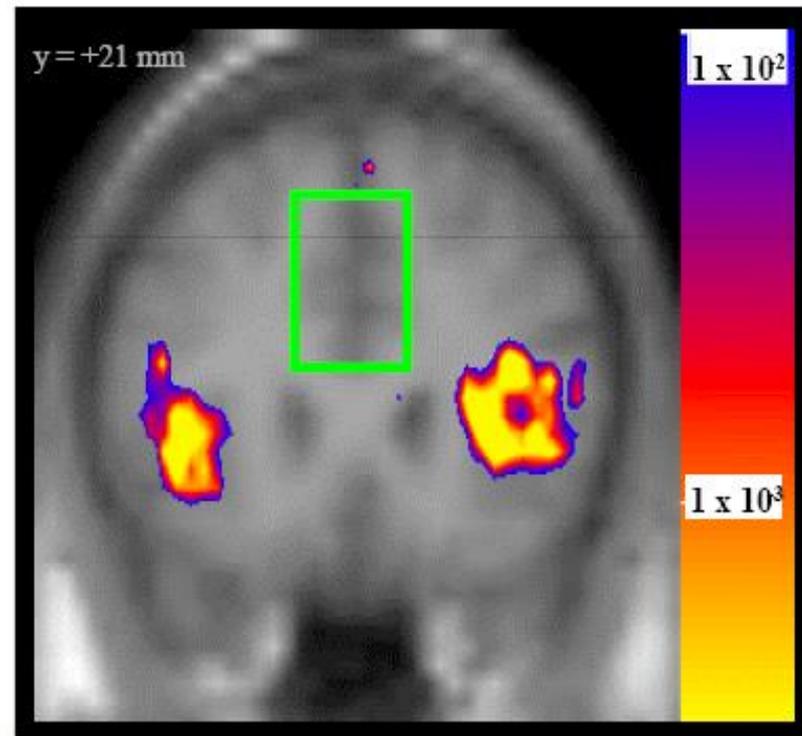
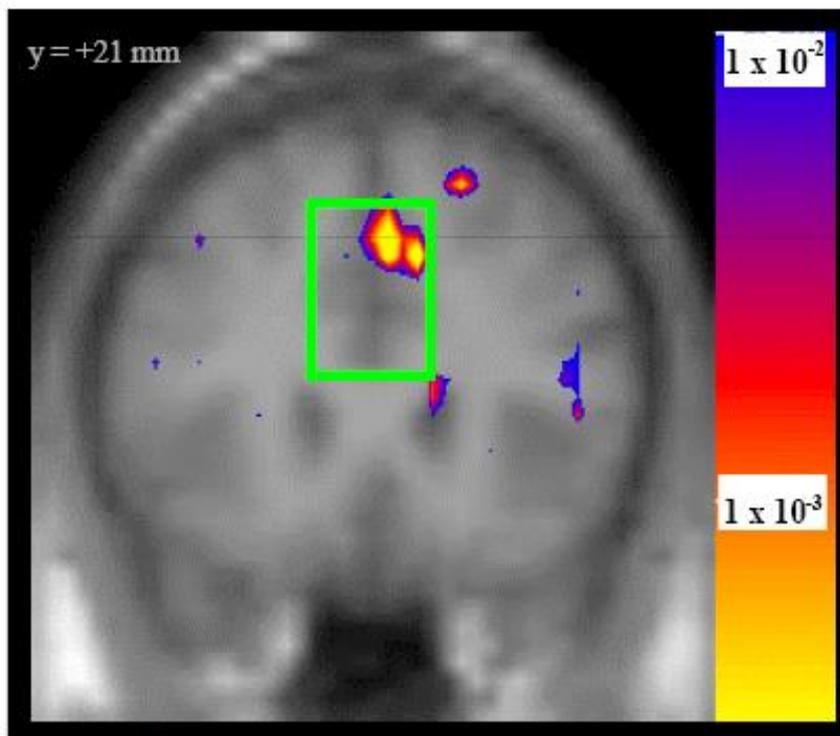
Bush et al. Biological Psychiatry. 1999.

Faraone SV et al. Psychol Med. 2006;36:159-165

Hallazgos en el desarrollo cerebral

Normal Controls

ADHD



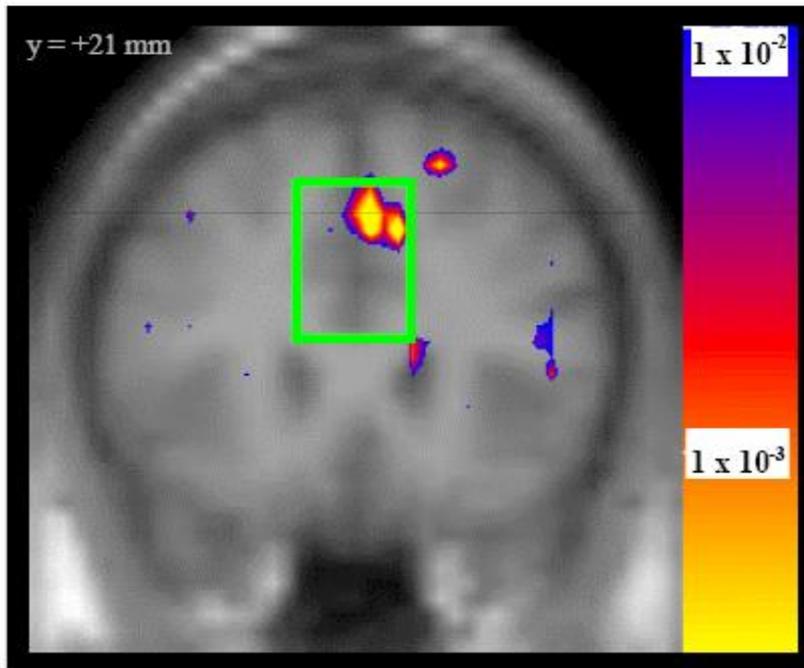
MGH-NMR Center & Harvard-MIT CITP

Bush et al. Biological Psychiatry. 1999.

Schaw et al., Proc Nati Acad Sci USA. 2007:104:19649-19654

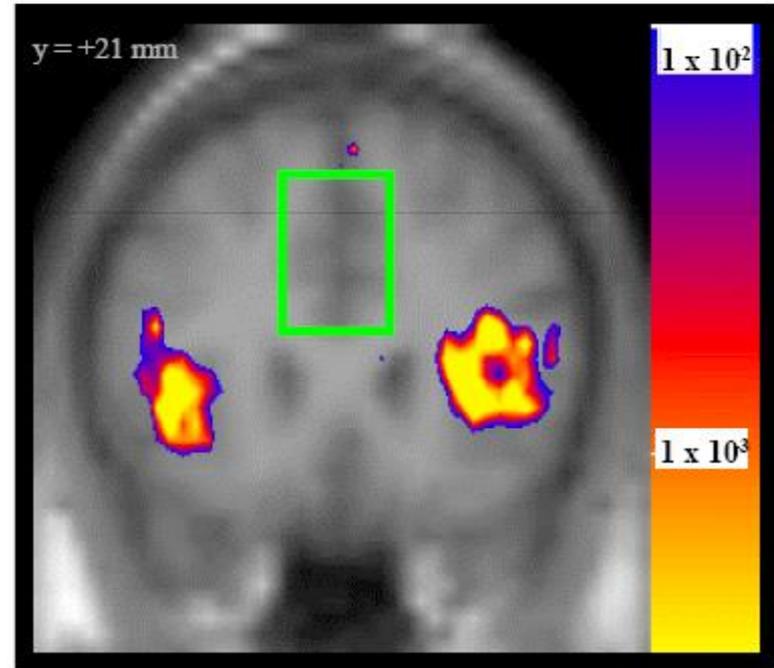
Hallazgos neuroquímicos

INITIAL CONTROLS



MGH-NMR Center & Harvard-MIT CITP

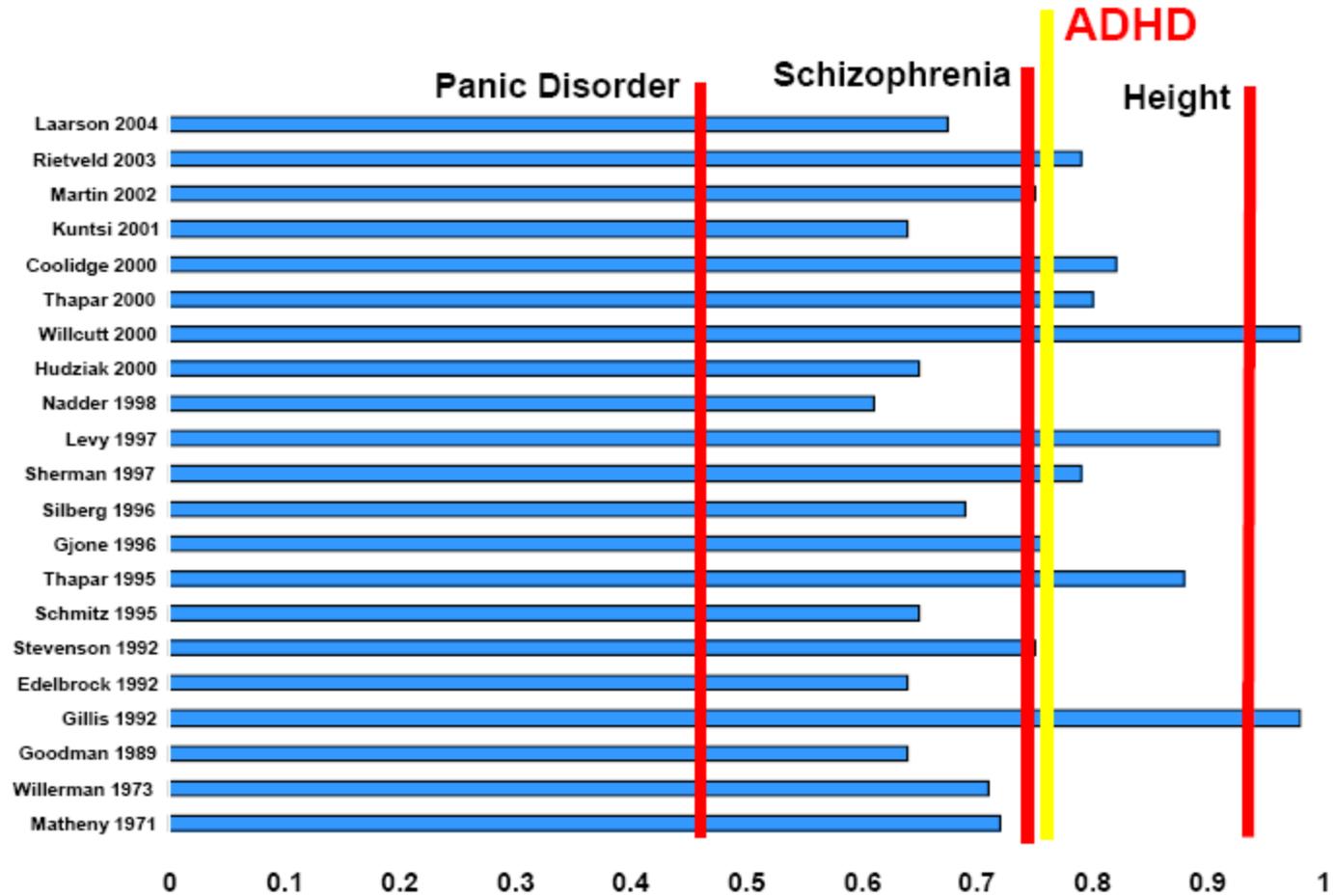
ADHD



Bush et al. Biological Psychiatry. 1999.

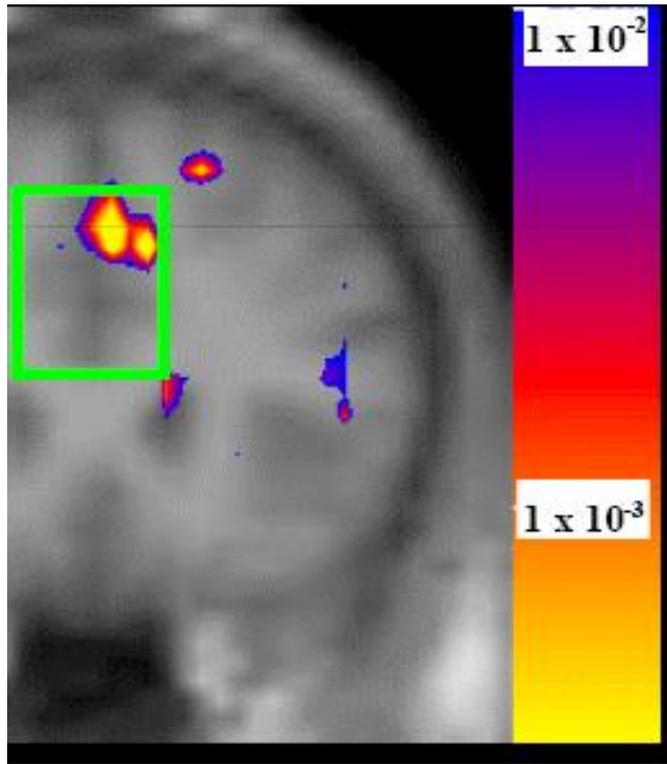
Bush et al. Arch Gen Psychiatry. 2008;65:102-114

Hallazgos genéticos

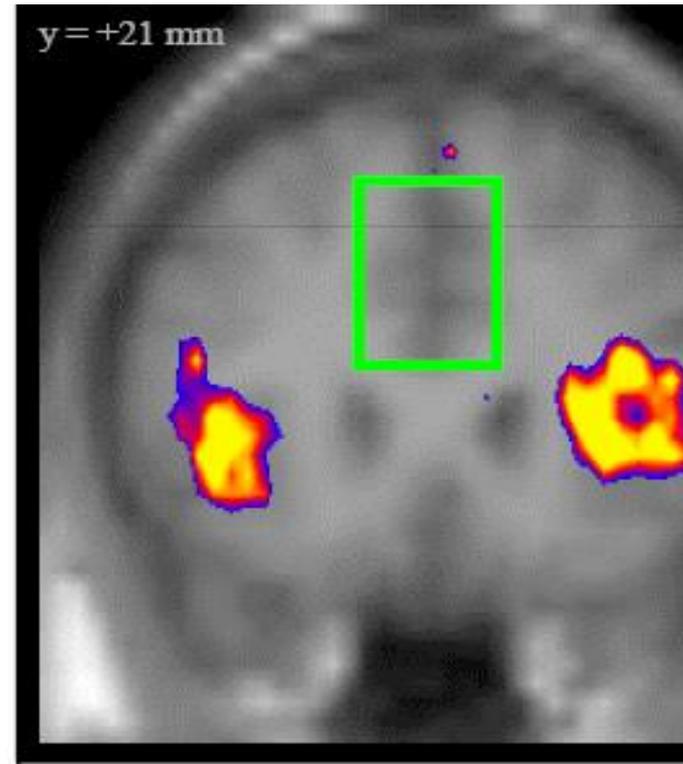


Hallazgos producidos por factores externos

Volumen cerebral en niños y adolescentes diagnosticados de TDAH y medicados vs no medicados



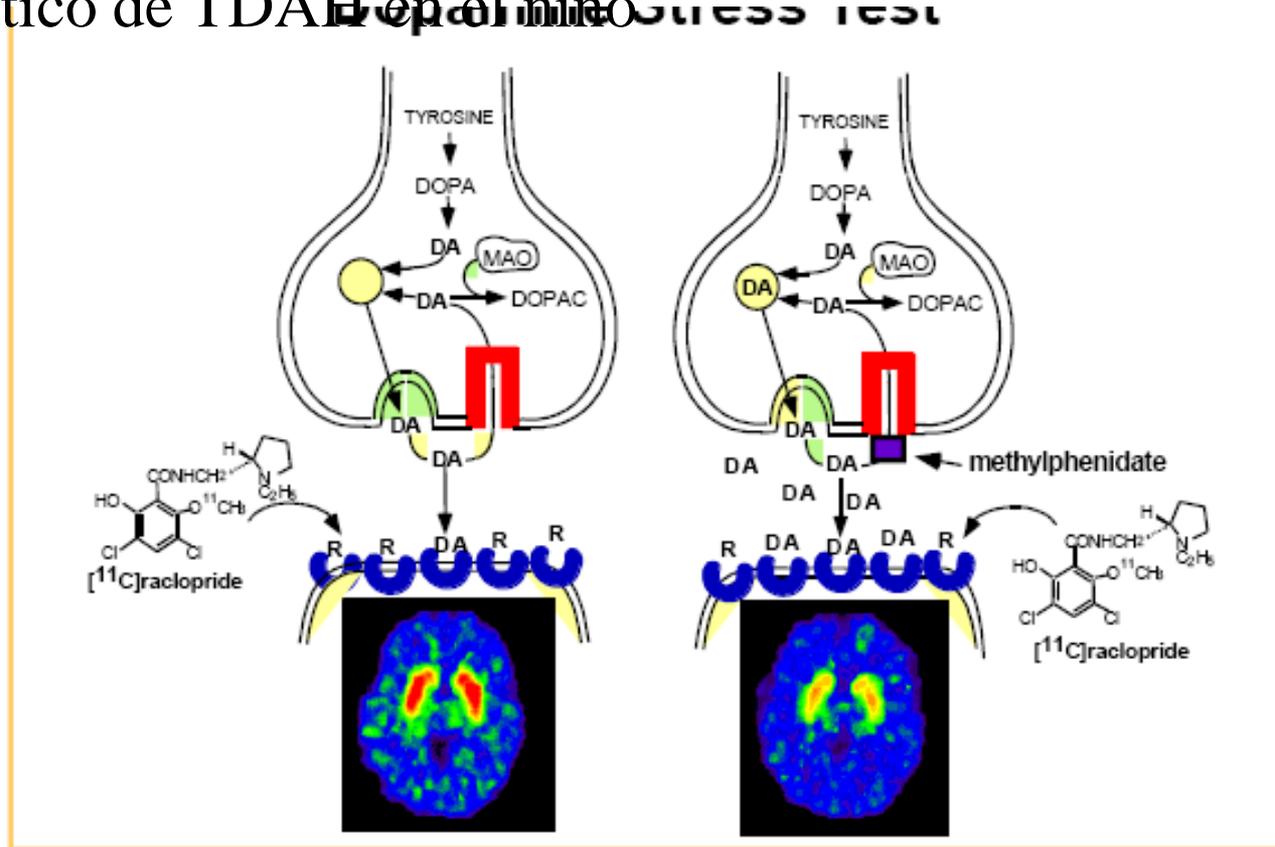
R Center & Harvard-MIT CITP



Bush et al. Biological Psychiatry.

Hallazgos producidos por factores externos

Historia de consumo de tabaco durante el embarazo vs diagnóstico de TDAH en el niño

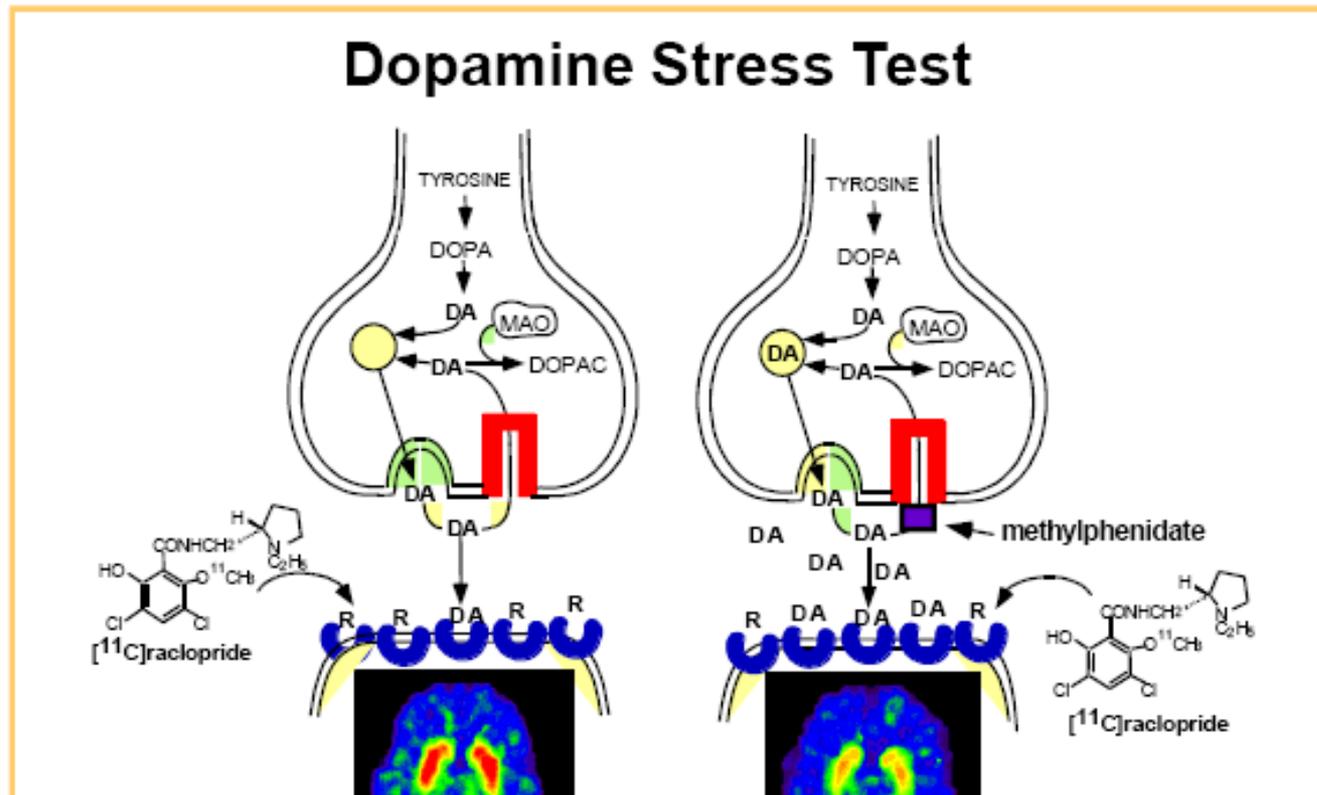


Volkow, Swanson. Am J Psychiatry. 2003 Nov;160(11):1909-18.

Milberger et al., Am J Psychiatry 1996;153:1138

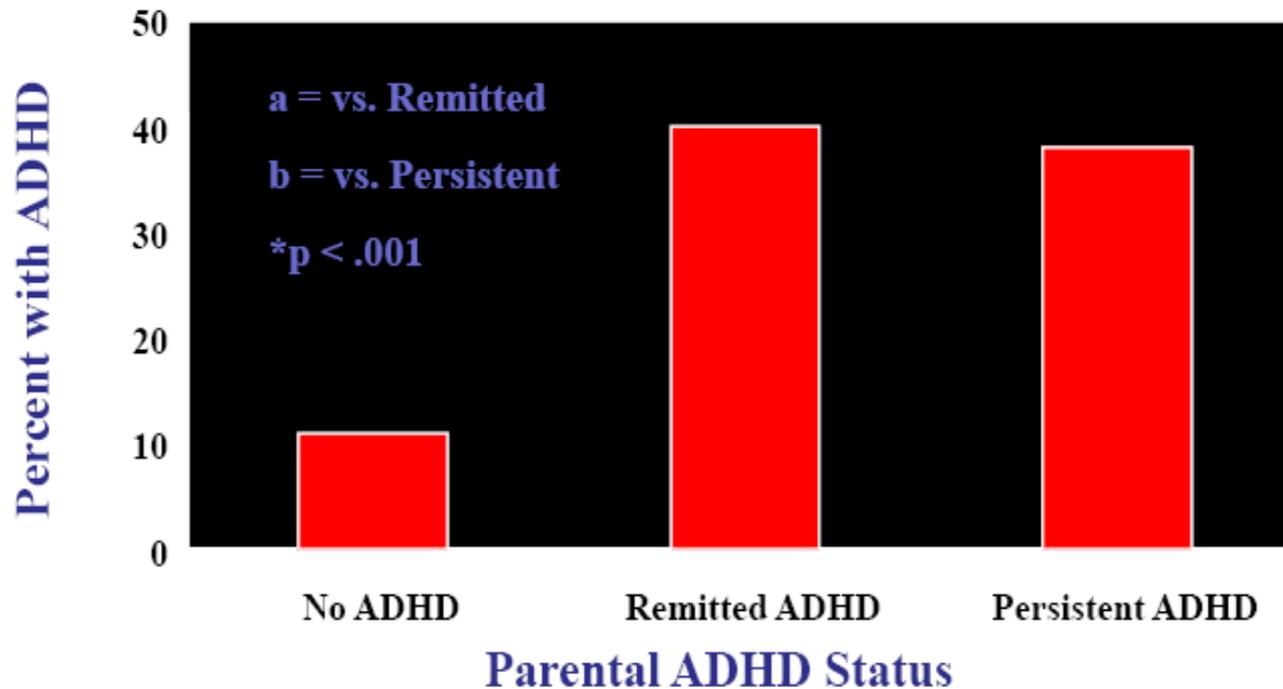
Hallazgos producidos por factores externos

Historia de consumo de tabaco durante el embarazo vs enfermedad psiquiátrica en el niño



Hallazgos producidos por factores externos

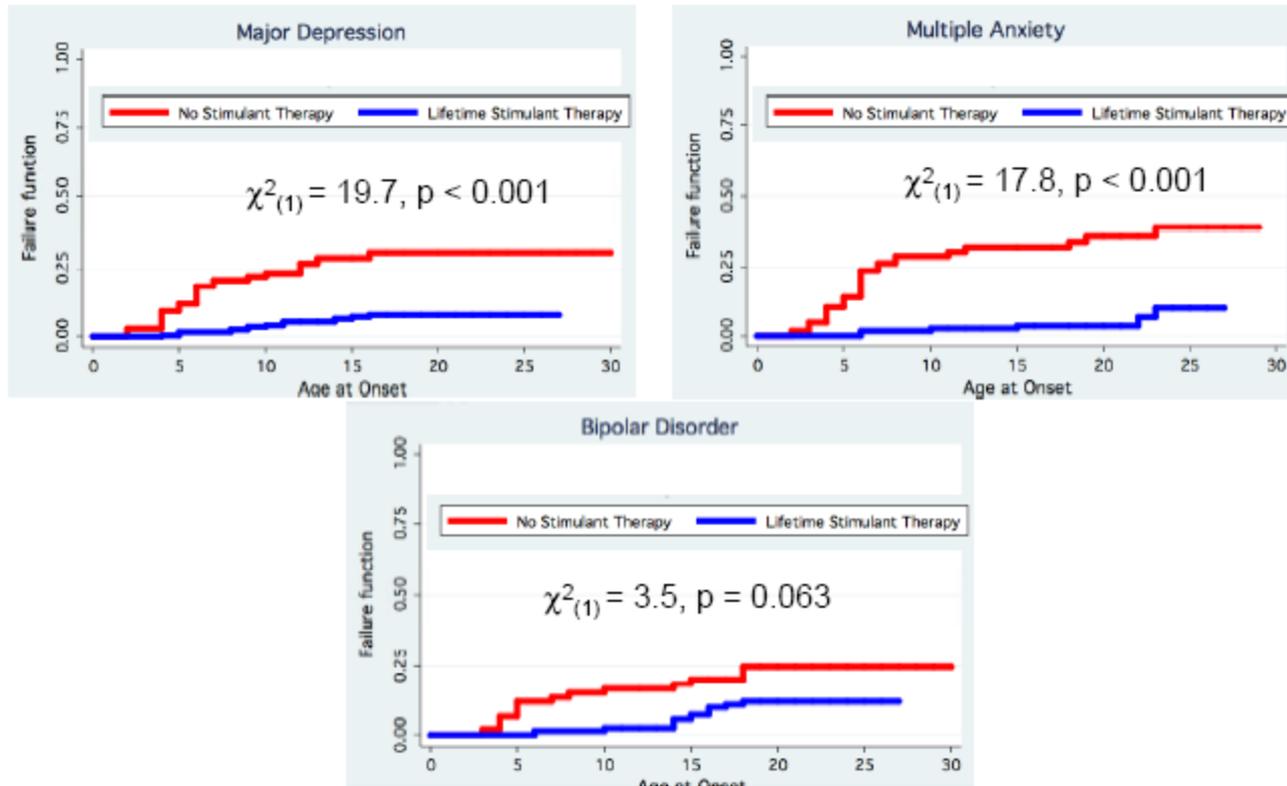
Control de TDAH del padre vs presencia de TDAH en el niño



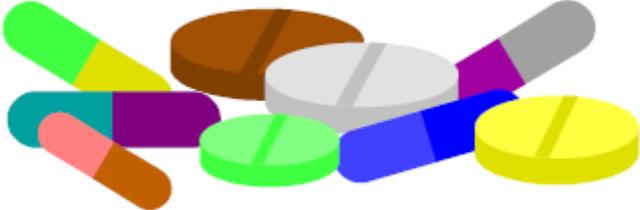
Exploración y pruebas diagnósticas

- **Imprescindible**
 - Entrevista y evaluación clínica
- **Recomendable**
 - Diferencia entre C.I. Verbal y manipulativo
 - Evaluación pedagógica y pruebas de aprendizaje
 - Test de atención
 - Analítica general
- **Necesario si sospecha de otro problema**
 - Electroencefalograma (EEG)
 - Resonancia Magnética Cerebral
 - Análisis genético

Tópicos acerca del tratamiento del TDAH



Biederman et al., 2012



Comorbilidad (consideraciones especiales)

TDAH & Tics

MPH & MPH + clonidina mejor que placebo

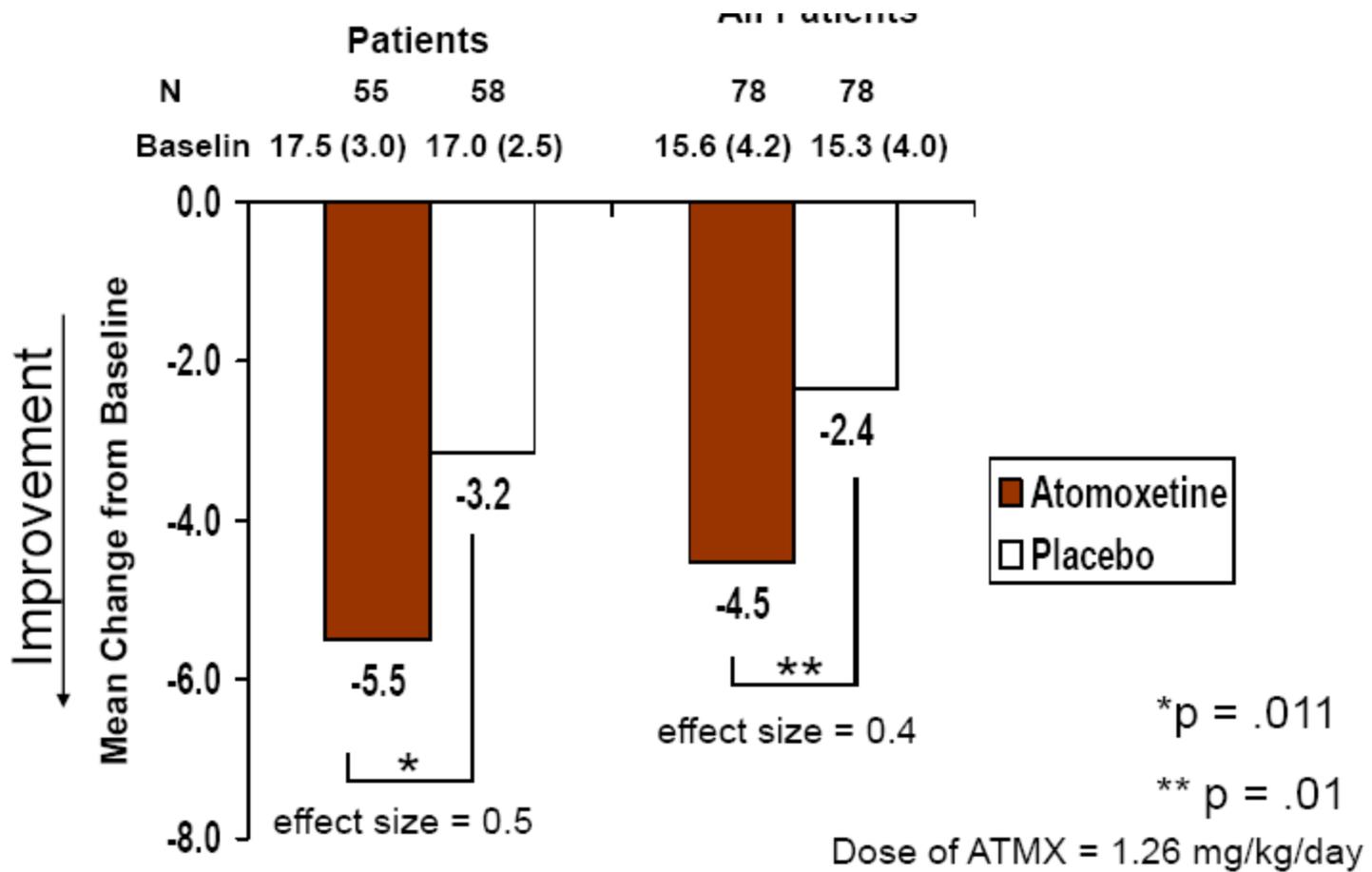
✓ **Valorar ansiedad como precipitante**

(Tourette's Syndrome Study Group, Neurology, 2002; 8(4):527-536)

✓ **Valorar Atomoxetina, 1ª opción**

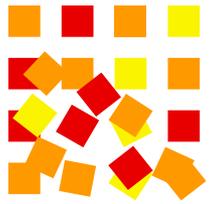
(Spencer et al., J Atten Dis 2008; 11(4):470-481)

Resistencia al tratamiento/Remisión parcial



Investigaciones iniciales

Investigaciones iniciales



SÍNTOMAS ESENCIALES

...pero también pueden tener muchas ventajas



...abiertos a nuevas ideas



...se entusiasman



...llenos de energía



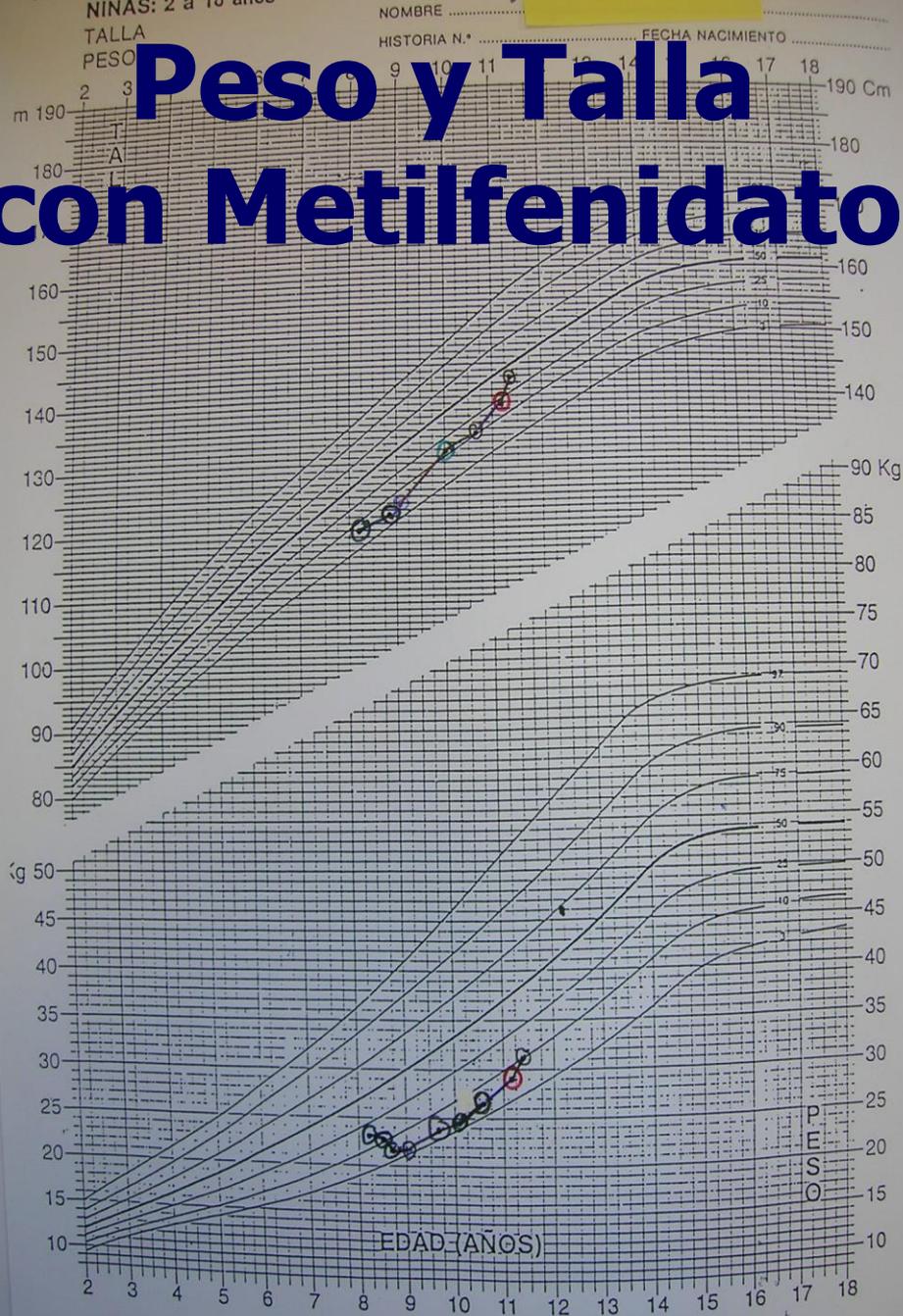
...bromistas

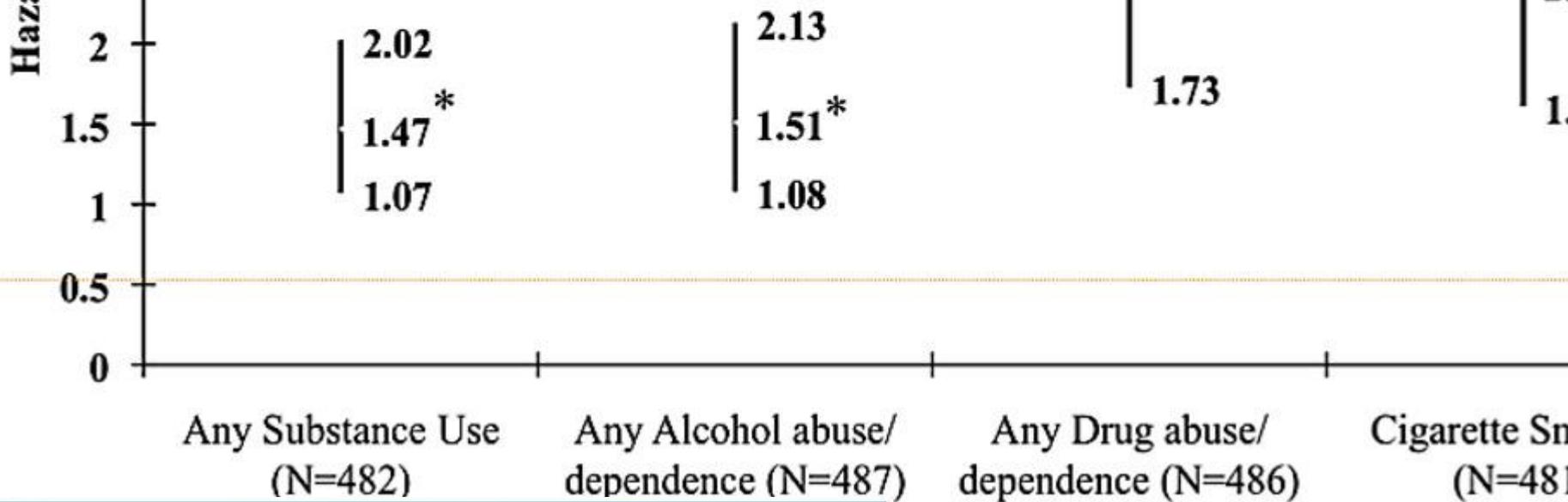
...pueden ser muy inteligentes

Döpfner y cols. 2000, 2002

ipción de un caso **Síntomas esenciales** Nacimiento de un concepto Clasificación Epidemiología Etiología Comorbilidad Costes Implicaciones

Peso y Talla con Metilfenidato





Developmental Relationship Between ADHD & Substance Abuse

Adolescent

- ADHD treatment may protect against cigarette and SUD
- Exposure to parental SUD increases SUD in ADHD



Adult

- ADHD linked to more cigarette smoking and SUD
- ADHD linked to more severe and chronic SUD
- ADHD linked to less remission from



Child

Table 2

Cumulative morbidity risks and hazard ratios for association between stimulant treatment and subsequent psychiatric comorbidity in ADHD males

Outcome	Age of Onset	Events prior to ADHD onset ¹	Subjects used in model	MR (95%CI)		Hazard Ratio	Test statistic, p value
	mean±sd, range			No Stimulant Therapy	Stimulant Therapy		
Major Depression	8.0±3.9, 2-16	20	107	0.69 (0.55, 0.82)	0.24 (0.15, 0.37)	0.22	$\chi^2(1) = 19.7, p < 0.001$
Conduct Disorder	10.8±4.0, 3-18	13	112	0.67 (0.53, 0.81)	0.22 (0.14, 0.34)	0.21	$\chi^2(1) = 21.4, p < 0.001$
MA Disorder	8.5±6.0, 2-23	18	108	0.60 (0.47, 0.75)	0.07 (0.03, 0.19)	0.15	$\chi^2(1) = 17.8, p < 0.001$
ODD	7.4±3.5, 2-18	46	79	0.88 (0.78, 0.95)	0.40 (0.25, 0.58)	0.21	$\chi^2(1) = 19.9, p < 0.001$
Bipolar Disorder	11.4±5.2, 3-18	9	116	0.42 (0.27, 0.61)	0.20 (0.12, 0.32)	0.47	$\chi^2(1) = 3.5, p = 0.063$
Repeated Grade	8.4±4.0, 4-18	2	122	0.63 (0.51, 0.75)	0.26 (0.16, 0.40)	0.25	$\chi^2(1) = 18.4, p < 0.001$

¹subjects excluded from given model

MR = Cumulative morbidity risk of disorder by age 21 as estimated by Kaplan-Meier failure function

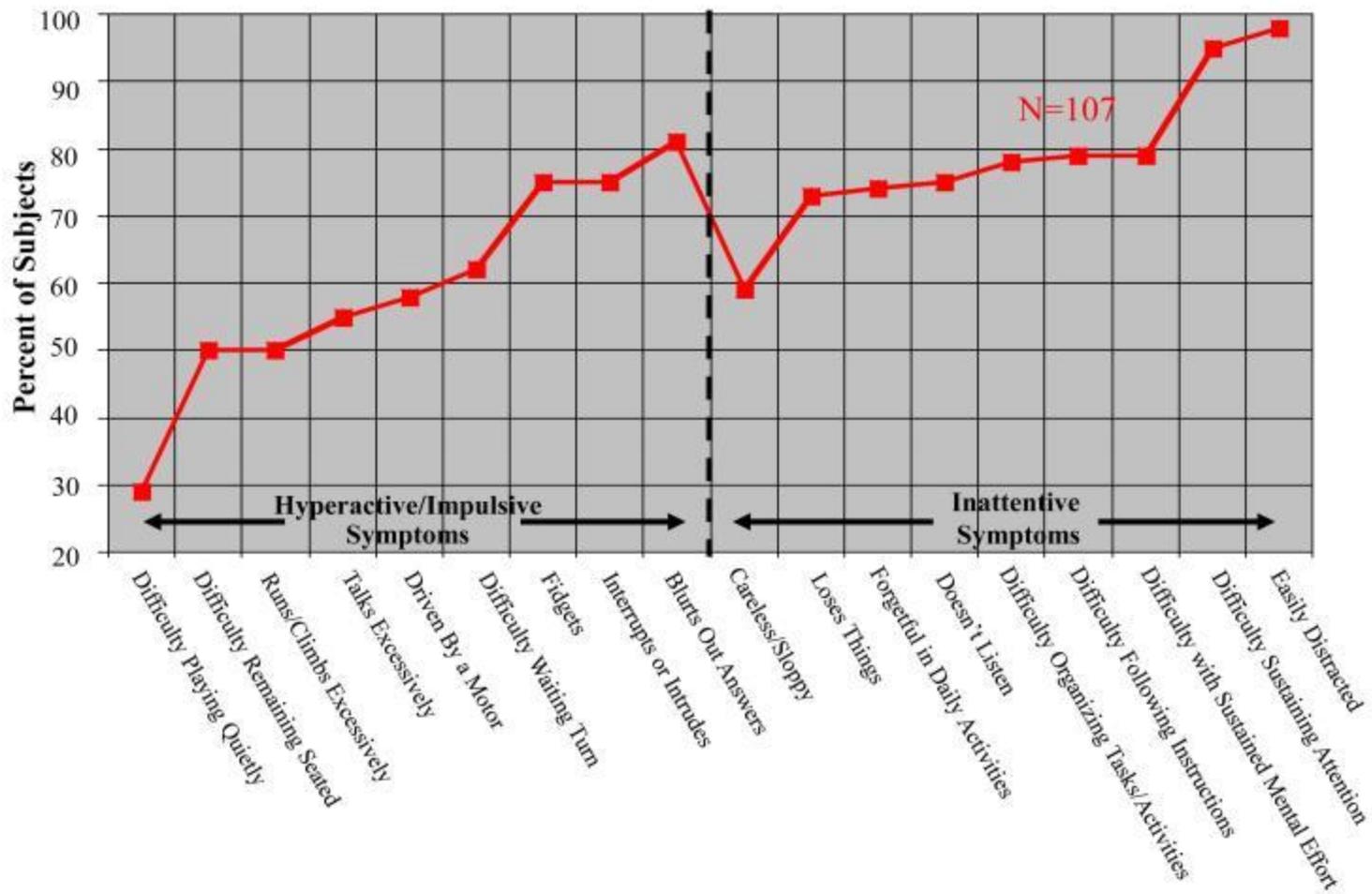
MA = Multiple (≥ 2) Anxiety

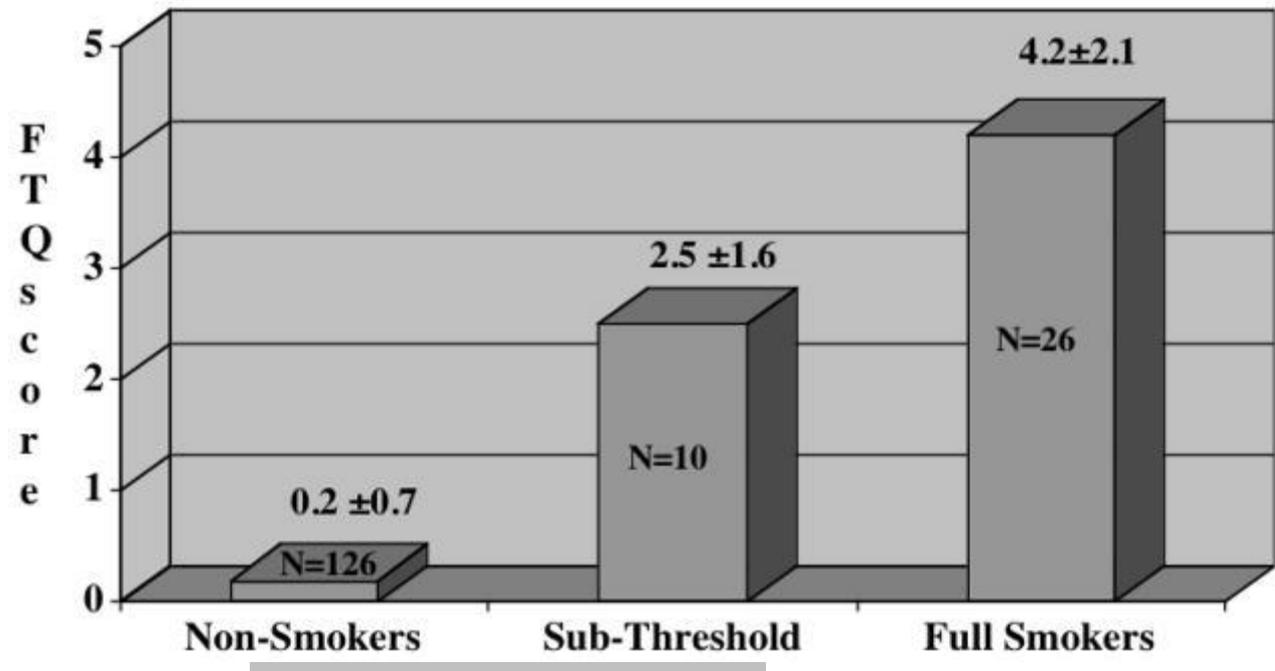
ODD = Oppositional defiant disorder

Table 2

Cumulative morbidity risks and hazard ratios for association between stimulant treatment and subsequent psychiatric comorbidity in ADHD males

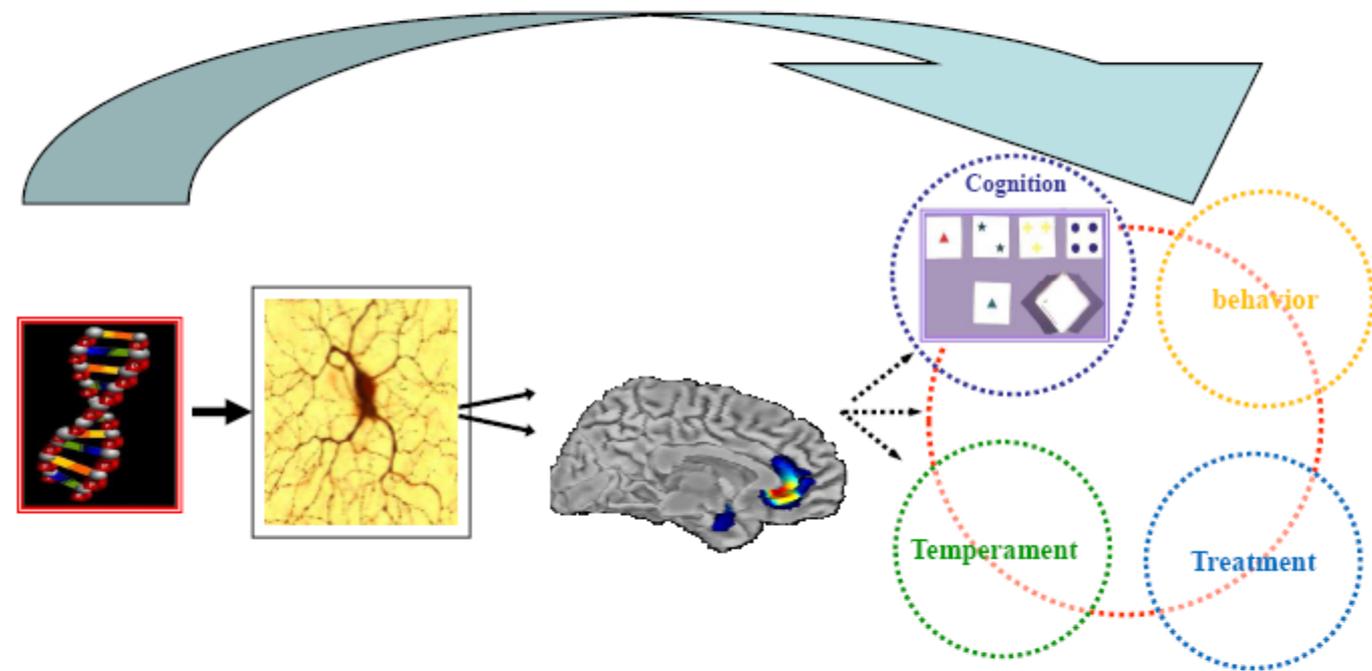
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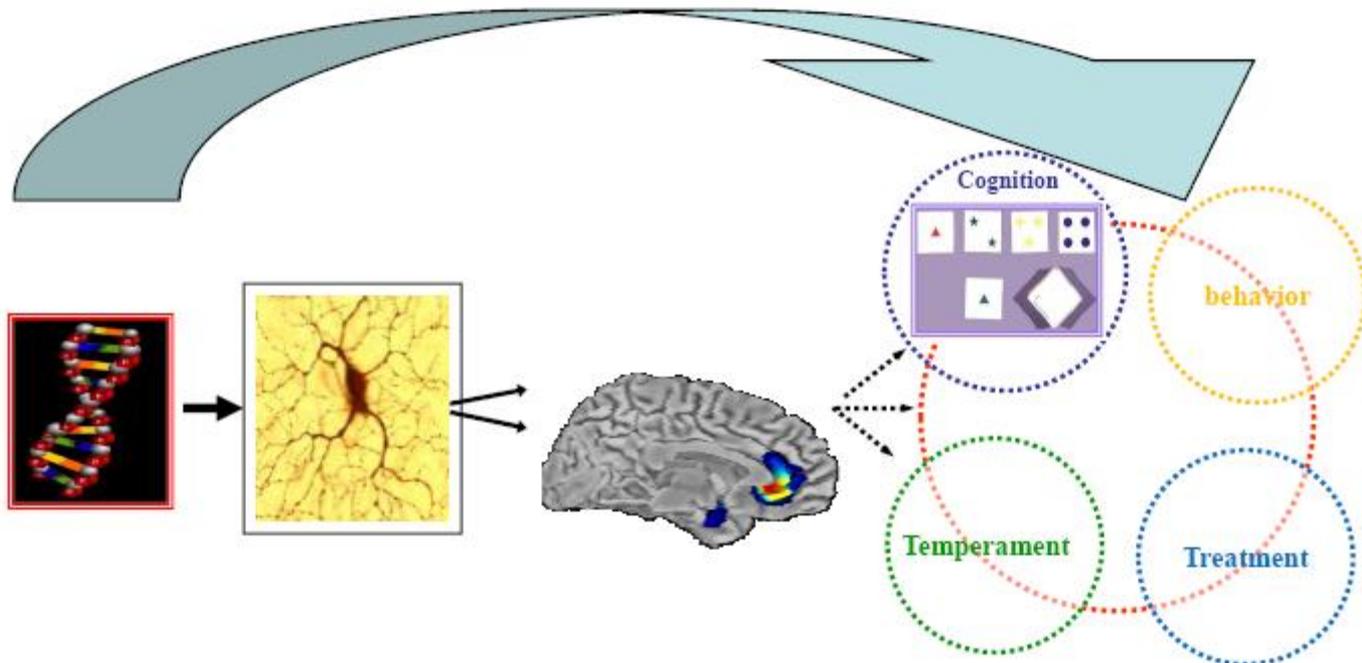


Neural Mechanisms Mediate between Gene and Behavior

Adapted from Andreas Meyer-Lindenberg



<p><u>Genes:</u> <i>Multiple interacting variants</i></p>	<p><u>Cells:</u> <i>Subtle molecular alterations</i></p>	<p><u>Systems:</u> <i>Interactions, neural plasticity, information processing</i></p>	<p><u>Behavior/Cognition:</u> <i>Performance, social integration, treatment response</i></p>
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Genes:
*Multiple
interacting
variants*

Cells:
*Subtle
molecular
alterations*

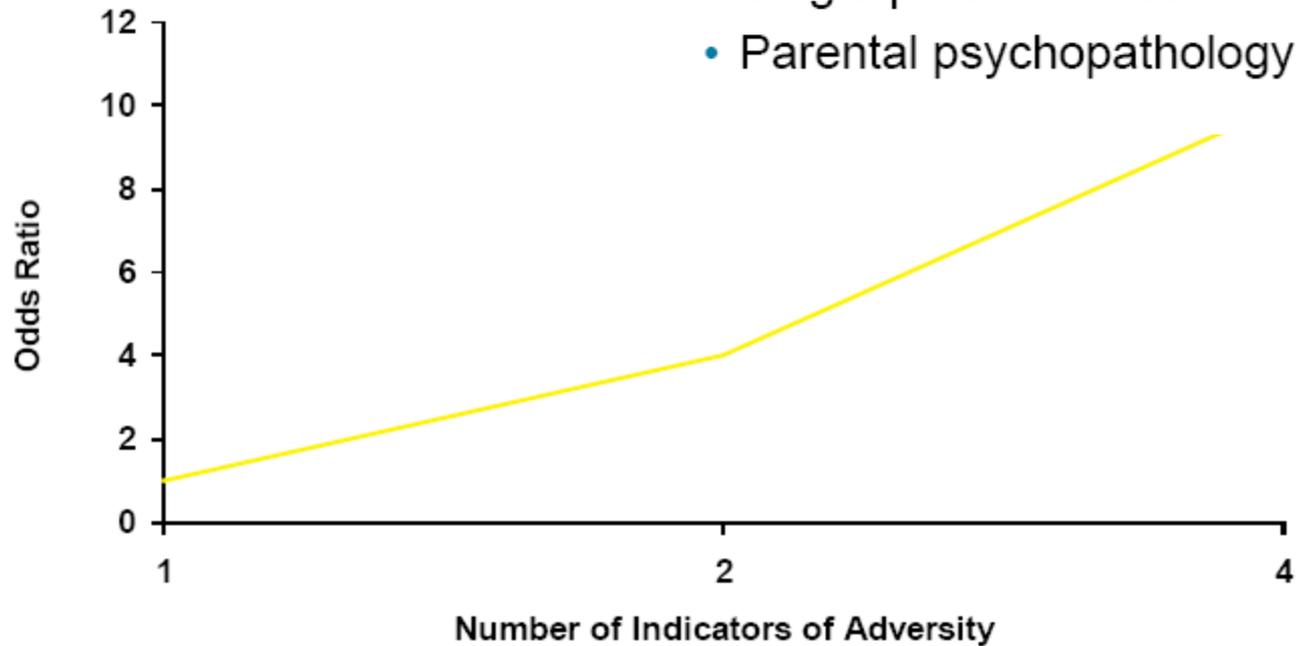
Systems:
*Interactions, neural
plasticity, information
processing*

Behavior/Cognition:
*Performance,
social integration,
treatment response*

Psychosocial Adversity

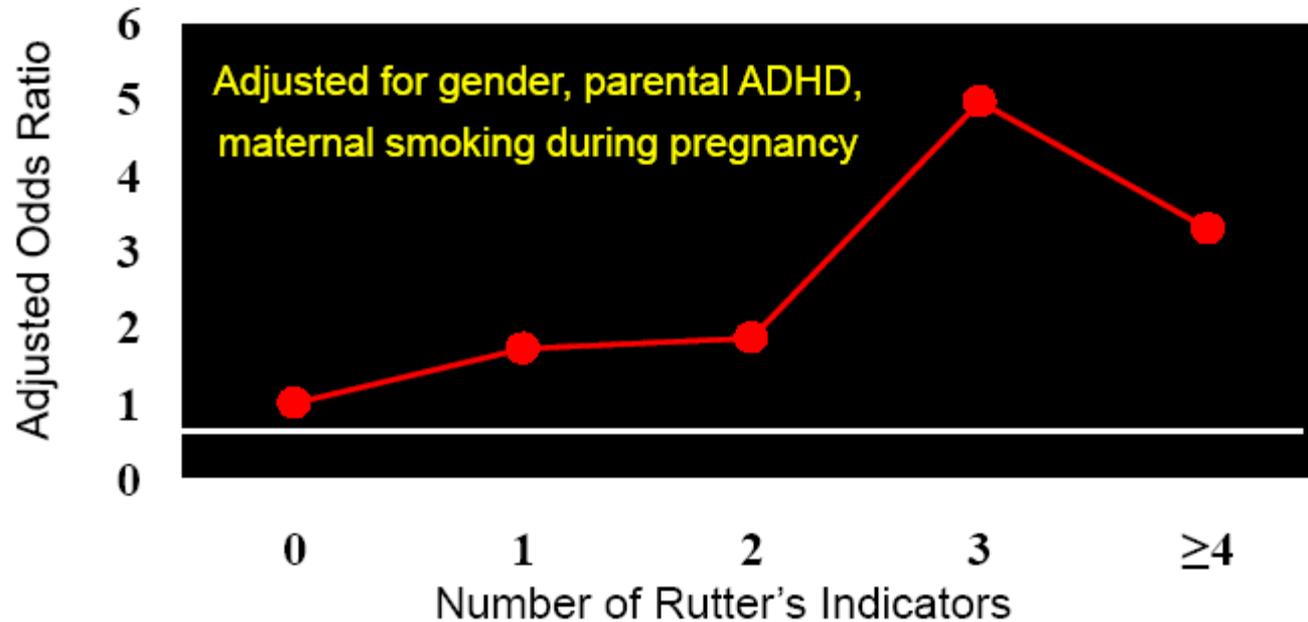
Risk for Child

- Low SES (poverty)
- Family conflict
- Single-parent homes
- Parental psychopathology

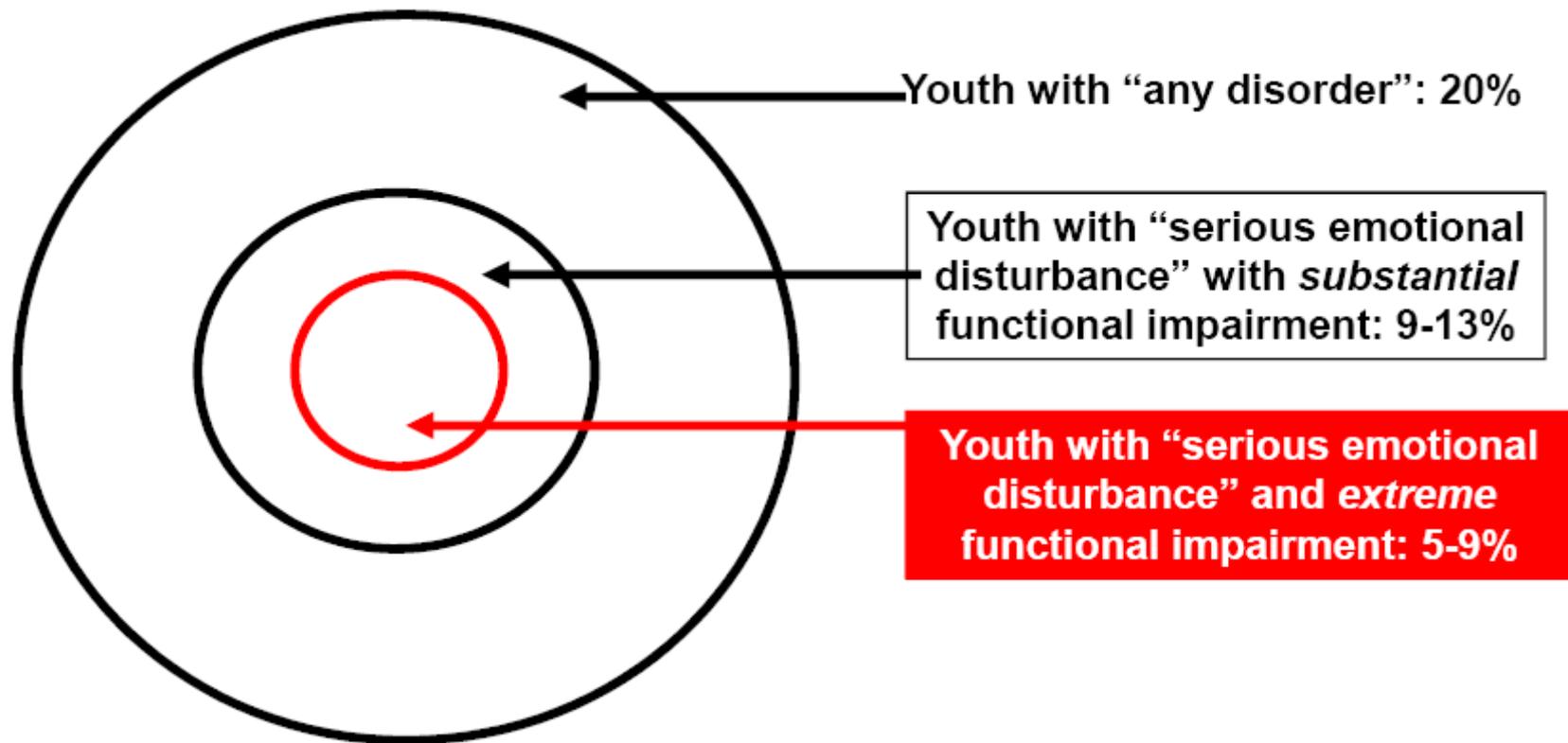


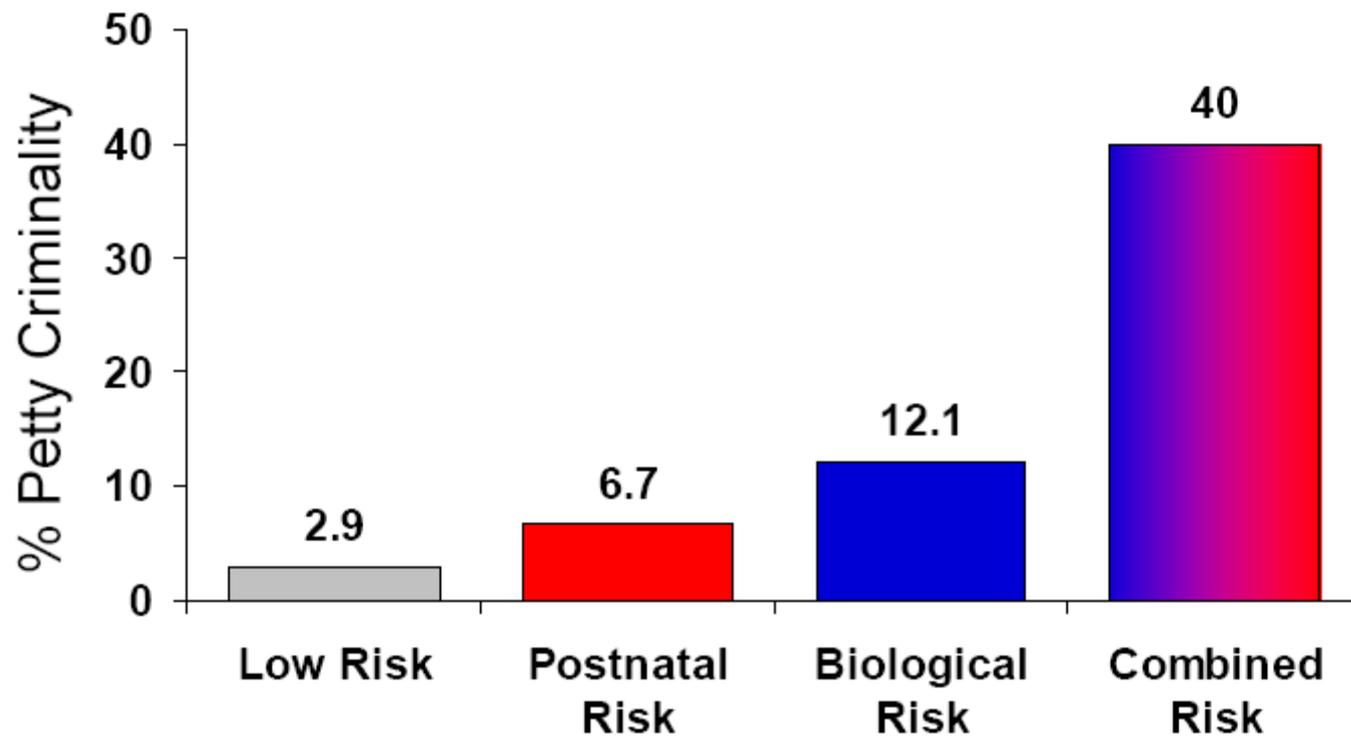
Biederman et al. Am J Psychiatry. 2002;159(9):1556-62.

Test for Linear Trend: $Z = 3.83, p < .001$

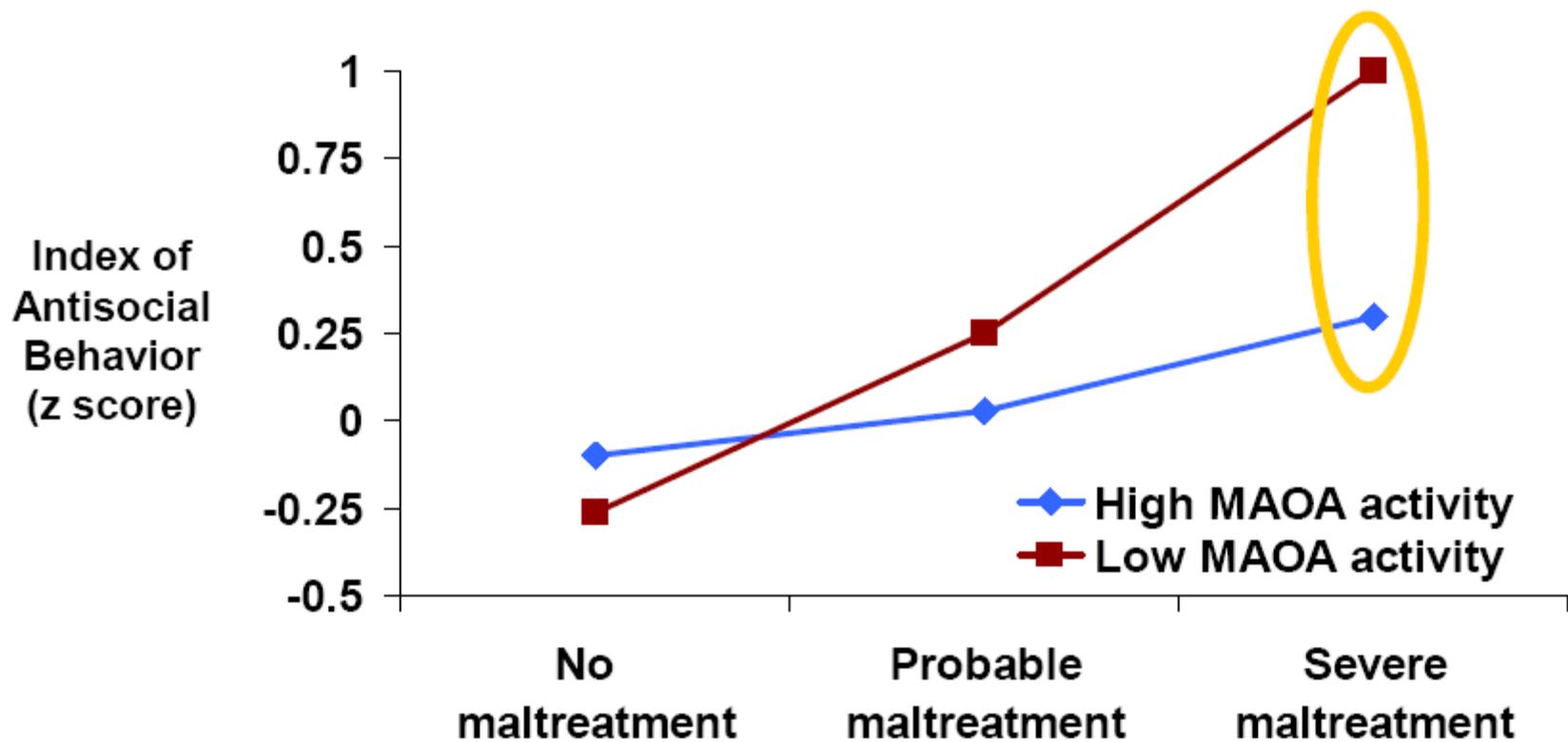


Biederman et al. Am J Psychiatry. 2002;159(9):1556-62.

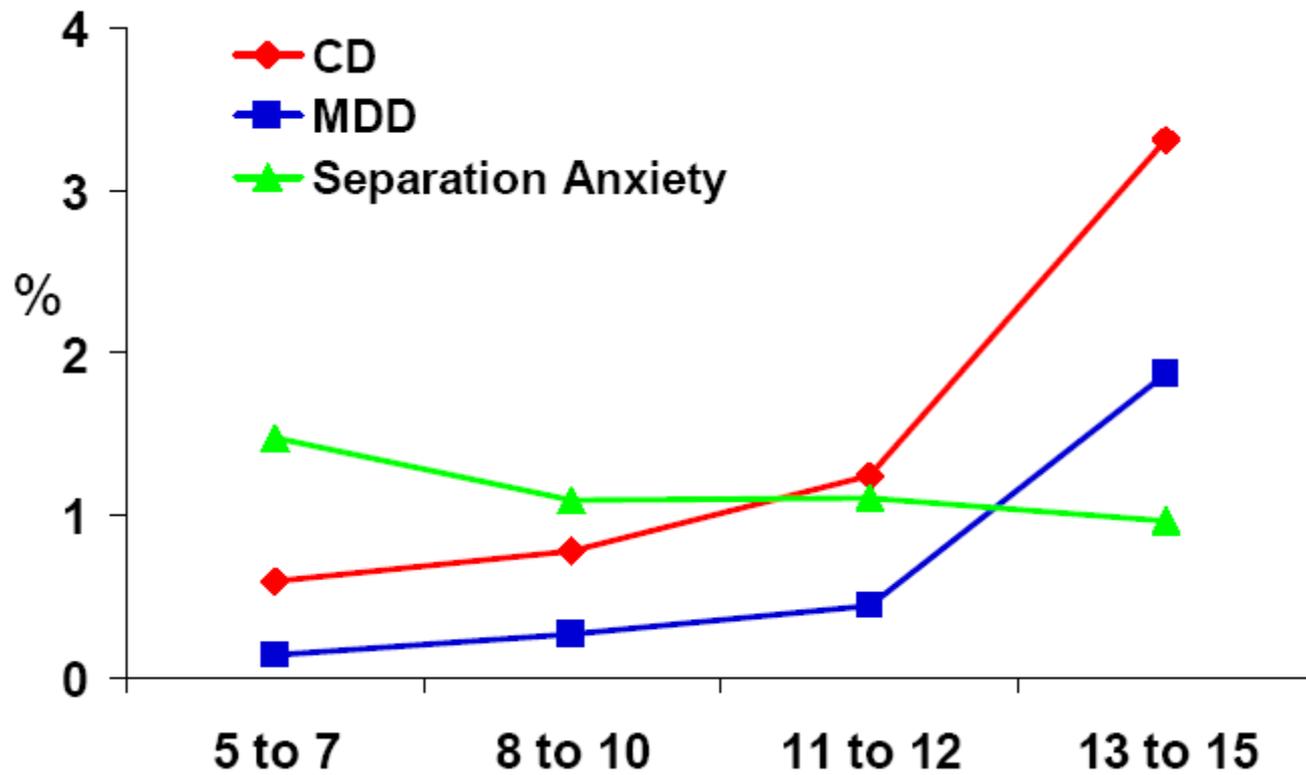




Bohman M. Predisposition to criminality: Swedish adoption studies in retrospect.
Ciba Foundation Symposium. 1996;194:99-109.

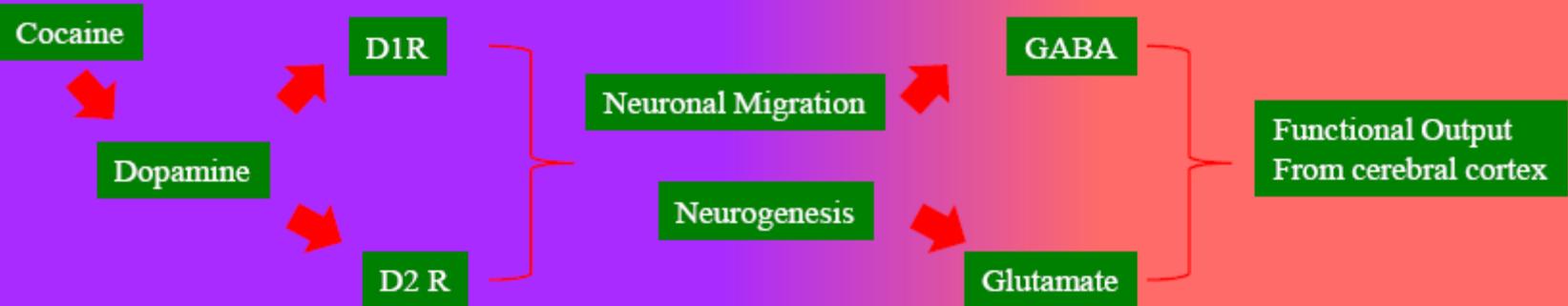


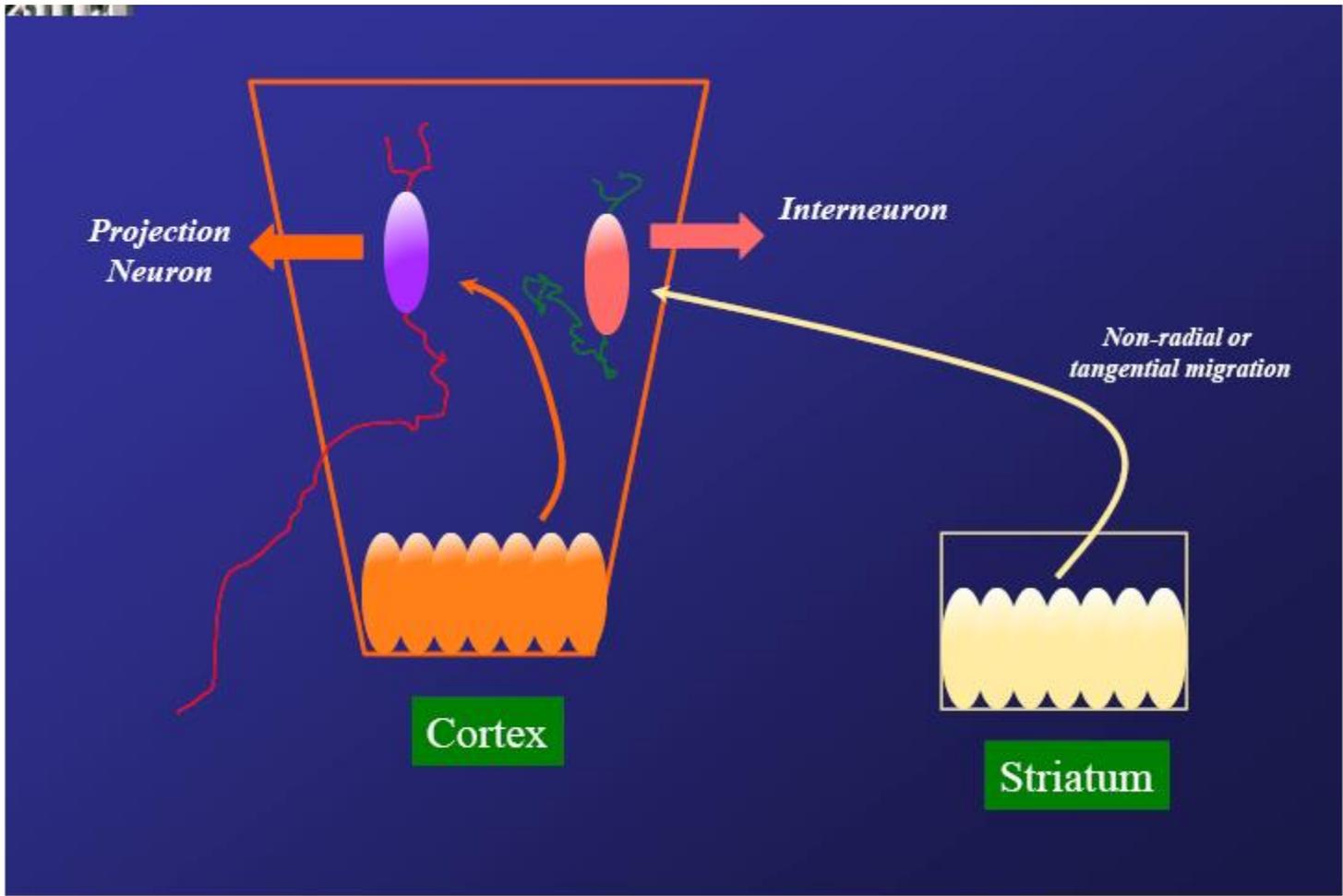
Adapted from: Caspi et al. Role of genotype in the cycle of violence in maltreated children. Science. 2002;297(5582):851-4.



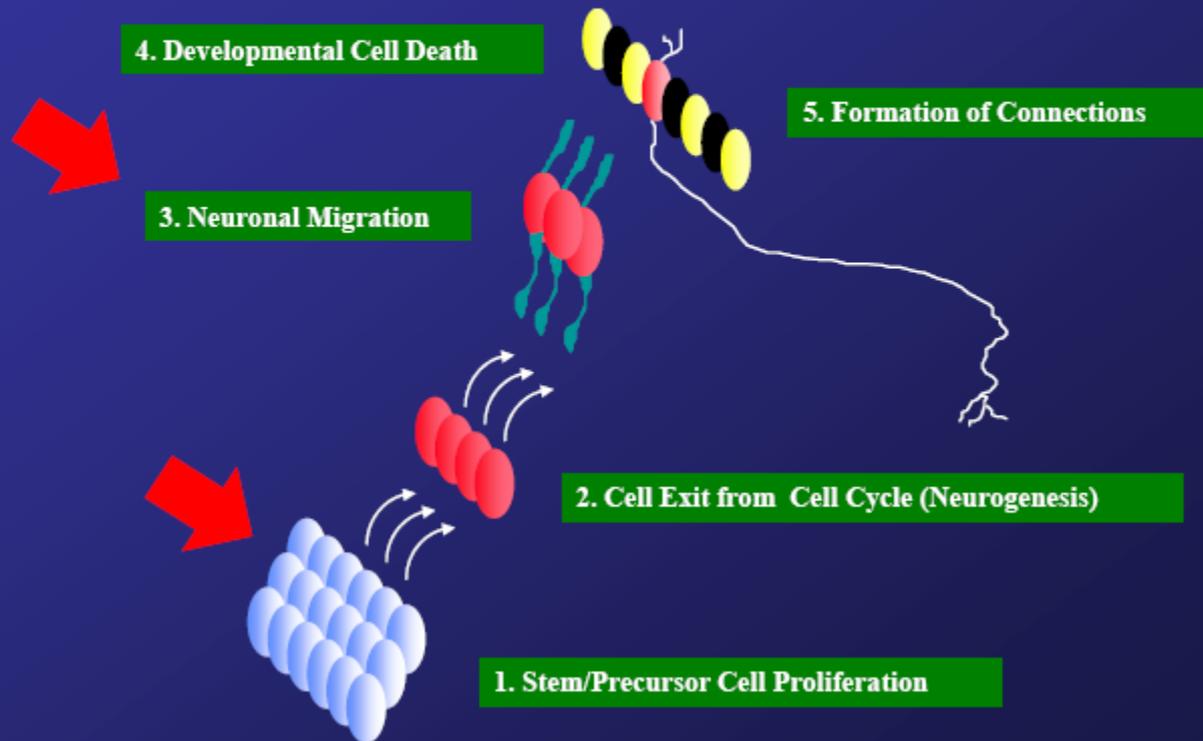
Ford T, Goodman R, Meltzer H. The British Child and Adolescent Mental Health Survey 1999: the prevalence of DSM-IV disorders. *J Am Acad Child Adolesc Psychiatry*. 2003;42(10):1203-11

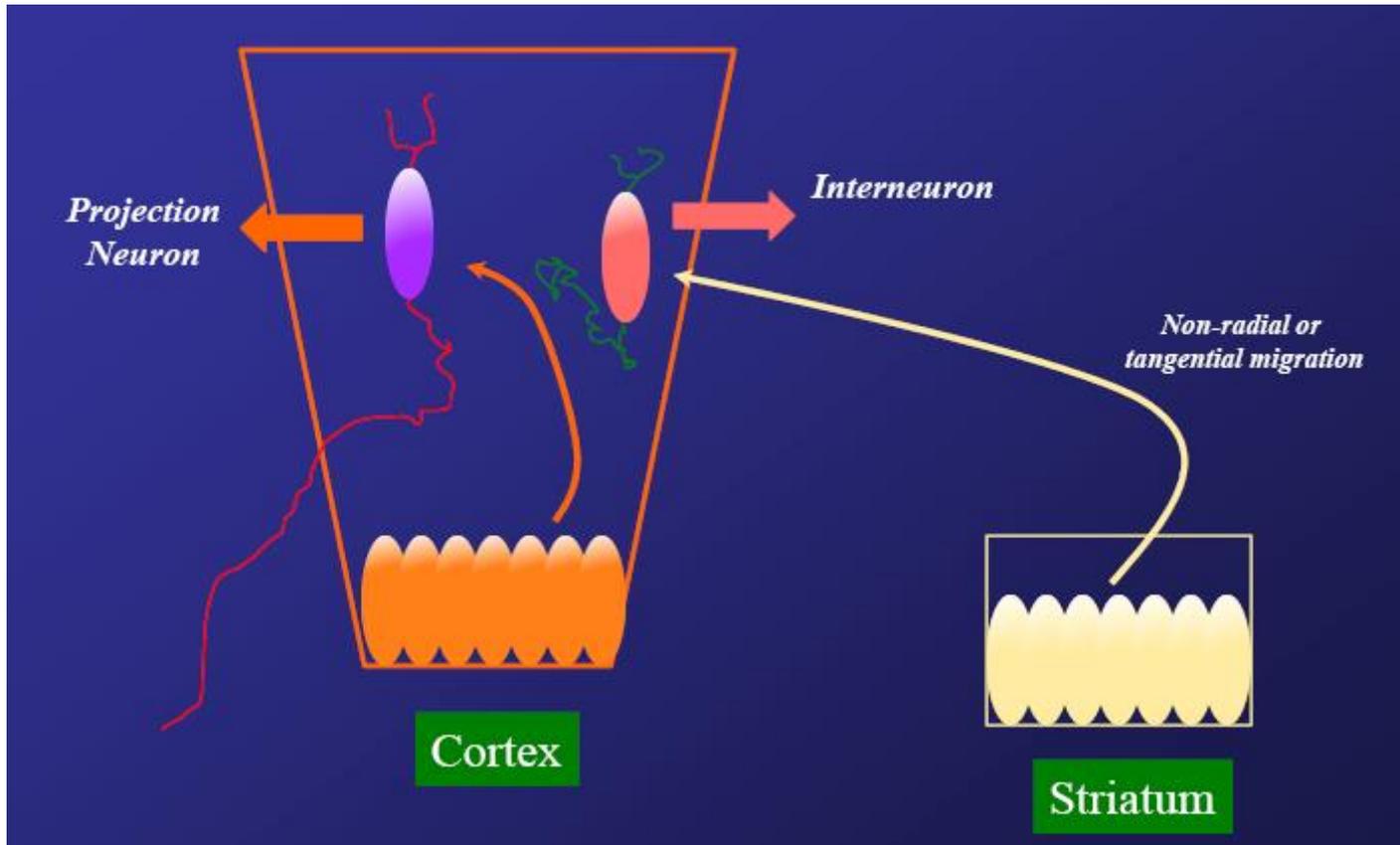
Prenatal cocaine exposure
Long-term effects
Mouse Studies





Developmental processes vulnerable to fetal neurotransmitter imbalance



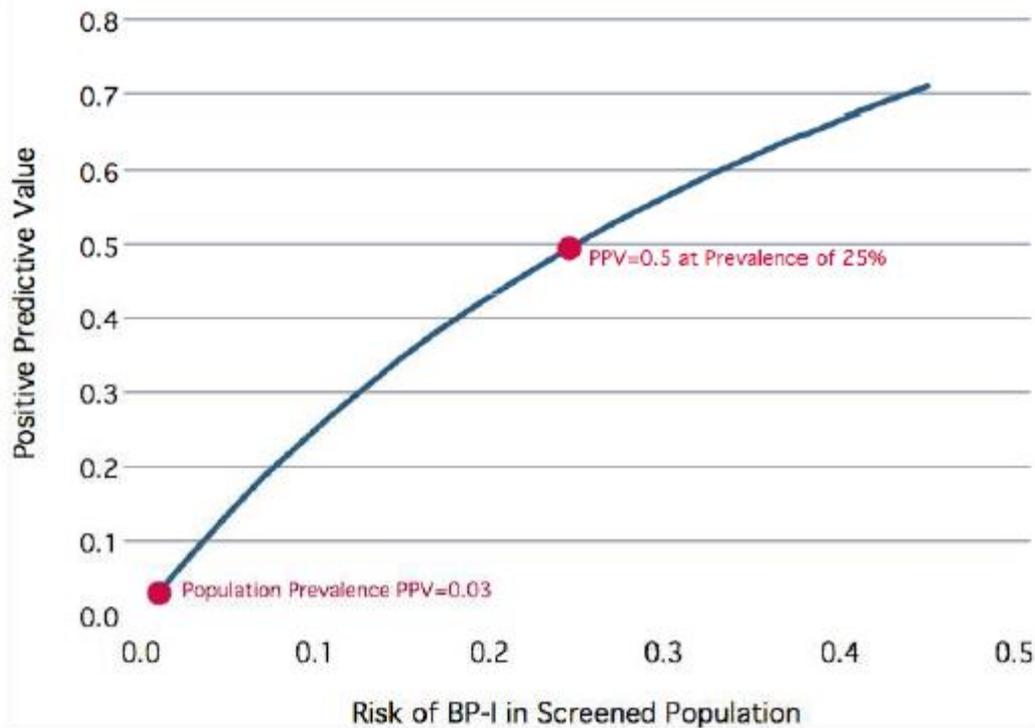




*Cocaine blocks dopamine transporter
function in the fetal brain*



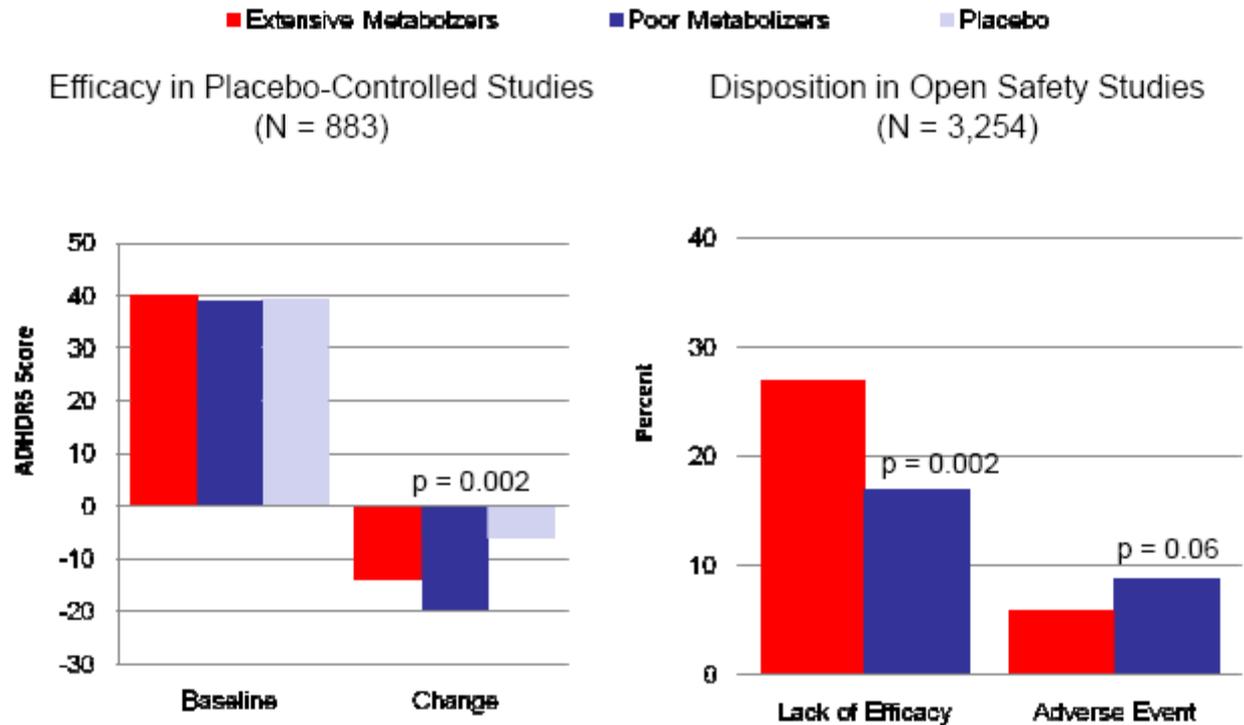
*Increased extracellular
dopamine*



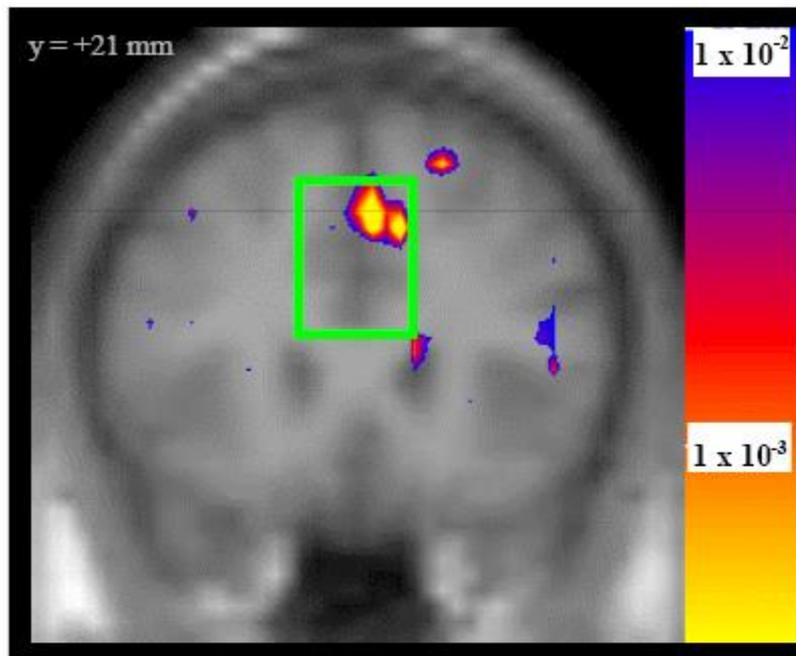
Since then, Kelsoe has hit on a combination of four SNPs in *GRK3* that together seem to be associated with a doubling of disease risk and are more common. They were found in 15% of bipolar patients (and 5% of those without the disorder) in 181 Caucasian families. That work was published last month.

Psynomics's CEO May frames this as an opportunity: "We would like to establish that as a brand, this is the destination for information, for diagnostics, for therapeutics" in psychiatric illness.

CYP2D6 Genotypes and Atomoxetine

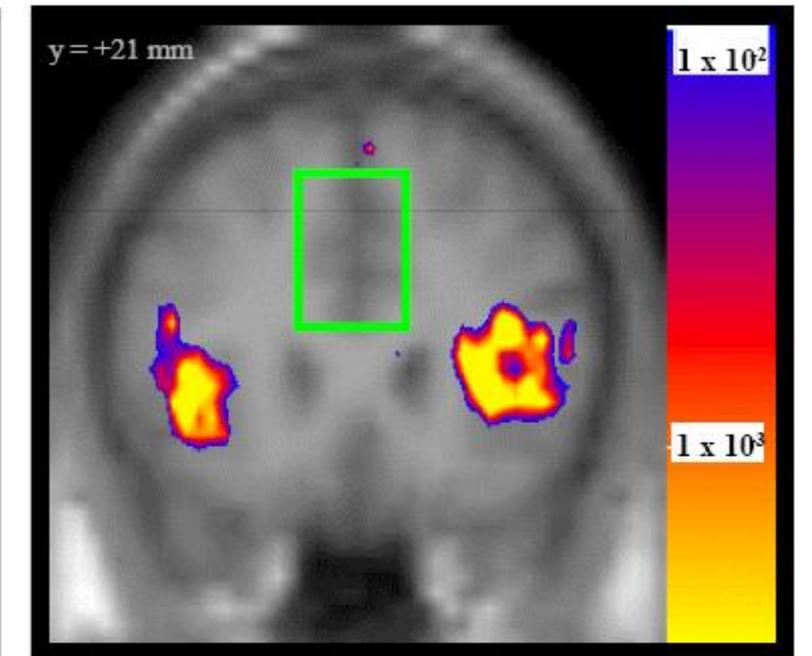


Normal Controls



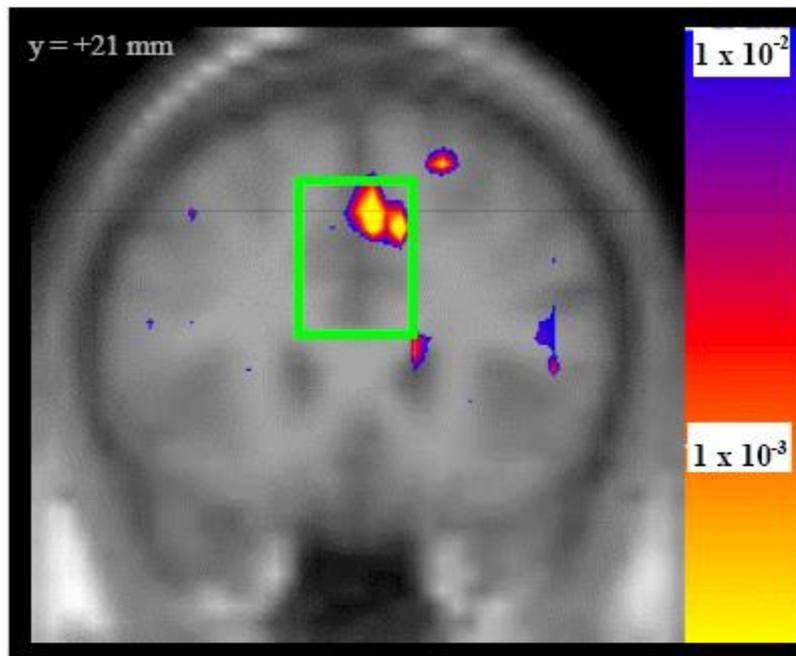
MGH-NMR Center & Harvard-MIT CITP

ADHD



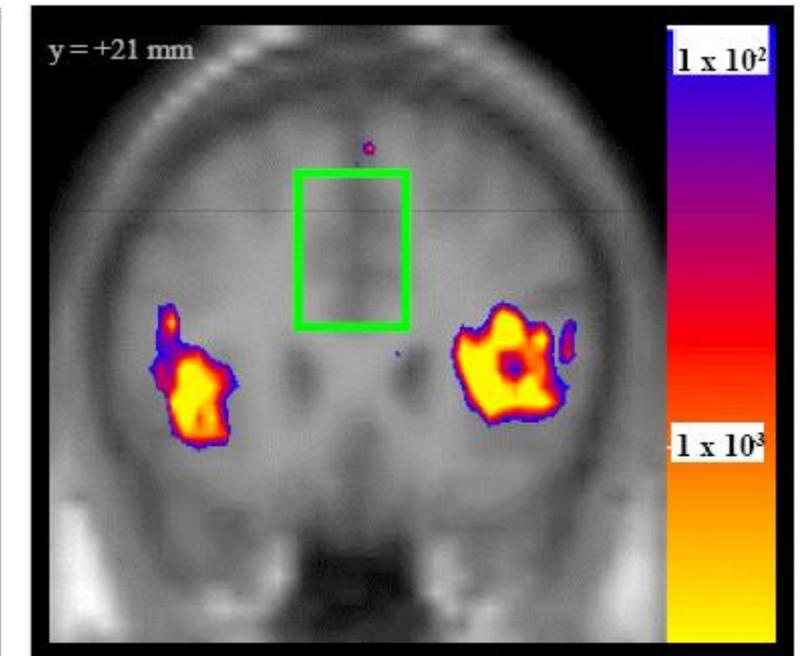
Bush et al. Biological Psychiatry. 1999.

Normal Controls

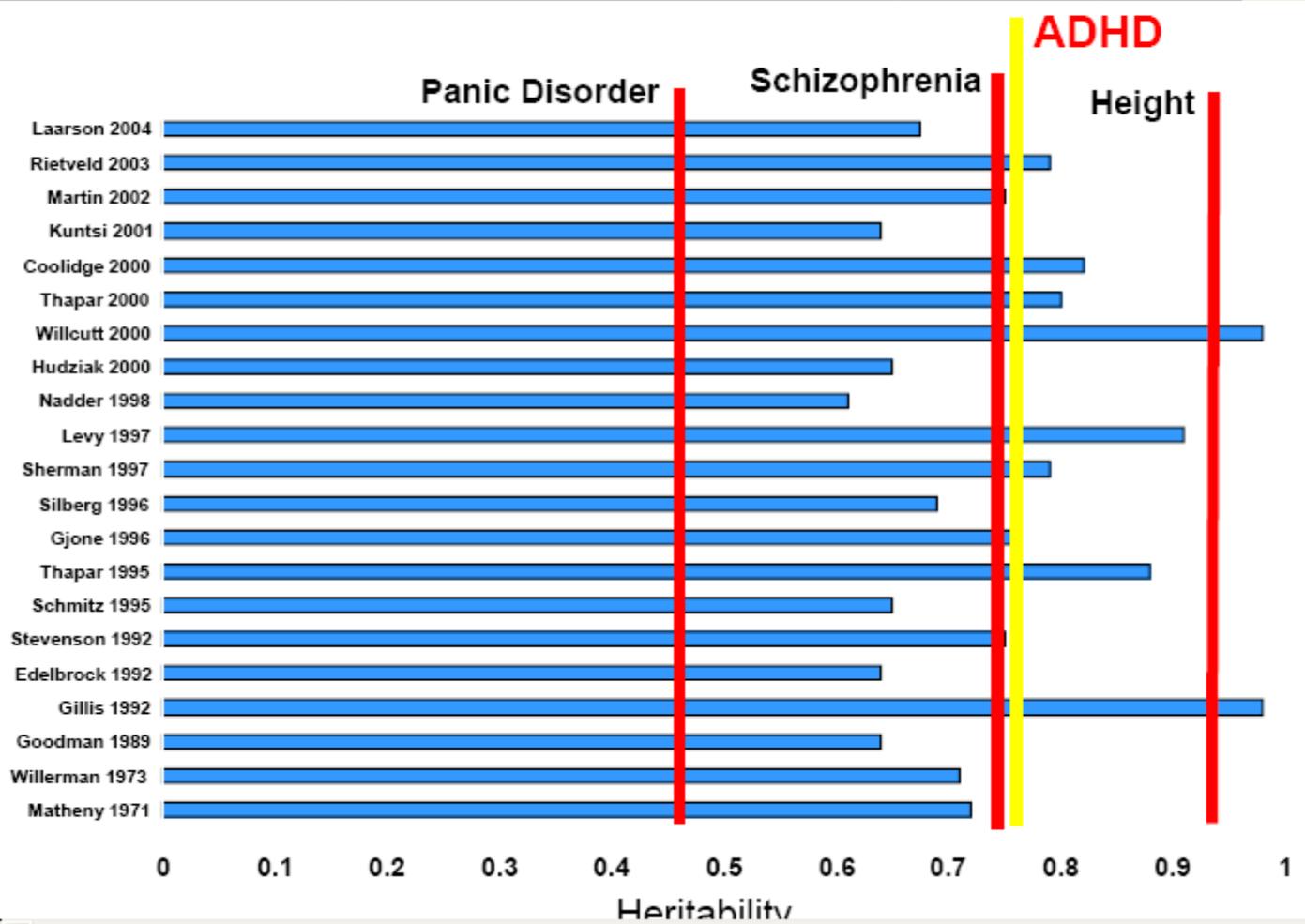


MGH-NMR Center & Harvard-MIT CITP

ADHD



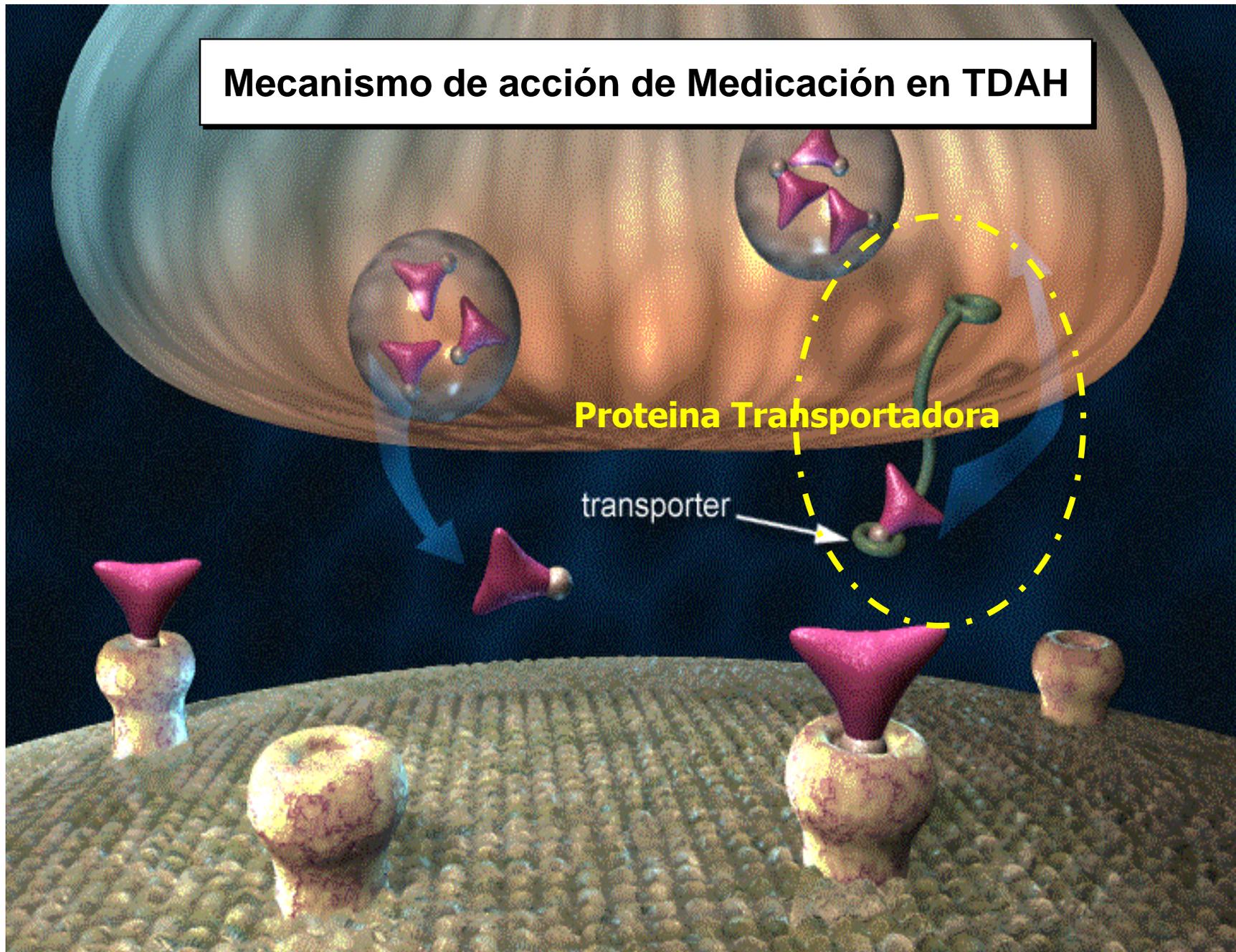
Bush et al. Biological Psychiatry. 1999.

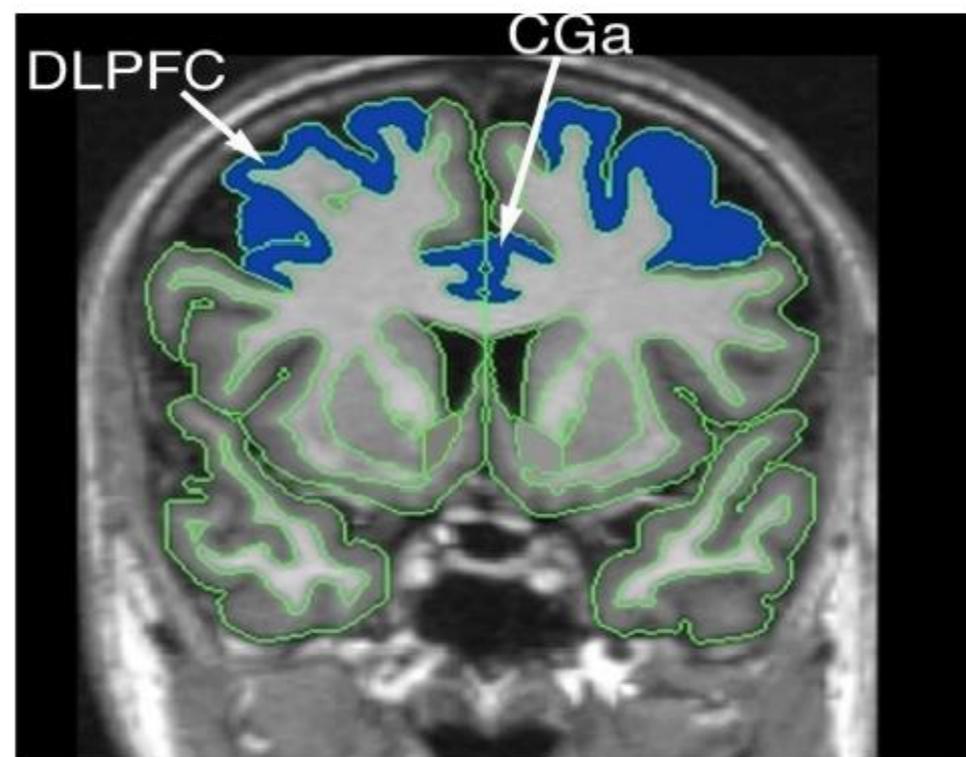


Mecanismo de acción de Medicación en TDAH

Proteína Transportadora

transporter





Dorsolateral Prefrontal Cortex (DLPFC): Blue
Anterior Cingulate Gyrus (CGa): Blue

Comorbilidad (consideraciones especiales)

(Scheffer, Kowatch, Carmody et al. Am J Psych:2005 162:58-64)

Study of BPD Spectrum youth

Age 6-17 years ($9 \pm 2.4y$)

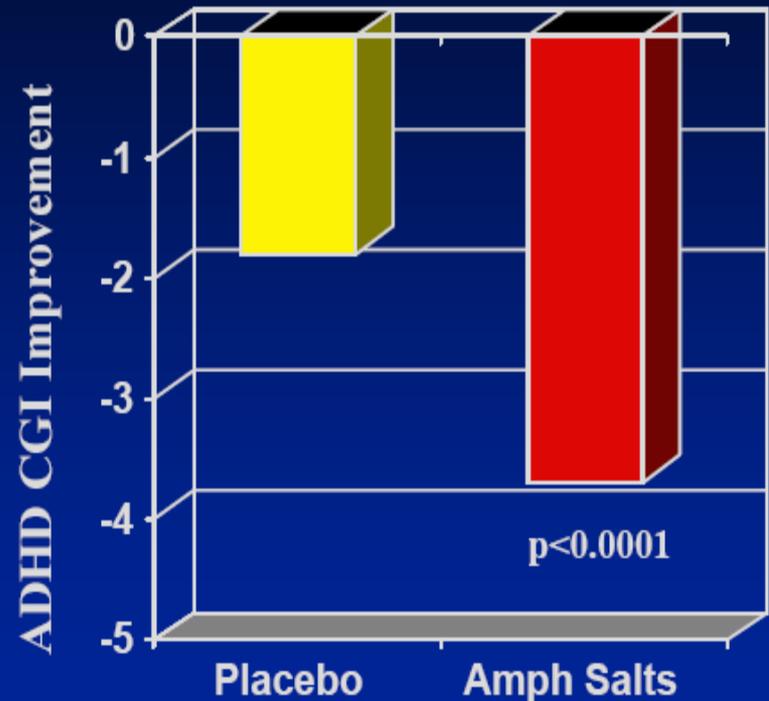
Design:

8 Wk open (N=40) with DPK

4 Wk double blind (N=30)

DPK+Adderall (5mgBID)

or PBO



YMRS scores (endpoint):
PBO 5.9, Amph 7.1 (pNS)

Hallazgos funcionales

Atención mantenida

Atención dividida

