ADHD:

Developmental Paths, Underlying Mechanisms, Sex Differences, and Rising Prevalence

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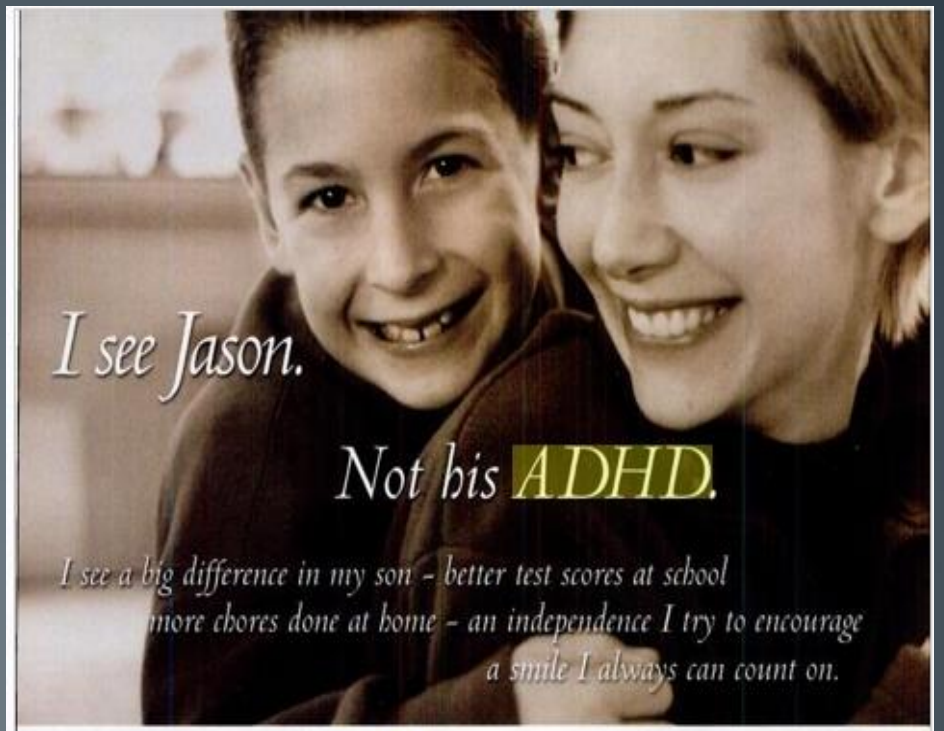
HELP Group Summit
October 15, 2021

Controversies/Myths

- How many times have you heard…
  - Everyone's diagnosed these days
  - It's all about bad schools…or permissive parents
  - Medications poison children's minds…we should never use them for behavior control
  - When topic is kids/adults who 'misbehave'—and when there are no objective markers (as with all mental disorders)—controversy abounds
- Start with ads, and fair use
  - 1997-9: FDA and DTC advertising



If your child has been diagnosed with ADHD, talk to your doctor about your choices of medication.
Medical studies support the unique benefits of **CONCERTA®**

- ☑ **96% of patients did not report loss of appetite or sleep**
- ☑ **Higher scores when solving math problems and an overall improved classroom focus**
- ☑ **Fewer conflicts among adolescents with family members and friends**
- ☑ **Patented OROS® delivery system controls symptoms consistently for 12 hours with a single dose**

The Makers of CONCERTA® believe in the importance of proper diagnosis and treatment of ADHD. Only a doctor can decide whether medication is right for you or your child. CONCERTA® should not be taken by patients with: significant anxiety, tension or agitation; allergies to methylphenidate or other ingredients in CONCERTA®; glaucoma; Tourette's syndrome, tics or family history of Tourette's syndrome; current/recent use of monoamine oxidase inhibitors (MAOI). CONCERTA® should not be taken by children under 6 years of age. Abuse of methylphenidate may lead to dependence. Tell your healthcare professional if your child has had problems with alcohol or drugs. In the clinical studies with patients using CONCERTA®, the most common side effects were headache, stomach pain, sleeplessness and decreased appetite.

Please see important product information on adjacent page.

Talk to your doctor and see if CONCERTA® is the right choice for you.

ONCE-DAILY
CONCERTA®
(methylphenidate HCl)
There's only one.

Call 1-888-302-7739
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a FREE Success Stories DVD or CD-Rom
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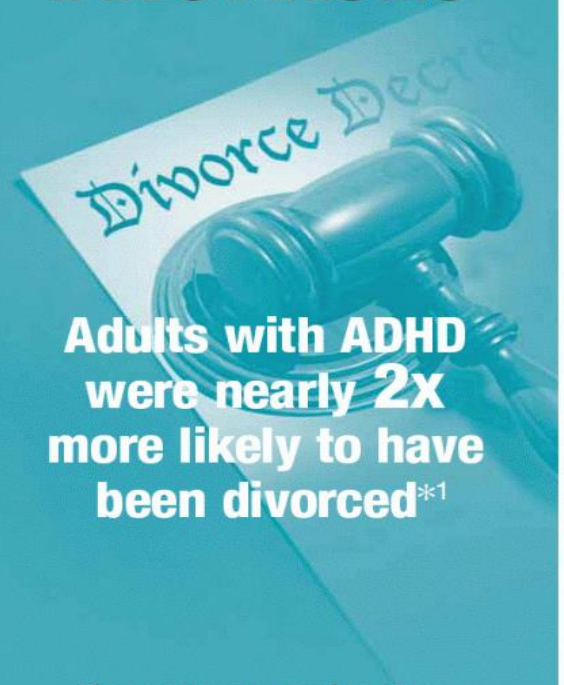
BROKEN PROMISES



Adults with ADHD were nearly 2x more likely to have been divorced*1

The consequences may be serious. Screen for ADHD.

Find out more at
www.consequencesofadhd.com
and download patient support materials, coupons, and adult screening tools.

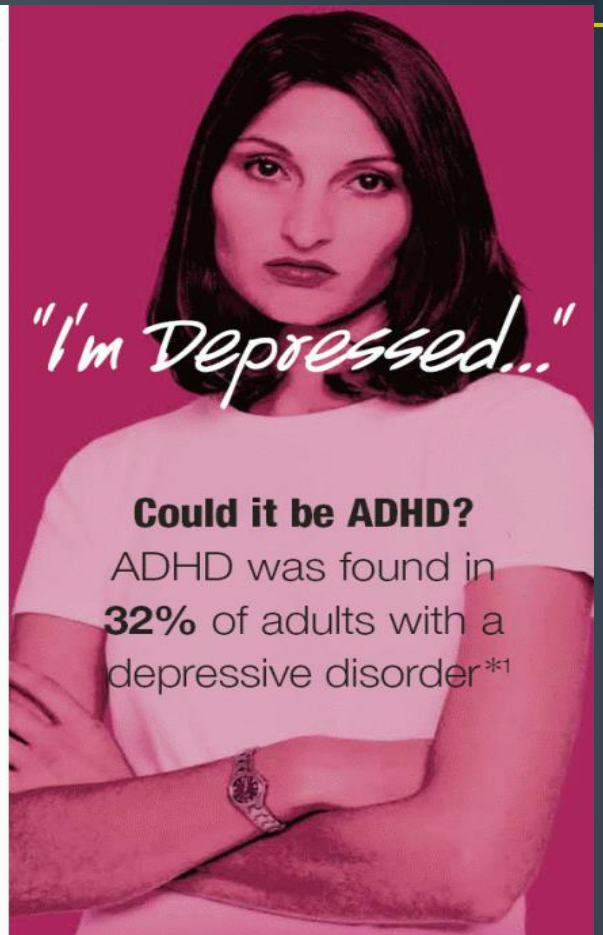
*Results from a population survey of 500 ADHD adults and 501 gender- and age-matched non-ADHD adults which investigated characteristics of ADHD and its impact on education, employment, socialization, and personal outlook.

Reference: 1. Biederman J, Faraone SV, Spencer TJ, et al. Functional impairments in adults with self-reports of diagnosed ADHD: a controlled study of 1001 adults in the community. *J Clin Psychiatry*. 2006;67:524-540.

Shire

Shire US Inc.
...your ADHD Support Company™

 A1410 11/06



Could it be ADHD?
ADHD was found in **32%** of adults with a depressive disorder*1

Look for ADHD in patients who present with depression.

Visit **www.depressionandadhd.com** for patient education kits and adult screening tools.

*From a retrospective survey assessing the prevalence, comorbidity, and impairment of adult ADHD in 3199 adults, age 18 to 44. Depressive disorder includes major depressive disorder and dysthymia.

Reference 1. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry*. 2006;163:716-723.

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Shire US Inc.
...your ADHD Support Company™

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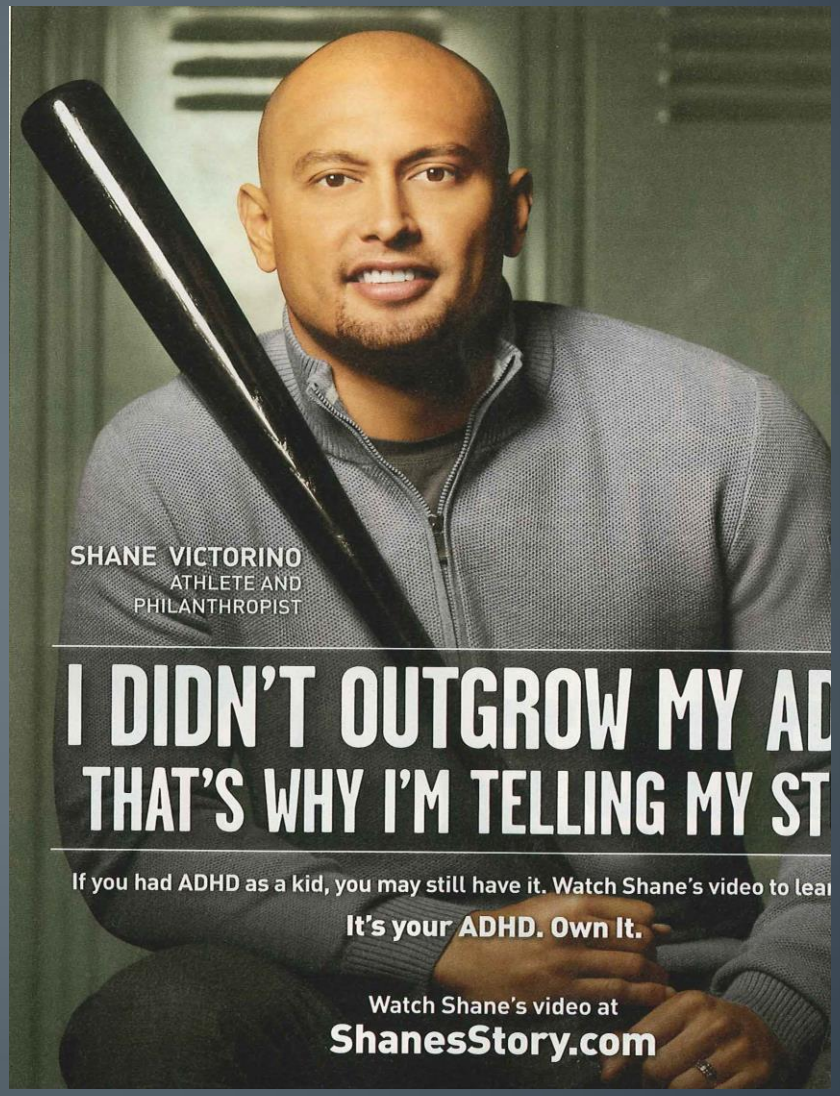
A third ad, from this decade



Clinical Manifestations

- Two partially independent domains of behavior
  - Inattention/Disorganization
  - Hyperactivity/Impulsivity
- Nine symptoms in each domain
  - Developmentally extreme and impairing levels, not explained by clear medical issues or severe deprivation, may warrant diagnosis
- Diagnosis of types/presentations:
  - Inattentive
  - Hyperactive/Impulsive
  - Combined

Impairment

- Academic (school failure)/Vocational
  - $100 billion/year (youth) indirect costs (justice, sp. ed, SUD)
  - $200 billion annually (adults) indirect costs (job problems)
- Social/peer/relationships
  - Most peer-rejected condition
- Family (reciprocal chains of bidirectional influences)
- Accidental injury (across the age span)
- Self-harm, suicide, lowered longevity

Key Issues

- **Clearly a syndrome, not a disorder: No single cause**
- **Sex differences: 2.5:1**
  - **Generally true for all neurodevelopmental conditions**
  - **By adulthood, closer to 1:1, even in general population**
- **Remarkably consistent prevalence, worldwide**
  - **In nations with compulsory education**
  - **Exceptions: US, Israel (stay tuned)**

DSM-5 vs. RDoC

- DSM-5 changes:
  - Neurodevelopmental disorder
  - Types (Inattentive, HI, Combined) now ‘presentations’
  - Adult examples of most symptoms (and only 5 symptoms per domain)
  - Age of onset of impairing symptoms: < 12 years, not < 7
  - **Each successive edition of DSM has loosened criteria somewhat
    - One reason for “ADHD explosion”
- NIMH Research Domains Criteria (RDoC)
  - Dimensional, multiple levels (genes to culture)
  - Search for underlying mechanisms
- Moral: Disorders don’t fit into neat ‘boxes’
  - Everyone on a spectrum

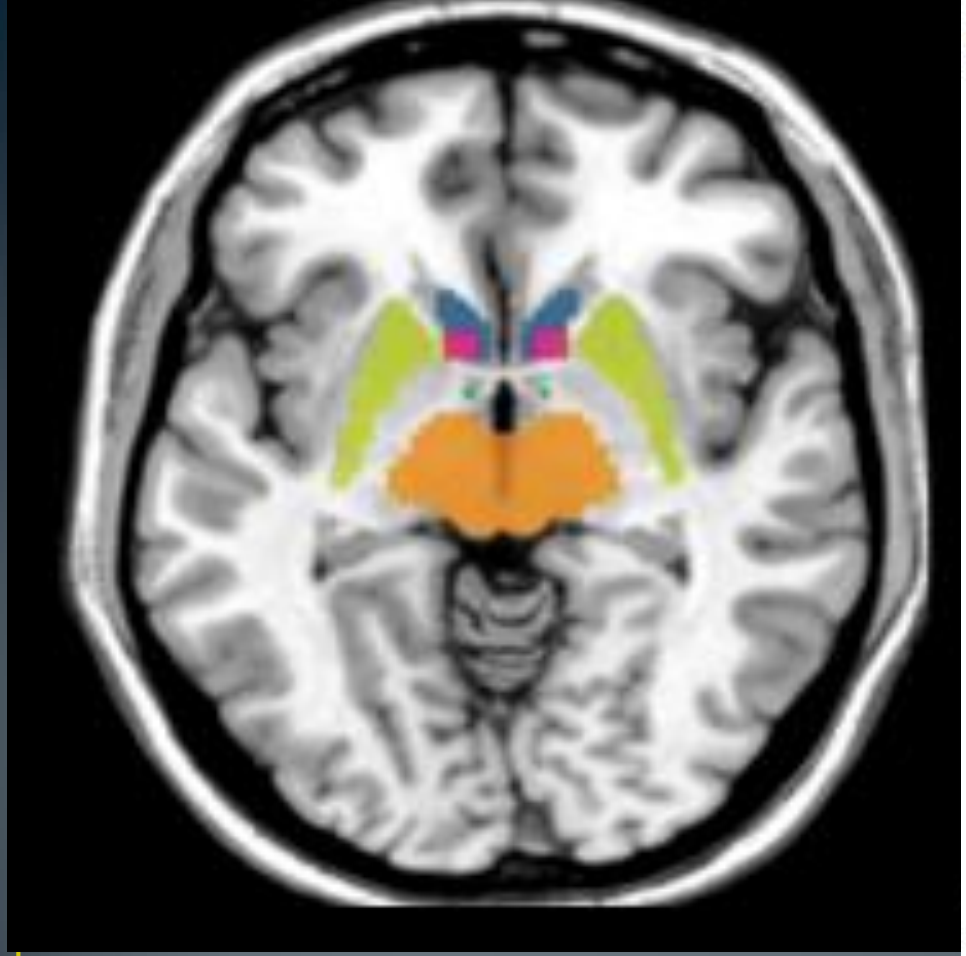
Nature of ADHD: Models

- 1. “Attention” models
  - But which form(s) of attention?
    - Sustained/selective/capacity
  - And ADHD is less about ‘deficient attention’ than ‘dysregulated’ attention
    - E.g., video games/hyperfocus?

- 2. “EF” models:
  - Executive functions/cognitive control
    - Planning
    - Interference control
    - Working memory
    - Error correction
  - Not specific to ADHD
    - Some who have ‘real’ ADHD do not show EF deficits

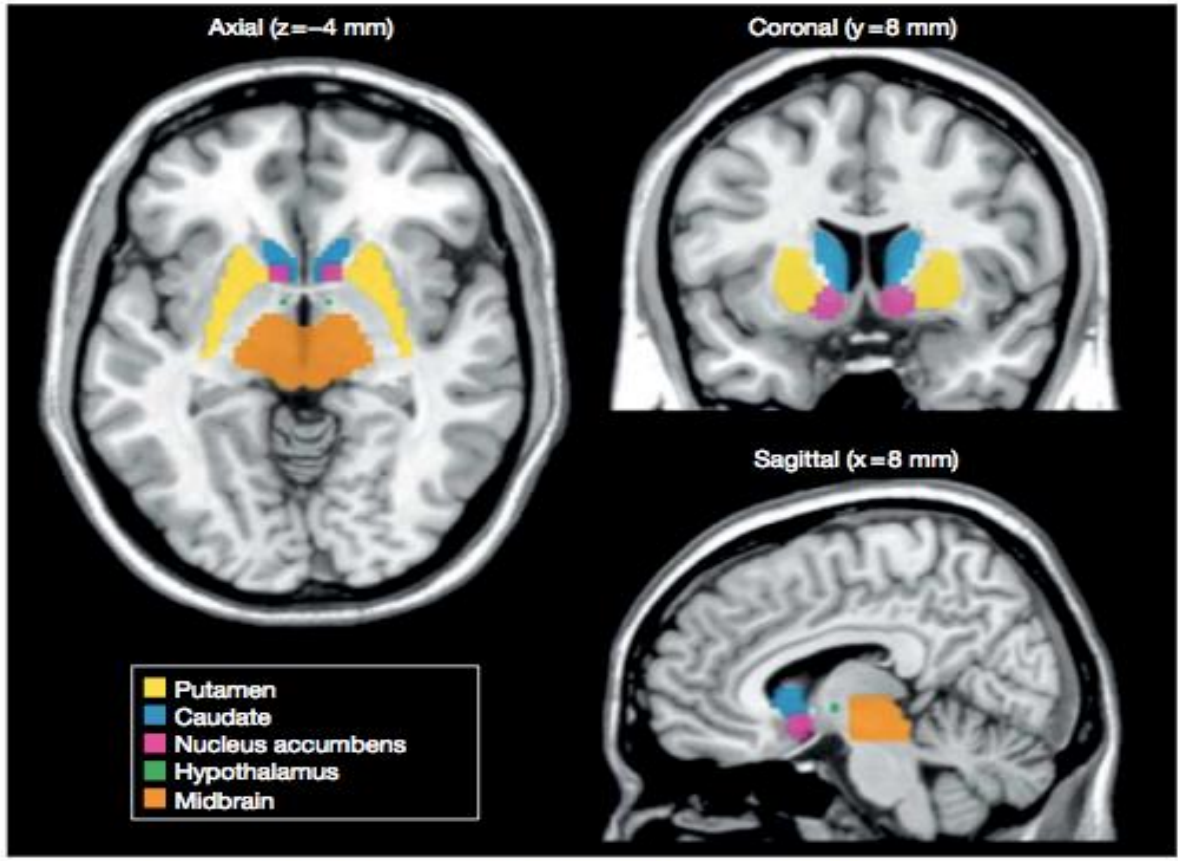
Models/Mechanisms #3

- 3. “Inhibition” models
  - Barkley’s theory
  - But is response inhibition actually an EF?
- 4. “Motivation” models: Reward undersensitivity/delay aversion
  - Volkow et al. (2009): large medication-naïve adult sample, PET
- **Key: Huge variability among/within individuals with ADHD
  - Inconsistency a major theme/dysregulation, not inattention per se
    - Resonates with brain imaging findings re: default mode/mind-wandering



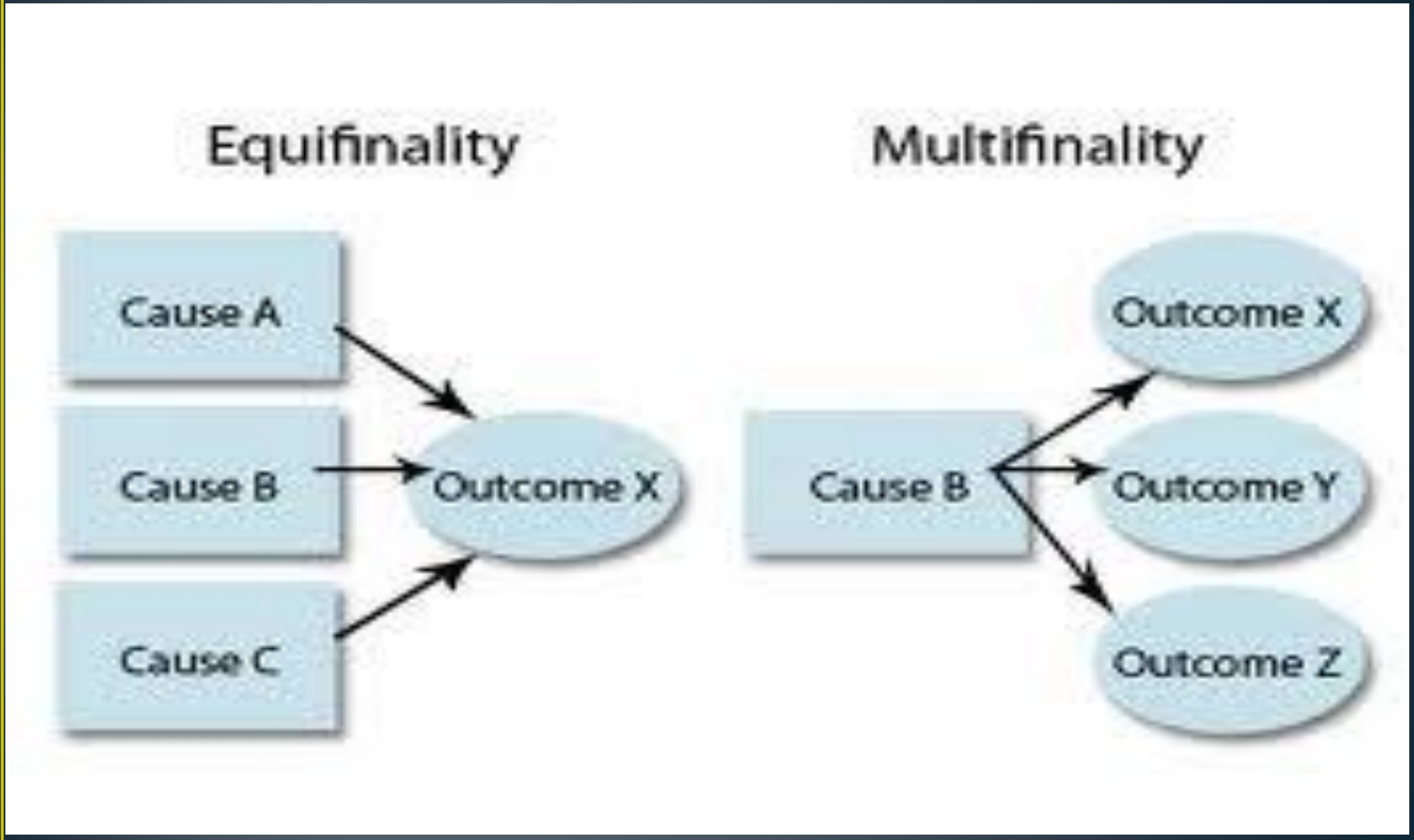
Transporter PET Image

Figure 1. Regions of Interest Used to Extract the D_2 / D_3 Receptor and Dopamine Transporter Measures

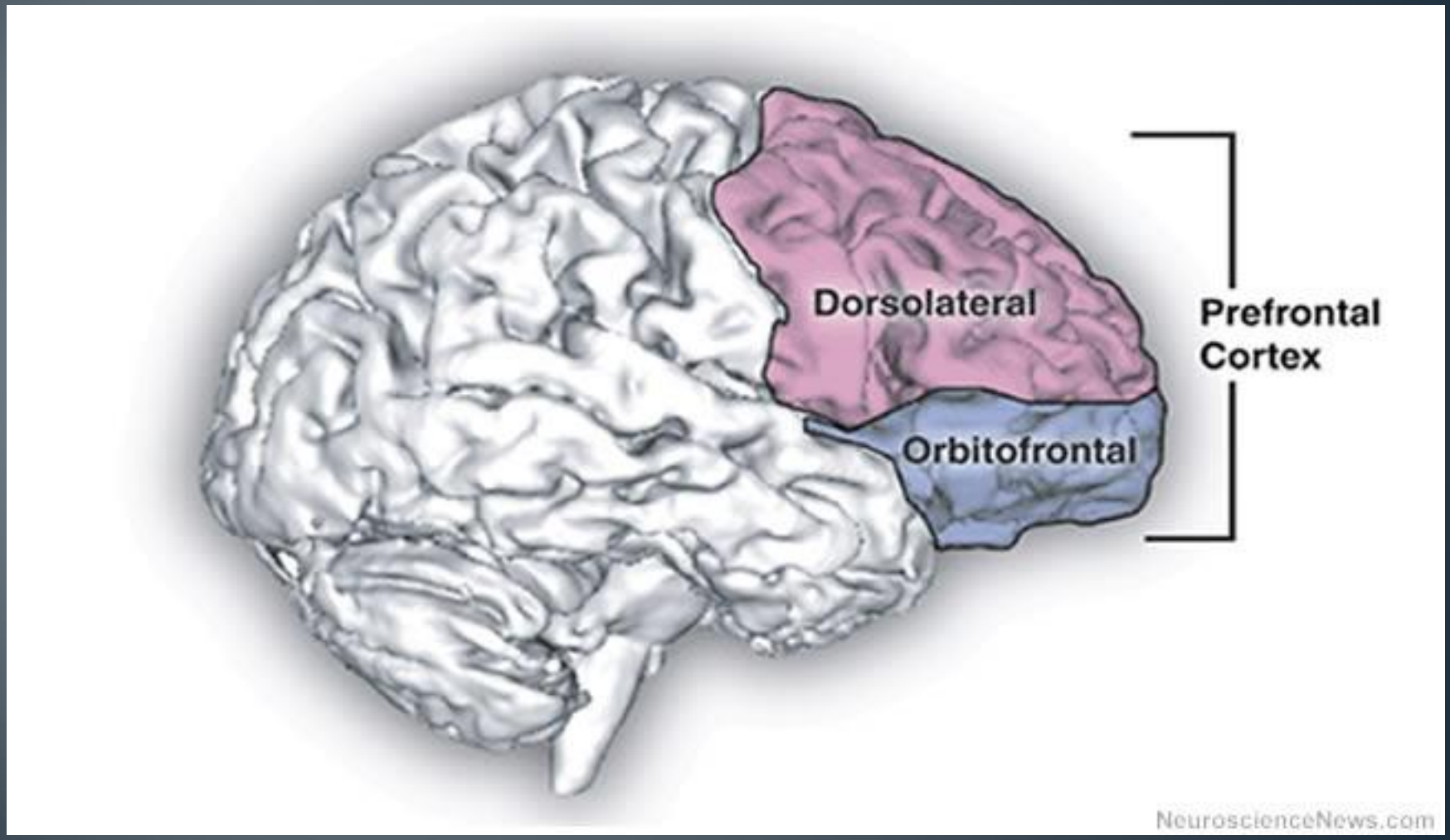


The regions of interest for the midbrain are obtained in several planes, and the shadow is projected to the axial image shown in the figure, which explains why the third ventricle is covered by the region. The x coordinate maps the left-right position; the y coordinate, the anterior-posterior position; and the z coordinate, the superior-inferior position

Dopamine transporter					
Accumbens (Motivation)	0.71 (0.16)	0.63 (0.11)	0.59	0.03 to 0.13	.004
Caudate (Attention)	0.66 (0.23)	0.53 (0.19)	0.62	0.04 to 0.22	.003
Midbrain	0.16 (0.10)	0.09 (0.11)	0.66	0.03 to 0.12	<.001
Hypothalamic region	–0.01 (0.10)	–0.05 (0.12)	0.36	–0.01 to 0.09	.08


Equifinality
Cause A
Cause B
Cause C
Outcome X
Multifinality
Cause B
Outcome X
Outcome Y
Outcome Z

Prefrontal Cortical Thickening: Shaw et al.

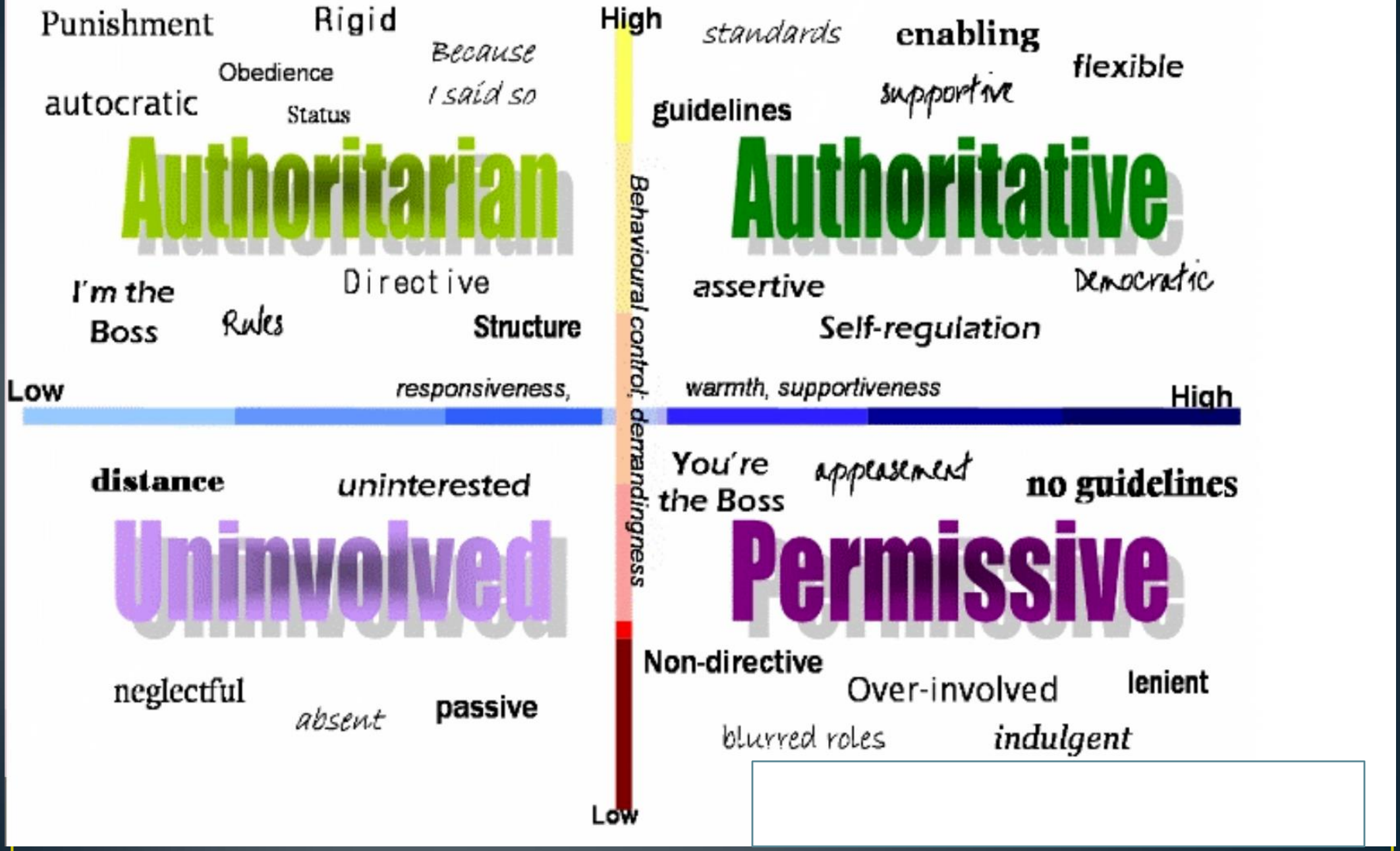


Etiology

- **Heritability and Genes:**
  - **H^2 of ADHD near .8**
    - **Such figures pertain to parent report of symptoms; but shared method variance/DZ twin contrast effects**
    - **Teacher ratings: Lower figures (still moderate to high)**
  - **So, assumption that ADHD is 'fixed' and largely immutable**
    - **I.e., "parenting can't matter"; parents as shepherds**
    - **Misreading of heritability**
- **Other risk factors:**
  - **Low birthweight, fetal alcohol, environmental toxins**
    - **Lead, perhaps pesticides**

Ultimate cause—or at least, the factor that 'reveals' ADHD?

- **Compulsory education (same as for LD)**
  - **Certainly, 'attention' or 'impulse control' genes have been around for the history of our species, but extremes not salient until we made children sit and learn to read**
  - **Entirely possible to posit genetic, neurobiological, AND cultural forces as responsible**
  - **Many forms of mental disorder: 'mismatch' between vulnerability and current context**


Punishment
Rigid
High
standards
enabling
Because
Obedience
flexible
autocratic
I said so
supportive
Status
guidelines
Authoritarian
Authoritative
Behavioural control; demandingness
I'm the
Boss
Directive
assertive
Democratic
Rules
Structure
Self-regulation
Low
responsiveness,
warmth, supportiveness
High
distance
uninterested
You're
the Boss
appeasement
no guidelines
Uninvolved
Permissive
Non-directive
neglectful
Over-involved
lenient
absent
passive
blurred roles
indulgent
Low

Parenting Influences on Positive Peer Status

Hinshaw, Zupan, et al. (1997, *Child Development*)

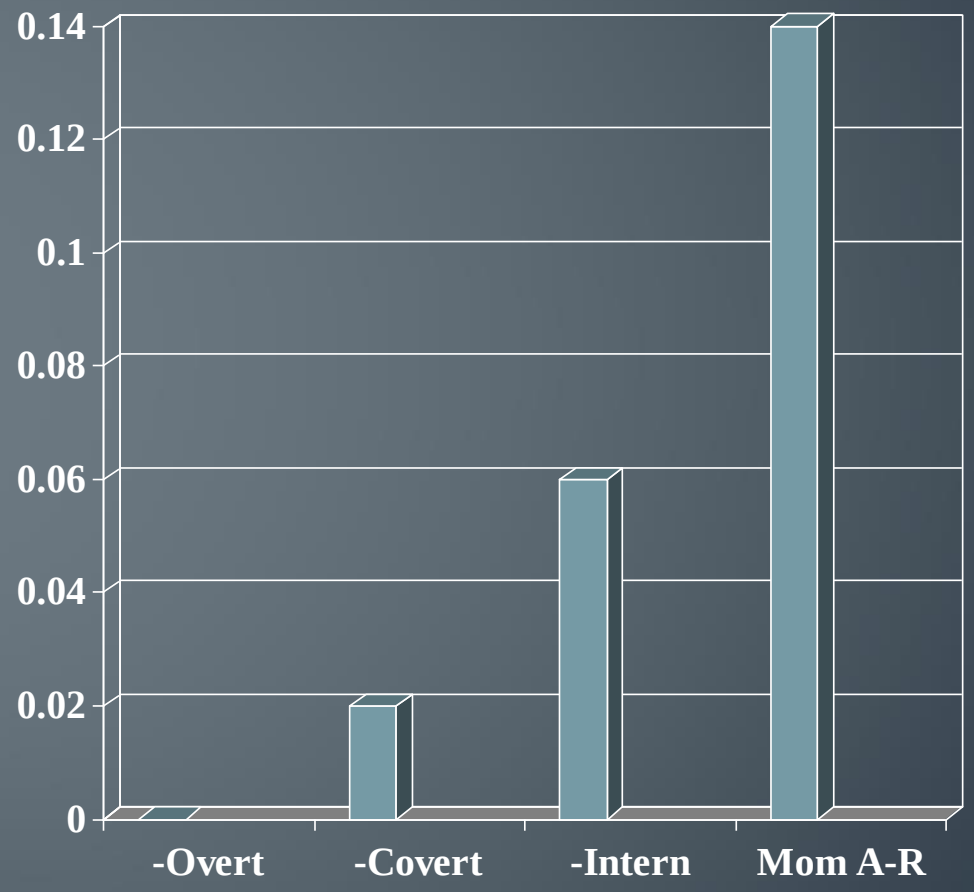
- **Aim: Predict peer acceptance from parenting**
  - **Ideas About Parenting (Heming et al., 1989)**
  - **3 factors = Authoritarian, Authoritative, Permissive**

- **Authoritative Factor: 15 items**
  - ***Warmth, Limits, Autonomy Encouragement--e.g.,***
    - **"I encourage my child to be independent of me"**
    - **"I expect a great deal of my child"**
    - **"I have clear, definite ideas about childrearing"**
    - **"Raising a child is more pleasure than work"**
    - **"When I am angry with my child, I let him know"**
    - **"I reason with my child regarding misbehavior"**

Findings

- Mothers of ADHD boys: lower on Authoritative (ES = .75)
  - Yet variance in ADHD group equivalent to comparison group's
- Tested predictive power of parenting factors, observed overt and covert behavior, and internalizing score (CDI, observed withdrawal) via hierarchical regressions
  - Neither Authoritarian nor Permissive beliefs predicted peer nominations, but Authoritative beliefs did so (beta = .3), even with diagnostic group controlled
- Moderation: strong prediction (B > .4 in ADHD group)
  - But near zero in comparisons

Explained Variance--Positive Nominations



Important Findings

Harold et al. (2013a, 2013b); Sellers et al. (2021)

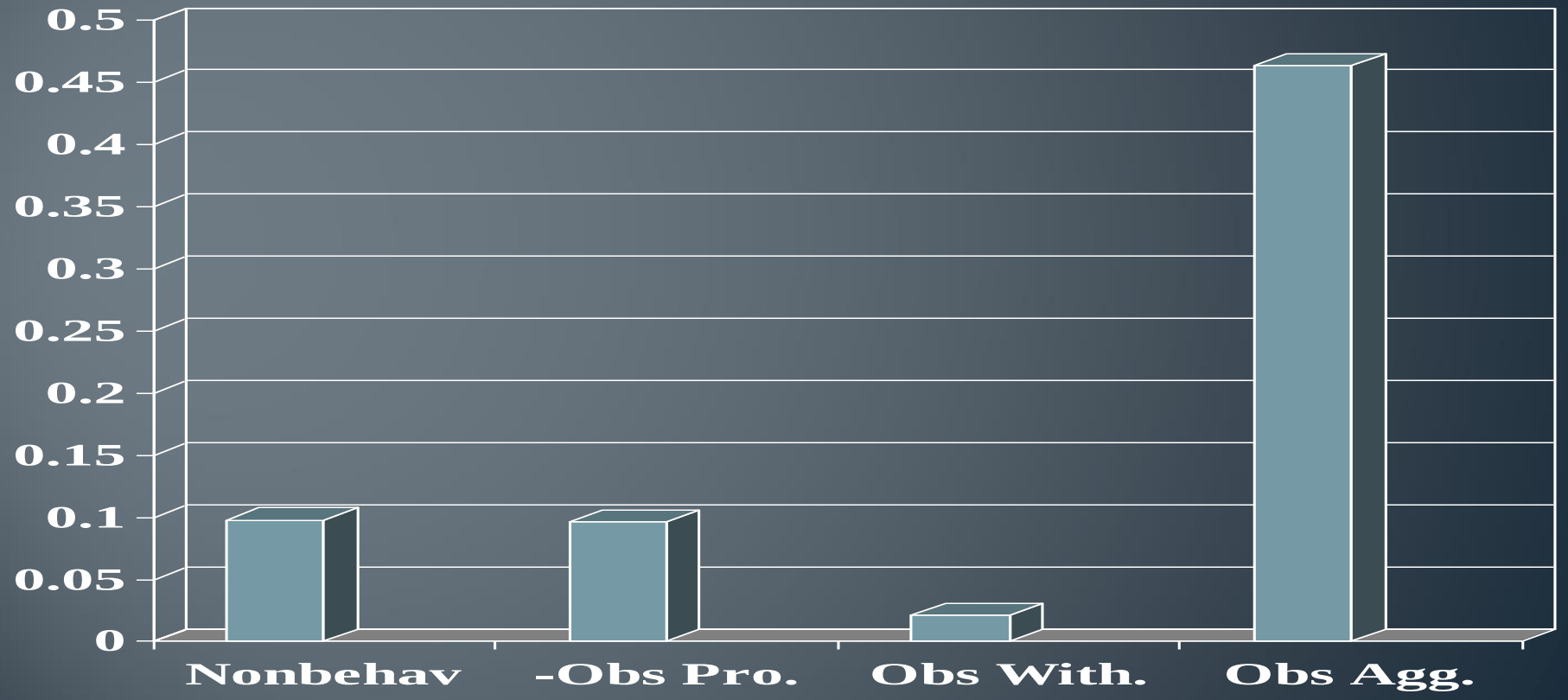
- **Adoption studies in UK**
  - **Adjust for biological relatedness and gene-env. correlation**
- **Even in adoptive families, kids' levels of ADHD elicit overcontrolling parenting from parents**
- **AND, levels of harshness predict further ADHD symptoms, and achievement deficits, over time**
- **It's not all in the genes!**

Quick Peer Rejection

Erhardt & Hinshaw (*JCCP*, 1994)

- **Initial sociometric nominations, for previously unfamiliar ADHD and comparison boys attending camp**
- **On Day 1 (& Day 3), boys with ADHD (n = 25) 4.5 times greater rate of negative nominations than comp (n = 24)**
- **r between Day 1 and final day negative noms = .7**
  - ***Implication: Don't perform no-treatment trial for successful intervention at start of school year!**

Explained Variance in Day 3 Negative Nominations



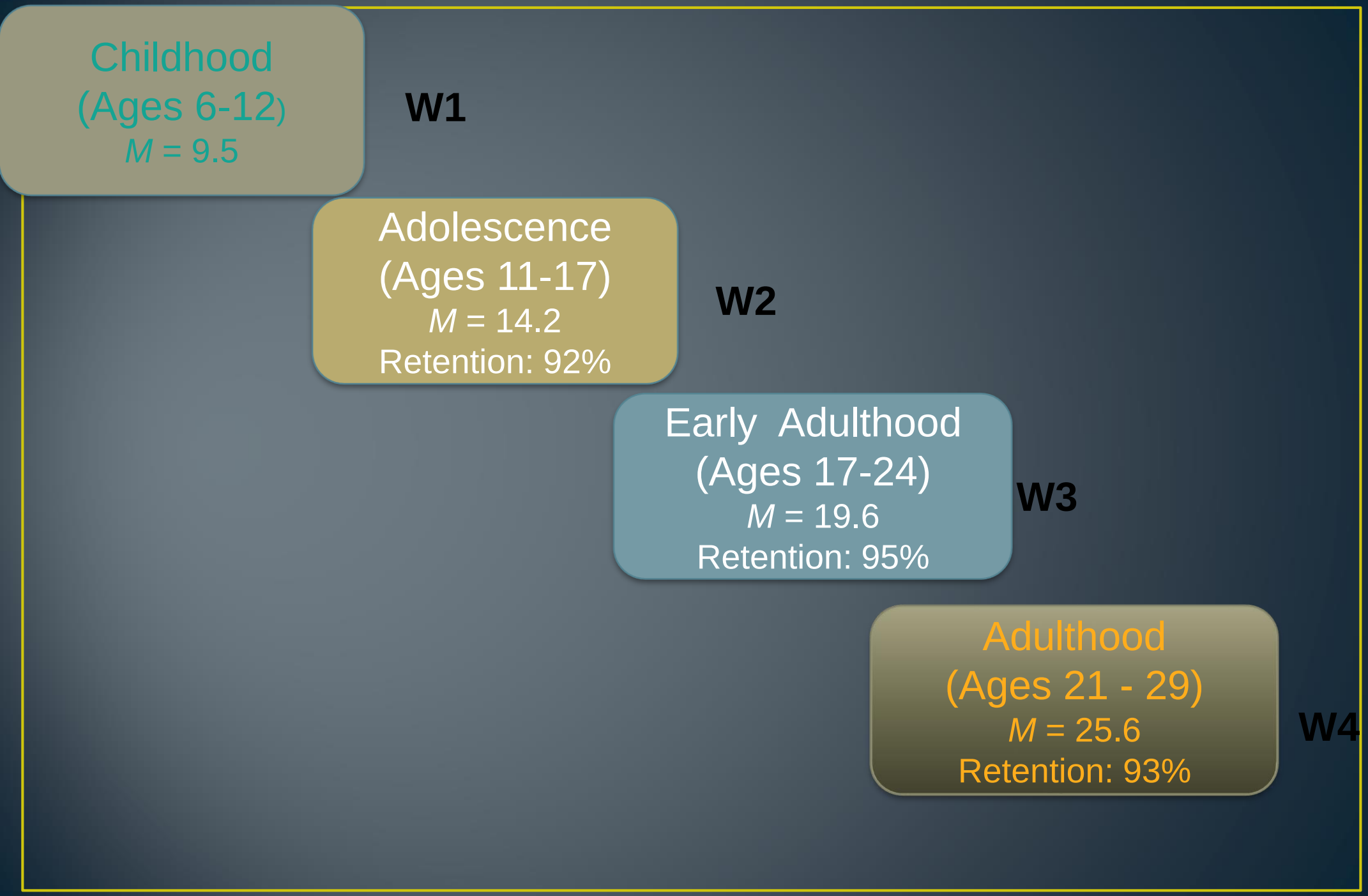
Implications

- Quick accrual of negative peer status
- Explanatory factors:
  - Weak role of nonbehavioral predictors of peer rejection (poor achievement, low athletic skills, low attractiveness)
  - Strong role of aggression (beta = .75)
- Preliminary: Even stronger pattern for girls

ADHD in Girls and Women

See Hinshaw et al. (2022), Annual Research Review, *Journal of Child Psychology and Psychiatry*

- **Longstanding neglect of females in human and even animal research**
- **1990s: Try to ascertain a large, diverse, viable female sample**
  - **NIMH grant: Carefully dx-ed ADHD group plus matched comparison sample**
- **Naturalistic summer research programs**
  - **Told families that we wanted to study their daughters for the rest of their lives**
- **Our sample (BGALS):**
  - **Largest in existence of preadolescent girls with ADHD (140, with 88 matched comparison girls)**
  - **Baseline: marked impairments across symptoms, impairments, neuropsych measures**
    - **Initial article: Hinshaw (2002), *Journal of Consulting & Clinical Psychology***


Childhood
(Ages 6-12)
M = 9.5
W1
Adolescence
(Ages 11-17)
M = 14.2
Retention: 92%
W2
Early Adulthood
(Ages 17-24)
M = 19.6
Retention: 95%
W3
Adulthood
(Ages 21 - 29)
M = 25.6
Retention: 93%
W4

BGALS Follow-ups

Hinshaw et al. (2006), Hinshaw et al. (*JCCP*, 2012), Owens et al. (2017)

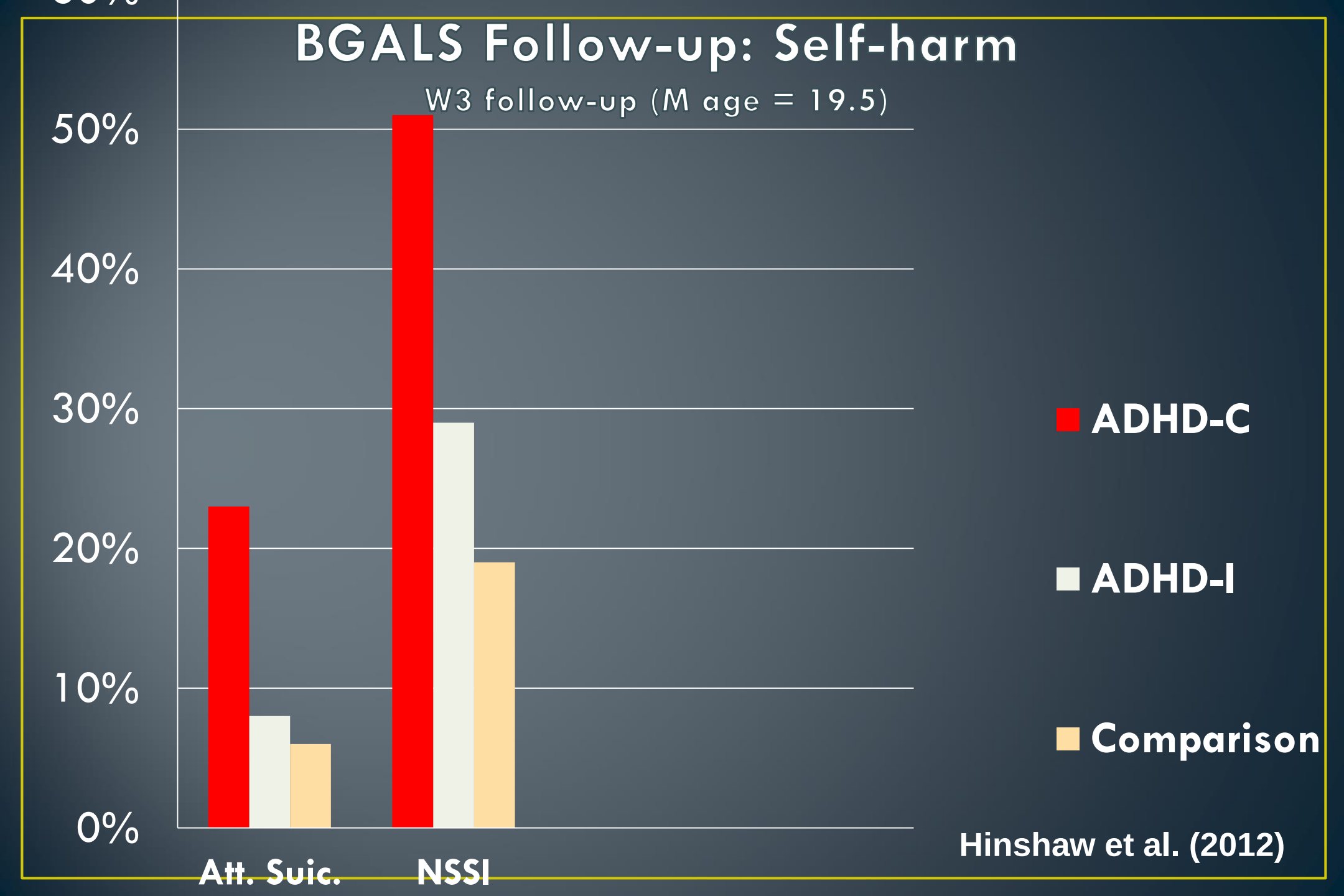
- **Adolescence:**
  - **All domains reveal that impairments maintained**
  - **E.g., academic/social/comorbidities/self-perceptions/parenting/EF**
- **Early adulthood:**
  - **Keep most measures same, BUT expand into developmentally salient domains**
  - **Impairments still pronounced, but NOT re: substance abuse**
- **Mid-late 20s:**
  - **Still, significant and medium/large effect sizes for ADHD vs. comps**
  - **Few effects of baseline subtype/presentation:**
    - **Exceptions: antisocial behavior, peer rejection**
  - **Even for neuropsychological/EF measures:**
    - **NO effects of type/presentation, with tiny ESs**
  - **All analyses: rigorous adjustment for baseline SES, even IQ**

Heterotypic Continuity: Self-harm as outcome

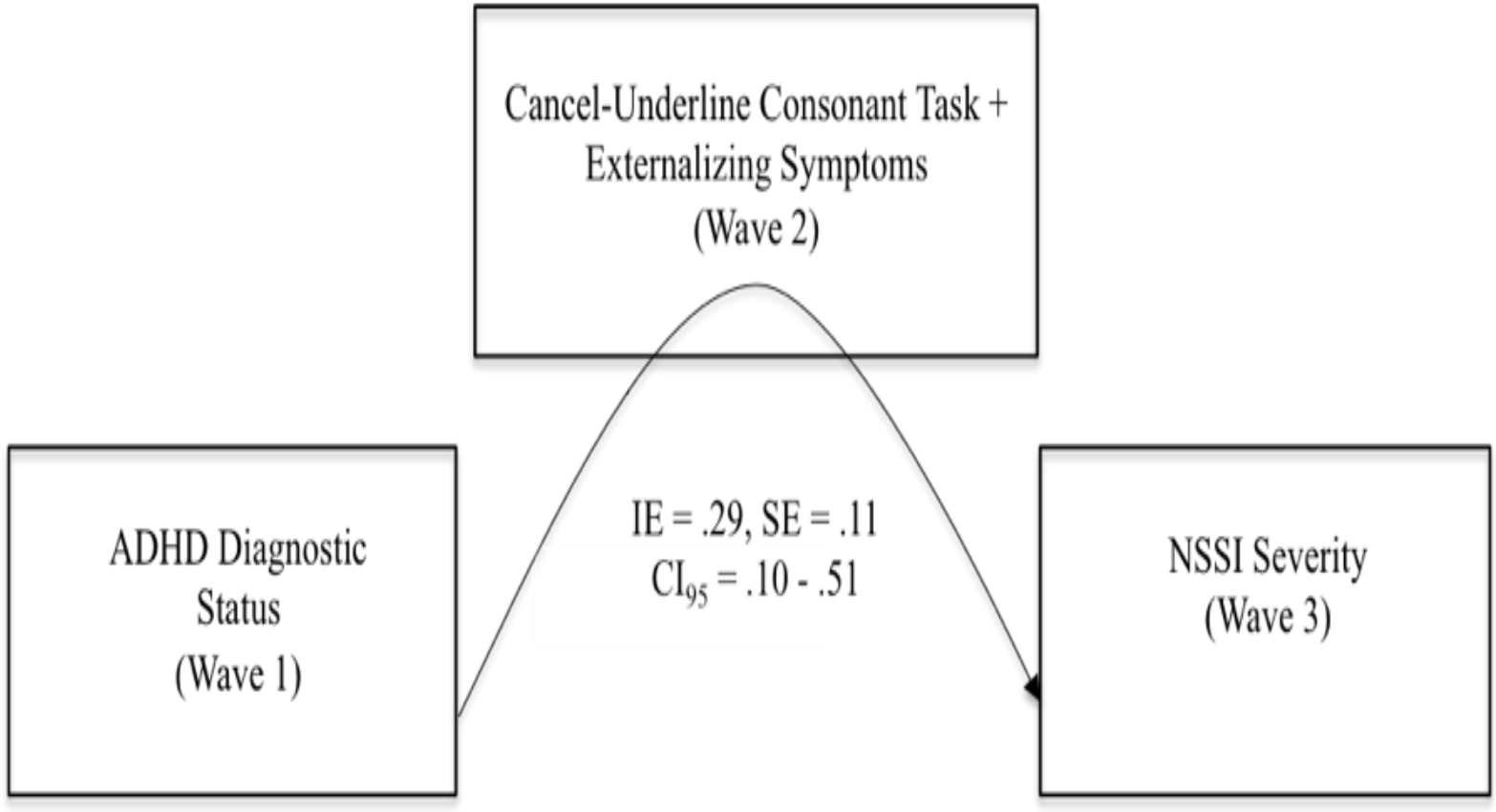
- **Suicidal behavior: intent is to die**
  - **Suicidal ideation (common)**
  - **Suicide attempt (rarer)**
- **Non-suicidal self-injurious behavior (NSSI)**
  - **No express intent to die, but to express (or ease) intense psychological pain**
  - **Linked to poor emotion regulation**
  - **Wide range—cuticles to cutting/burning**
- **Yet many suicide attempters have history of NSSI**
  - **NSSI stronger predictor of suicide attempts than previous attempts**
  - **NSSI may be lethal**

BGALS Follow-up: Self-harm

W3 follow-up (M age = 19.5)



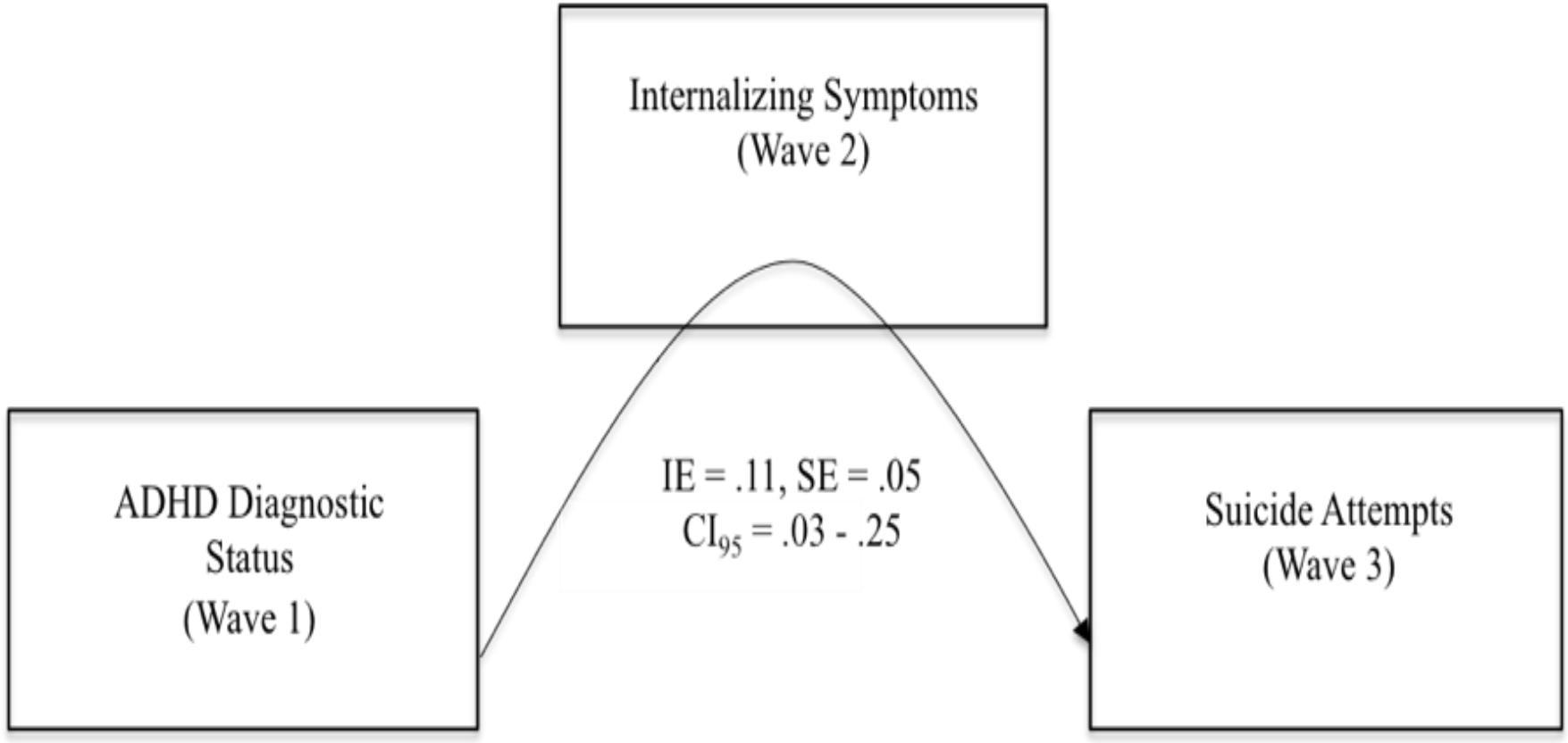
Hinshaw et al. (2012)



MEDIATION: WAVE 1 ADHD STATUS TO WAVE 3 NSSI

Data represent indirect effect and standard errors using 10,000 bootstrap samples to obtain bias-corrected and accelerated 95% confidence intervals.

Swanson, Owens, & Hinshaw (2014), *Journal of Child Psychology and Psychiatry*



MEDIATION: WAVE 1 ADHD STATUS TO WAVE 3 SUICIDE ATTEMPTS

Data represent indirect effect and standard errors using 10,000 bootstrap samples to obtain bias-corrected and accelerated 95% confidence intervals

Swanson, Owens, & Hinshaw (2014), *Journal of Child Psychology and Psychiatry*

Meza, Owens, & Hinshaw (2016)

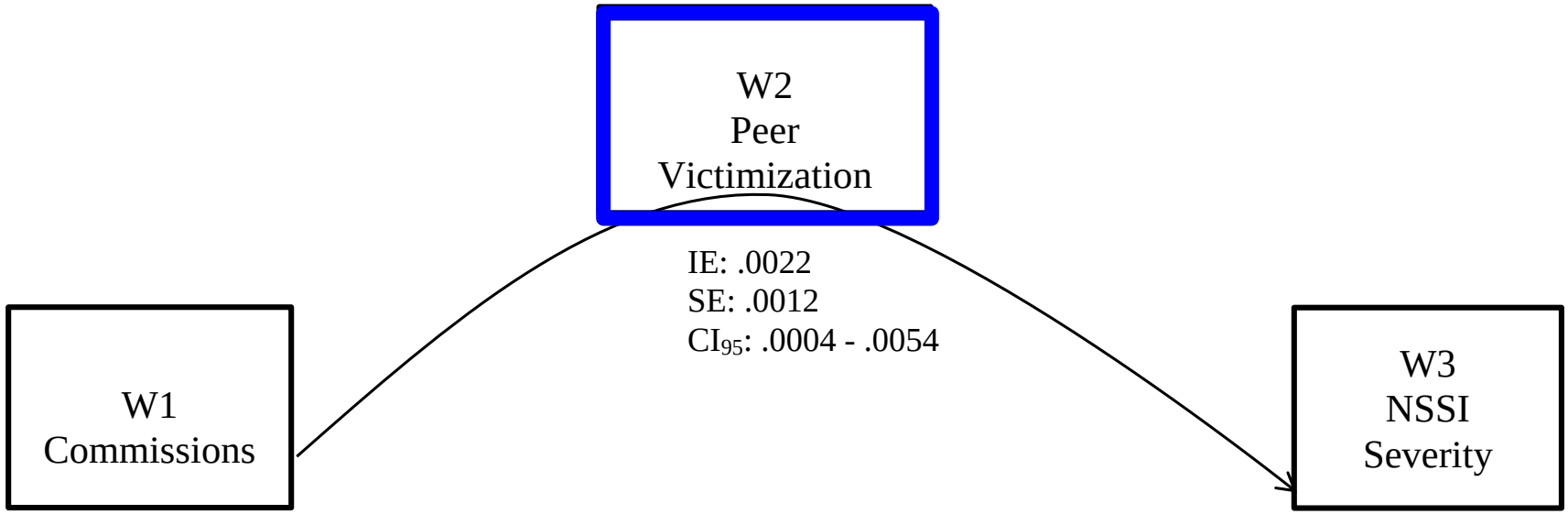


Figure 3. The relationship between W1 Commissions and W3 NSSI was partially mediated by W2 Peer Victimization over and above: WISC Full-Scale IQ, mother's education, household income, and age at W3. Data represent indirect effect and standard errors using 10,000 bootstrap samples to obtain bias-corrected and accelerated 95% confidence intervals.

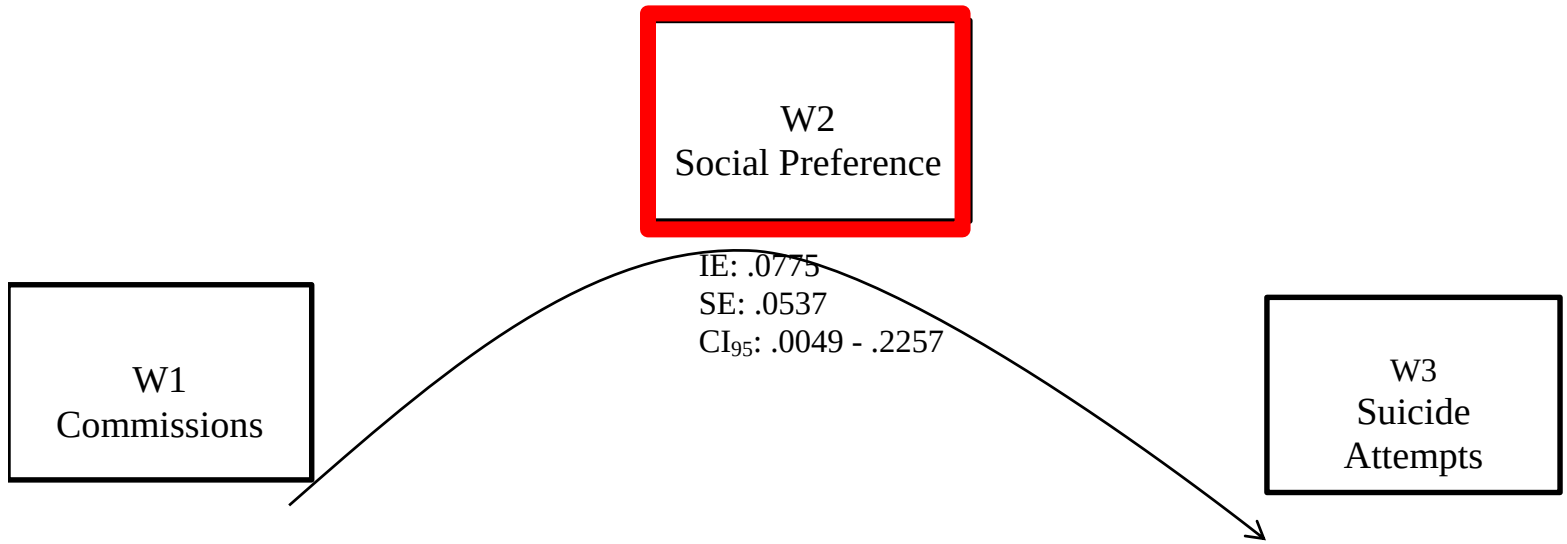


Figure 2. The relationship between W1 Commissions and W3 Suicide Attempts (y/n) was partially mediated by W2 social preference scores over and above: WISC Full-Scale IQ, mother's education, household income, and age at W3. Data represent indirect effect and standard errors using 10,000 bootstrap samples to obtain bias-corrected and accelerated 95% confidence intervals.

Predictors, Mediators

- Guendelman et al. (2016, *Devel. and Psychopathology*):
  - Physical abuse, sexual abuse, and/or neglect: > in ADHD than comp's
  - Within ADHD group, the maltreated subgroup more likely to show depression and suicide attempts (not externalizing behavior)
  - COMBINATION OF EARLY IMPULSIVITY AND MALTREATMENT PREDICTS SUICIDE ATTEMPT RATE OF OVER ONE-THIRD

- Meza, Owens, & Hinshaw (2020, *Devel. & Psychopathology)*
  - Lifetime rates of self-harm related to childhood…
    - ADHD severity
    - Externalizing problems,
    - Negative *father-child* interactions
    - EF deficits
    - Low self-esteem

Wave 4 (mid-late 20s)

Owens, Zalecki, Gillette, & Hinshaw, *JCCP* (2017)

- **Unplanned pregnancy rates:**
  - **Comparison : 10%**
  - **ADHD: 43%**
  - **REGARDLESS of persistence of ADHD symptoms across time**
  - **Owens & Hinshaw (2020): Key mediator: Low academic performance**
- **Owens & Hinshaw (2016, *Development and Psychopathology*)**
  - **Early cognitive vulnerability predicts adult comorbidity through**
    - **Adolescent poor self-control**
    - **Low delay of gratification**
    - **Low academic achievement**

Tidal Wave/ADHD Explosion

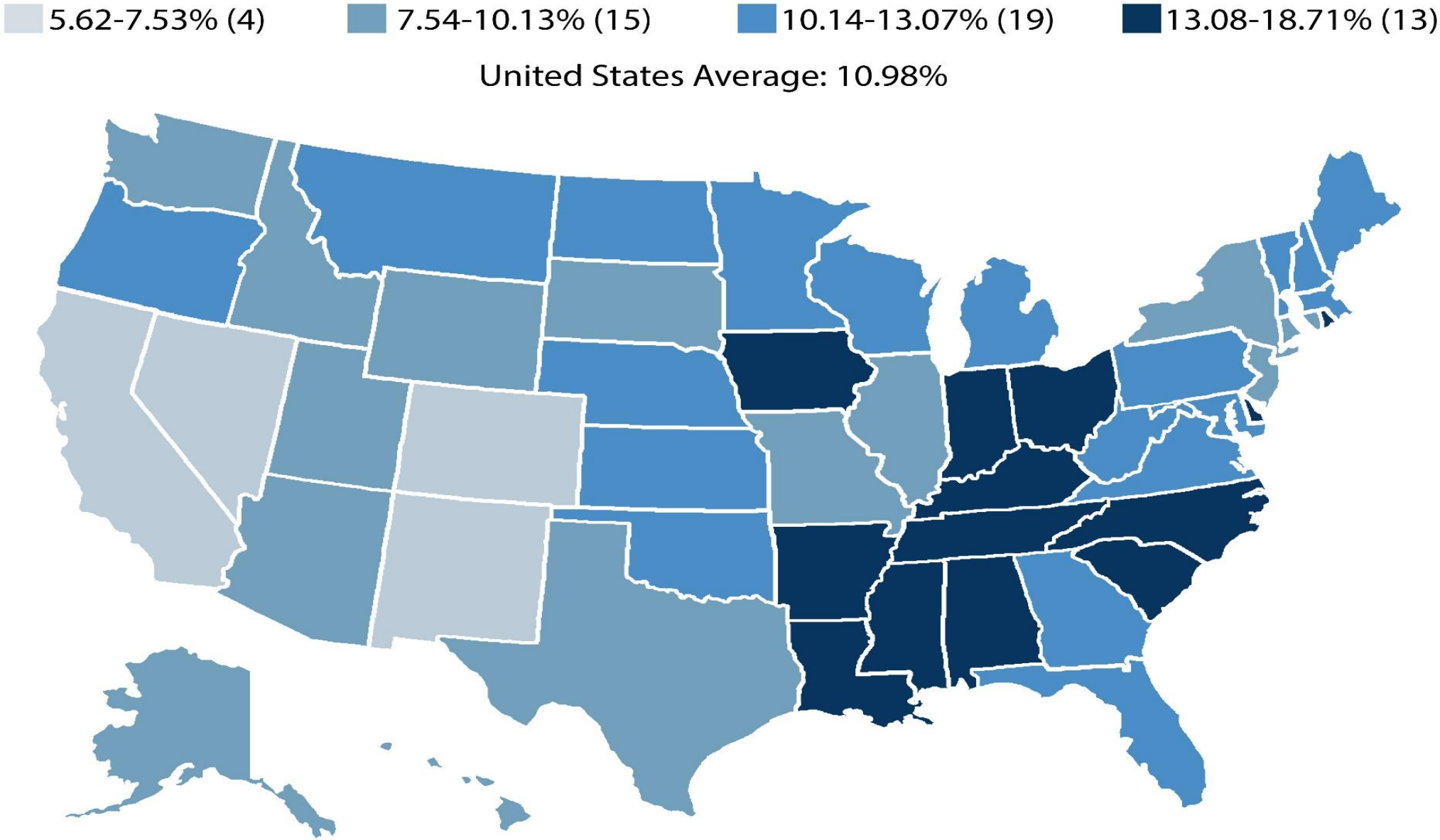
National Survey of Children's Health (Visser et al., 2014)
Journal of the American Academy of Child & Adolescent Psychiatry

- **Parent-reported ADHD 'ever diagnosed'**
  - **2003: 7.8%**
  - **2007: 9.5%**
  - **2012: 11.0%**
    - **41% INCREASE IN 9 YEARS, for all 4-17 year-olds**
  - **Low-income rates now = middle-class; Black = White**
    - **Hispanic lower (but fast growing)**
- **Medication rates higher, too:**
  - **Just under 70% of those 'currently diagnosed 'now receive medication**
  - **Largest medication increases: adolescents, adults**

Earlier Explosions: 1990s

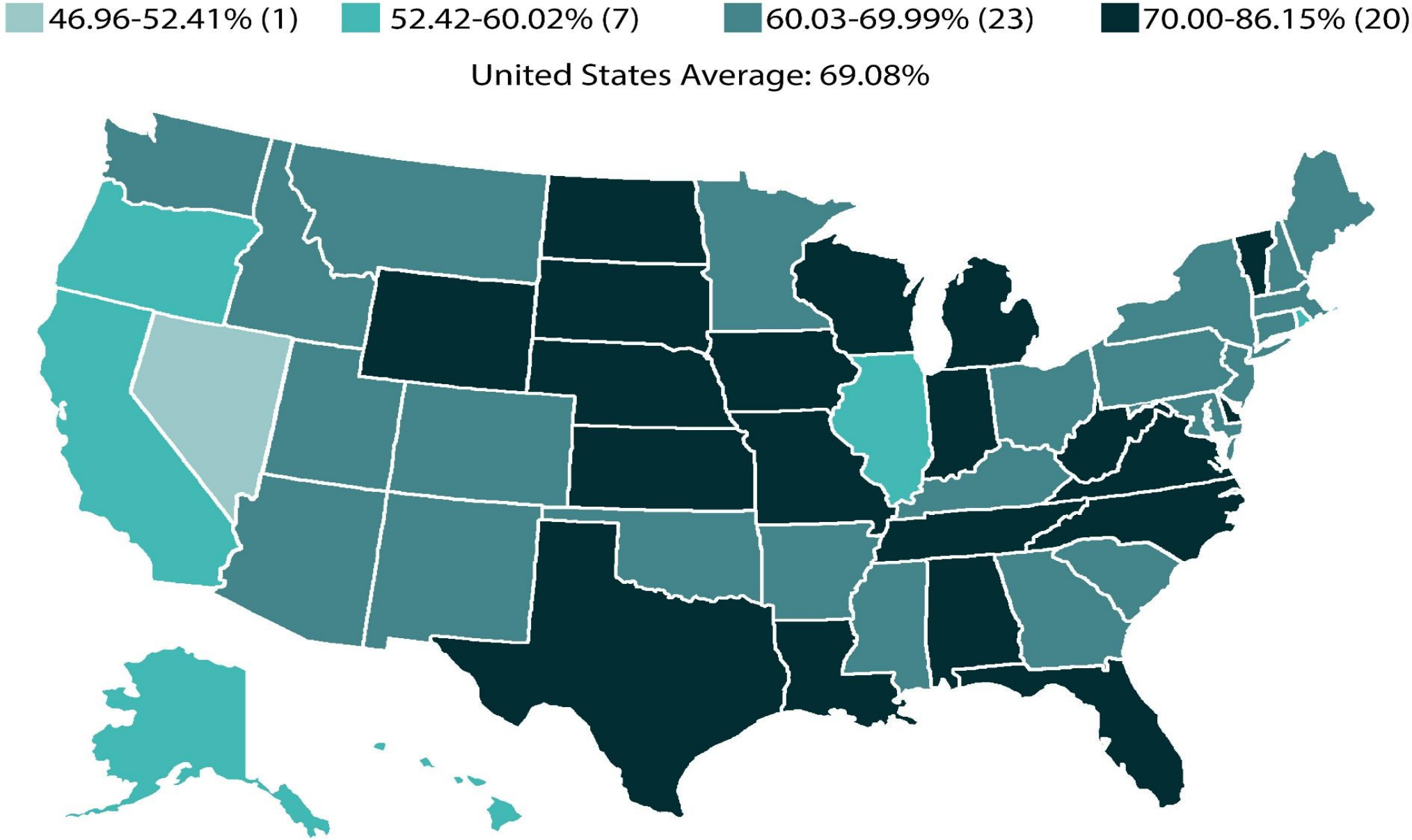
- **Policy shifts:**
  - **IDEA: ADHD as OHI**
  - **Medicaid: authorizes ADHD**
  - **SSI: ADHD (with other impairment) can qualify**
- **Late 1990s: FDA changes regulations on DTC ads**
- **2000: Concerta (first effective long-acting form)**
- **More and more LBW babies survive**
  - **Distinguish *TRUE PREVALENCE from DIAGNOSED PREVALENCE***

Diagnostic Prevalence:



Source: 2011-2012 NSCH, Children Aged 4-17

Medication Rate Given Current Diagnosis:



Source: 2011-2012 NSCH, Children Aged 4-17

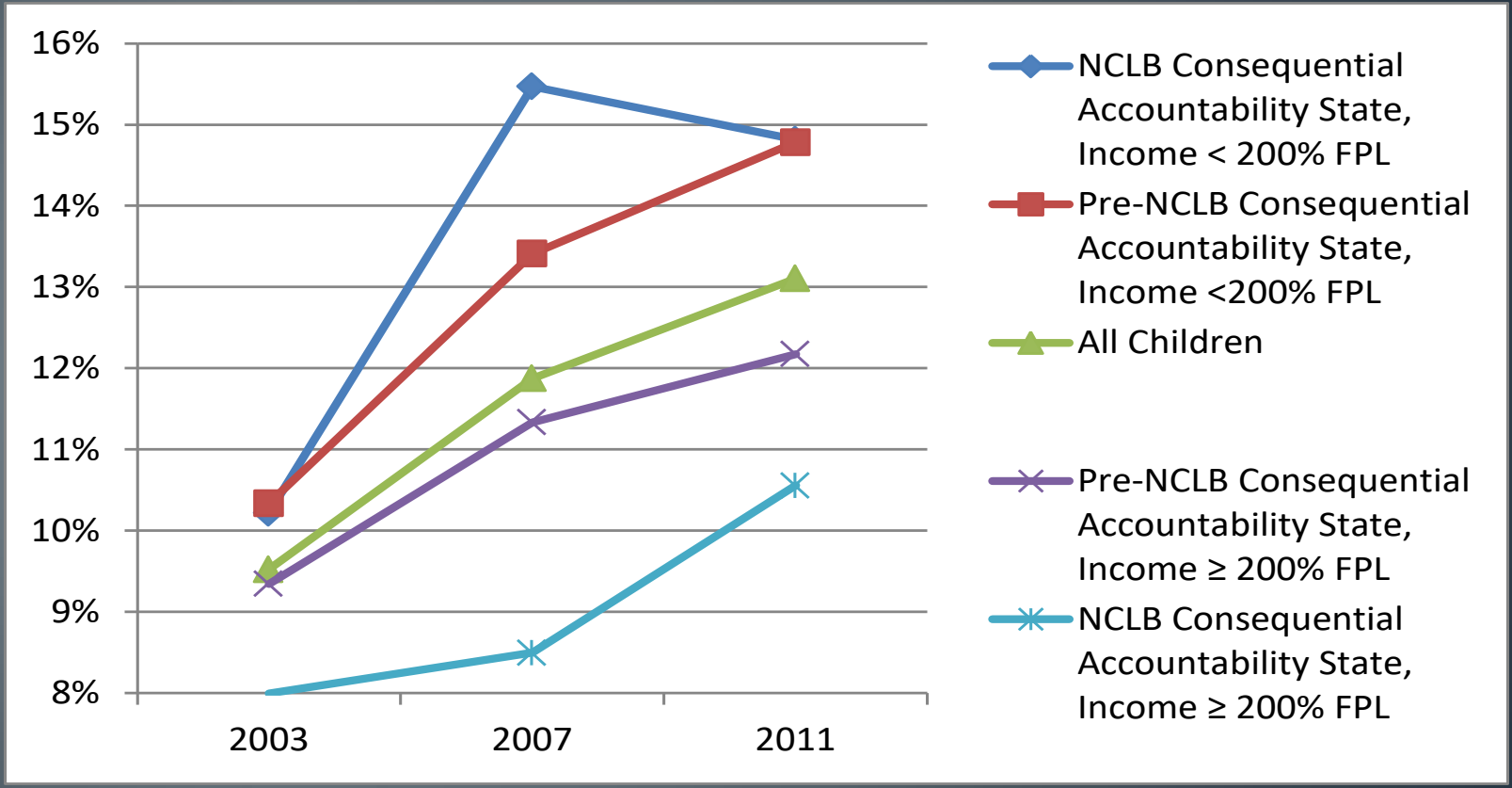
What does *not* explain "area variation"

- **Demographics**
  - Hispanic population clearly higher in California, and traditionally the lowest rates of diagnosis
  - Eliminated a little of the CA-NC difference but not most
  - **Hispanic rates growing FAST, esp. in California
- **Rates of health-care providers**
  - Explains other disorders, but not here
- **State "culture"**
  - May explain some regional differences (not state differences)

**Consequential accountability

- 1970s-80s: public school reforms “input focused”
  - Reduce class size, pay teachers more, etc.
- Results not consistent; shift in 1990s to “output focused”
  - I.e., incentivize test score improvements per se
- Consequential accountability—districts get ‘noted’ or even cut off from funds, unless test scores go up
  - 30 states implement such laws < 2000
- Then, becomes law of the land for all states with No Child Left Behind (takes effect 2002-3)

Consequential accountability introduced via NCLB was associated with higher ADHD diagnostic prevalence increases among low-income children aged 8-13 from 2003-2007, but there was no association from 2007-2011 (unadjusted results)



District of Columbia is included within the 21 No Child Left Behind consequential accountability states.
NCLB: No Child Left Behind; FPL: Federal poverty level
N=24,982 (2003), 22,467 (2007), 24,426 (2011)
Sources: 2003, 2007, and 2011 National Survey of Children's Health

"Unintended effect"

- Accountability laws encourage ADHD diagnosis for at least two reasons:
  - #1: Diagnosis may lead to treatment, which may help boost achievement test scores
    - Scheffler et al. (2009), Zoega et al. (2012)
  - #2: In some states/districts, diagnosed youth are excluded from the district's average test score!
    - Gaming the system, although NCLB eventually outlaws this
- Why poorest kids? NCLB targets Title I schools

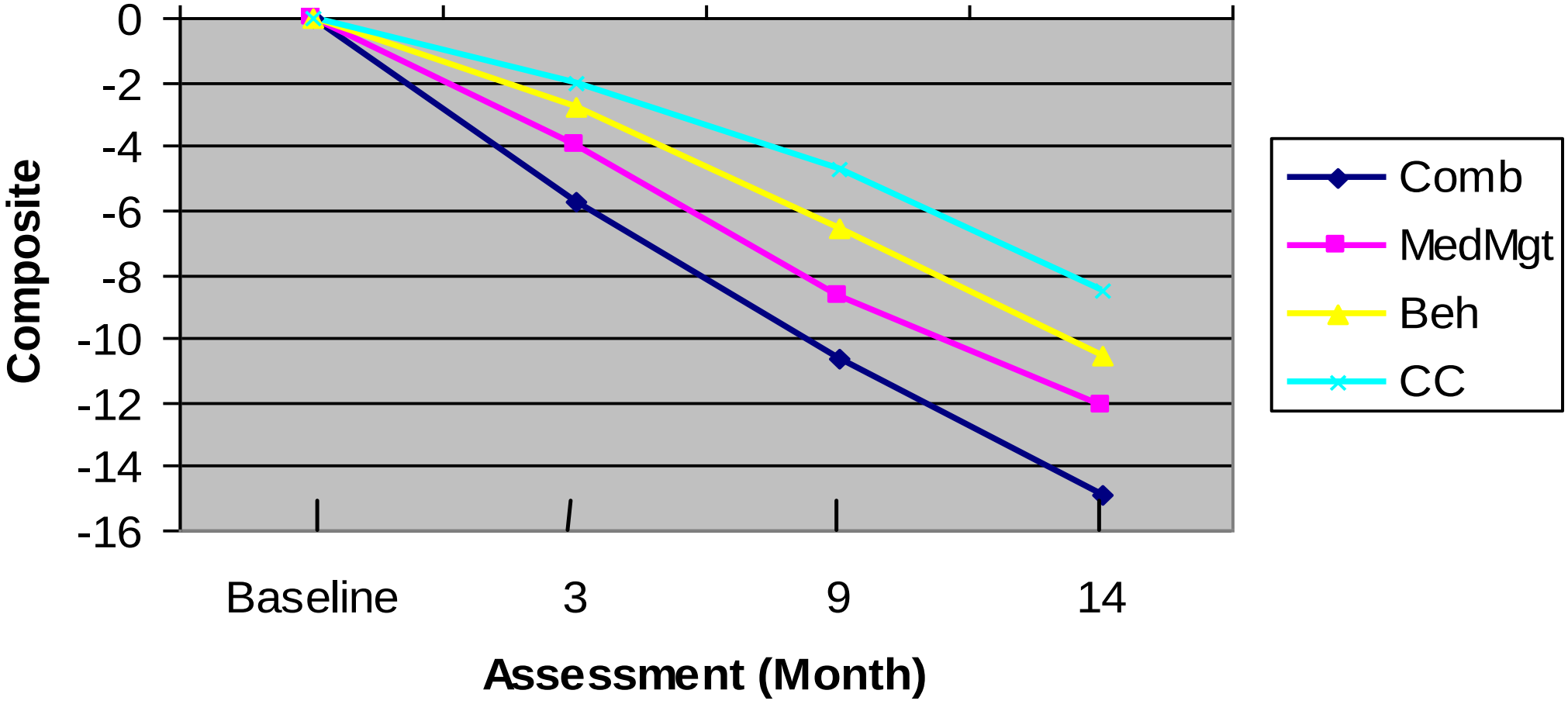
Main culprit-- Quick and dirty assessments?

- We haven't emphasized assessment, but it takes several hours to 'do it right'
  - Thorough developmental history
  - Normed parent and teacher rating scales
  - Medical eval: rule-outs
  - Achievement and cognitive testing re: learning issues
  - Yet computerized attention tests , brain scans not definitive
- In practice, however, 10-15' with non-specialist carries day
  - Lack of training, lack of reimbursement
  - Need 'team approach'

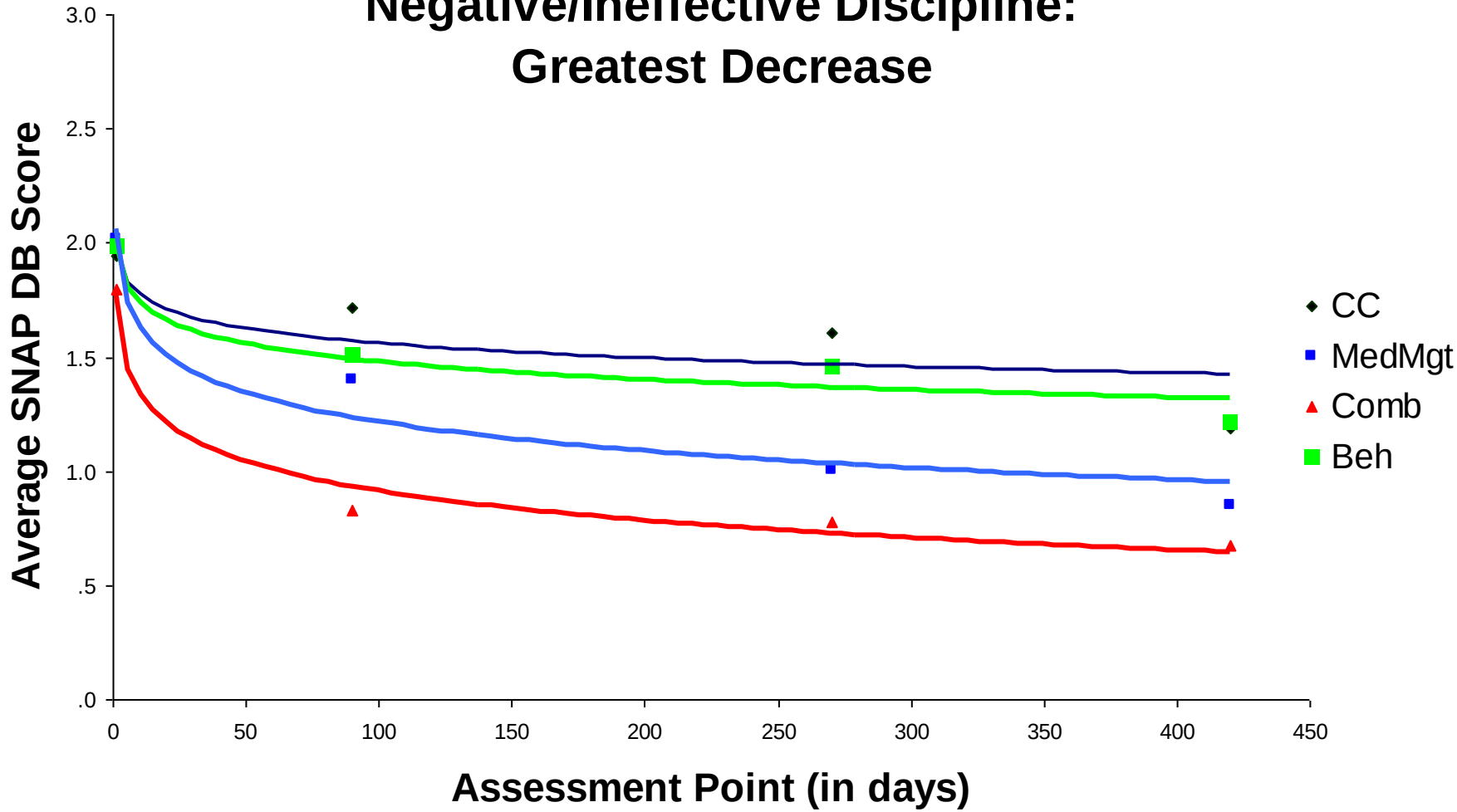
Treatment Strategies for ADHD… In Two Slides (!)

- **See next 2 slides....**

Composite Score
Adjusted for Baseline
Conners et al., 2001

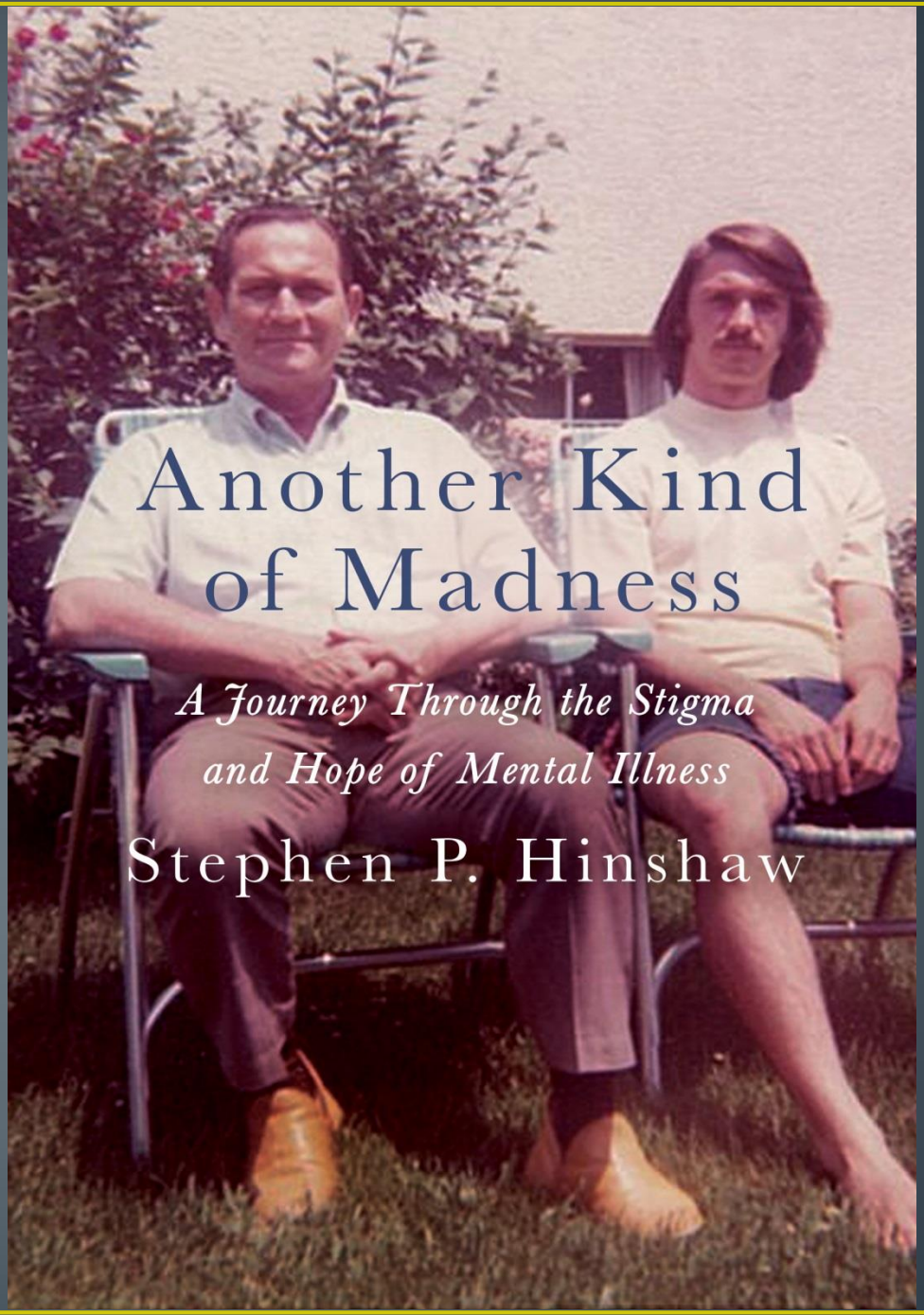


Outcomes Across 14 months
Teacher SNAP DB
Negative/Ineffective Discipline:
Greatest Decrease



Stigma and ADHD

- Wouldn't stigma pertain to ultra-severe disorders (e.g., psychosis), and not ADHD?
  - Paradoxically, inconsistency in behavior (with high expectations) may trigger strong stigma
    - E.g., high-functioning ASD
  - Overdiagnosis, paired with accounts of faking symptoms, stigmatize the entire condition
  - Parents still fearful of receiving the diagnosis for their kids, etc.


Another Kind of Madness
A Journey Through the Stigma and Hope of Mental Illness
Stephen P. Hinshaw

Shame, Silence, Stigma
This afternoon's session

- Idyllic childhood in Midwest, except for mysterious disappearances of dad for half-year to year at a time
- Began in 30's in Pasadena: At age 16 he believed he could save the free world from the Nazi threat by flying
- 6 months at Norwalk
  - Then Stanford and Princeton (Einstein, Russell)
  - Then Byberry
- Life of brilliance and madness had begun

As a boy…

- I knew nothing about his disappearances into hospitals
  - Doctor's orders: Children would be permanently destroyed
- Internalization
- Not until first spring break from college, back East, did he divulge the truth
  - I diagnosed him with bipolar disorder
- Moral: I went into psychology, yet terrified until I opened up
- WE MUST DO SCIENCE <AND> TELL OUR STORIES!

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- Colleagues with shared and contrasting ideas
- The HELP Group!