MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

ADHD & PTSD

Child & Adolescent Psychopharmacology

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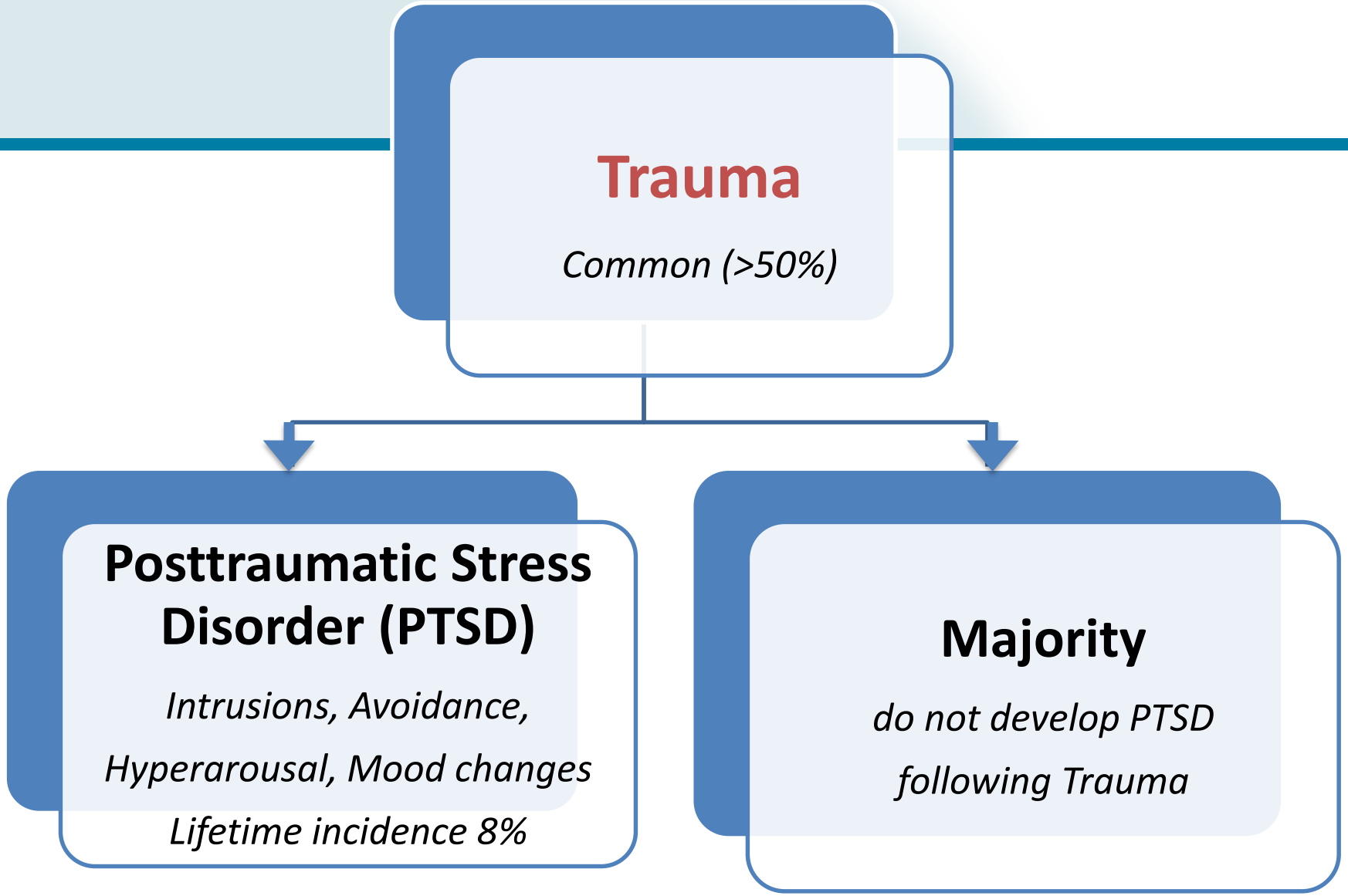
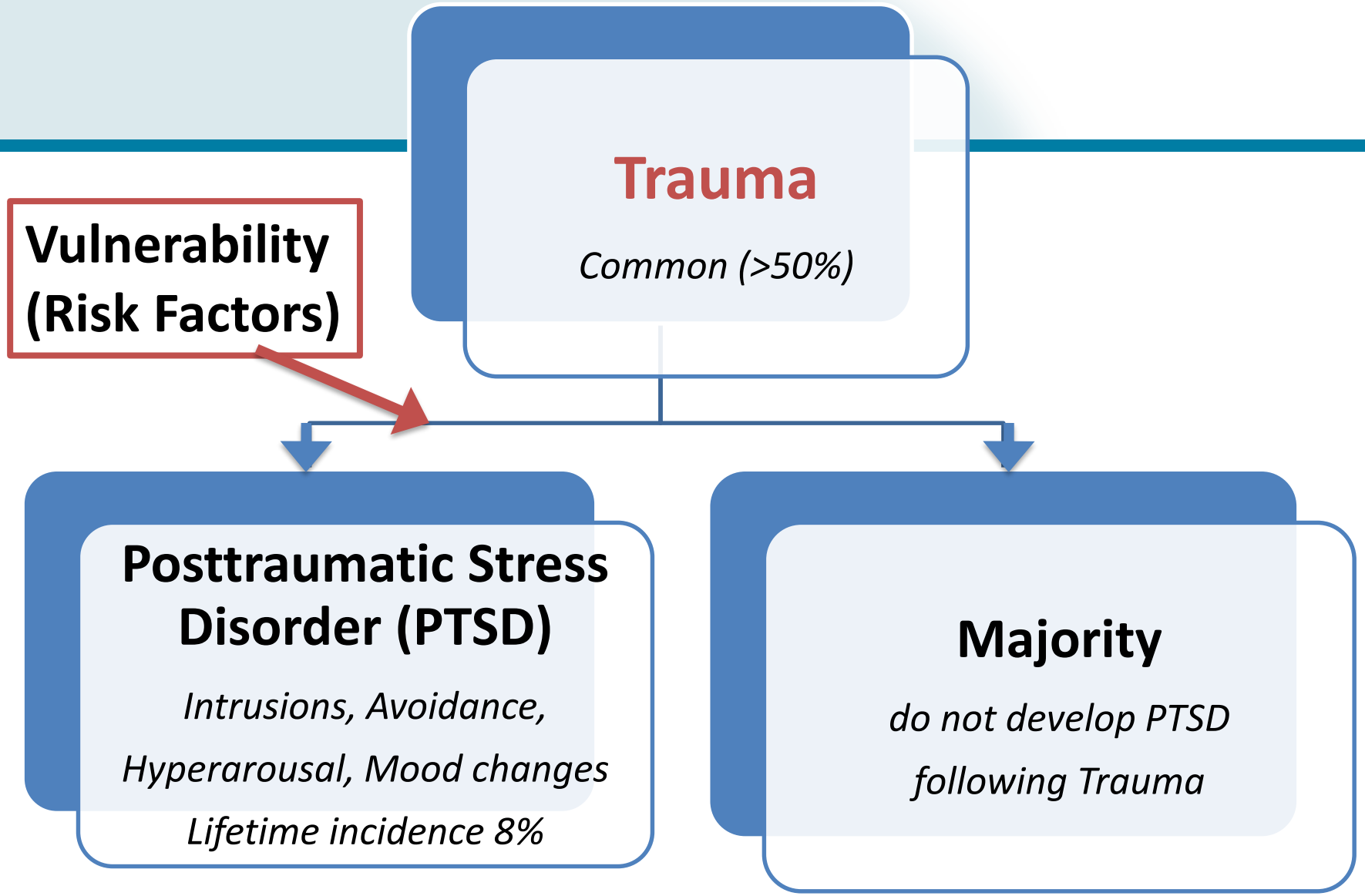
Objectives

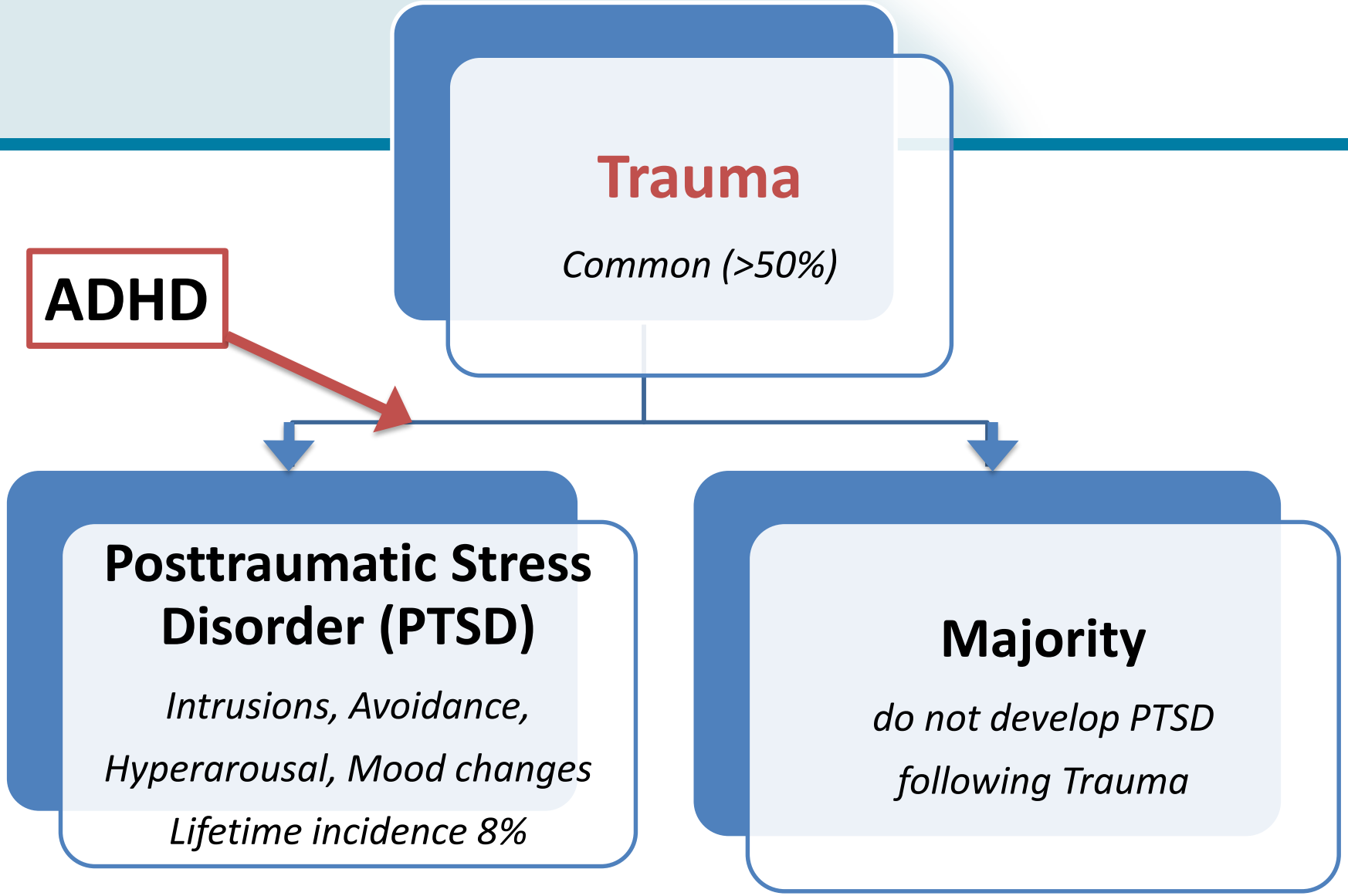
1) Describe evidence that ADHD is a ***risk factor*** for PTSD
2) Present evidence for ***neurobiological vulnerability*** to PTSD in ADHD
3) Discuss ***clinical implications***

Trauma

Common (>50%)


Trauma
Common (>50%)
Posttraumatic Stress Disorder (PTSD)
Intrusions, Avoidance,
Hyperarousal, Mood changes
Lifetime incidence 8%
Majority
do not develop PTSD
following Trauma


Trauma
Common (>50%)
Vulnerability (Risk Factors)
Posttraumatic Stress Disorder (PTSD)
Intrusions, Avoidance,
Hyperarousal, Mood changes
Lifetime incidence 8%
Majority
do not develop PTSD
following Trauma


Trauma
Common (>50%)
ADHD
Posttraumatic Stress Disorder (PTSD)
Intrusions, Avoidance,
Hyperarousal, Mood changes
Lifetime incidence 8%
Majority
do not develop PTSD
following Trauma

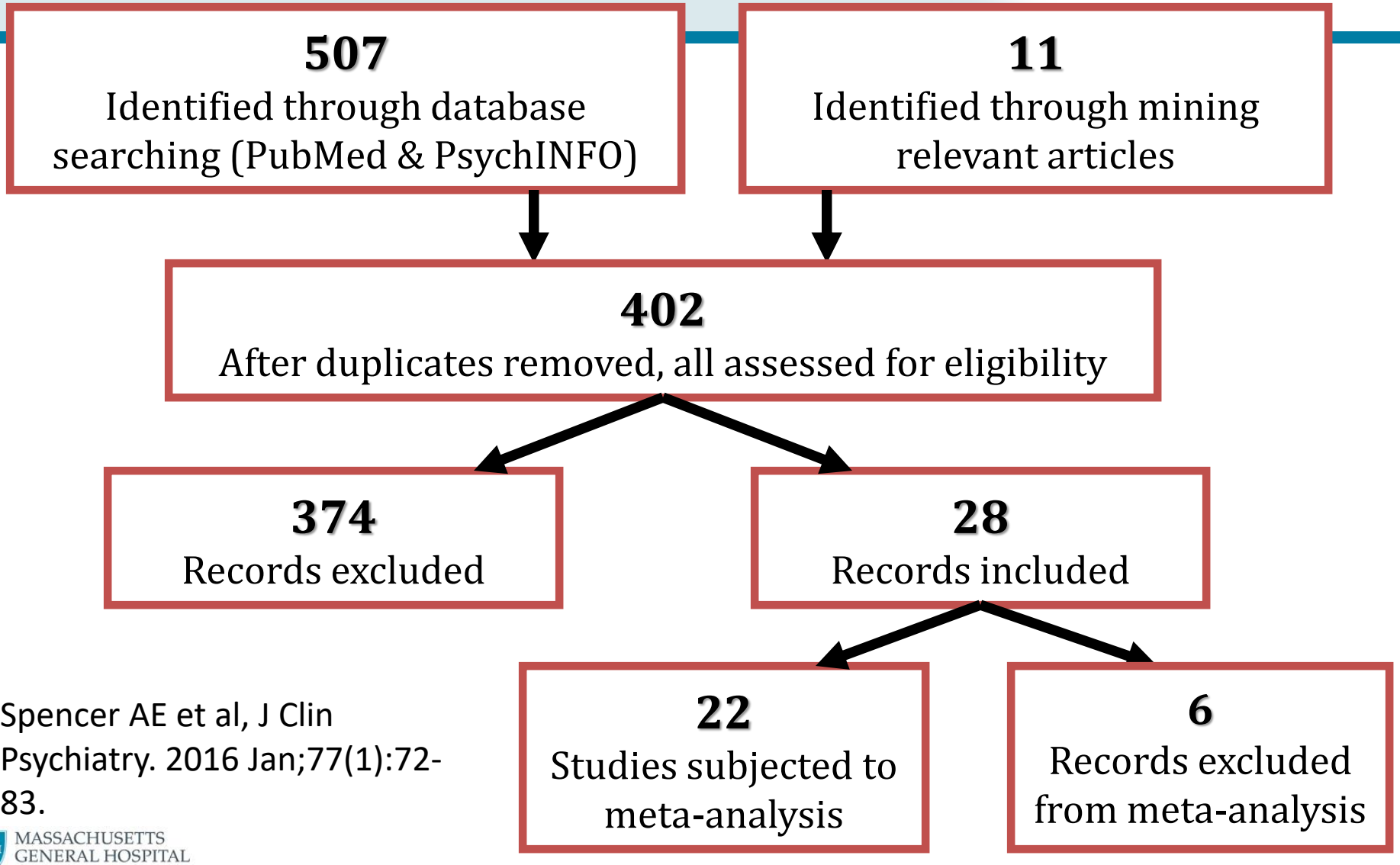
ADHD is a possible risk factor for PTSD

- ADHD is a prevalent neurobiological disorder that onsets in the preschool years, while PTSD more commonly develops in later years
- ADHD is associated with high levels of risk-taking and impulsivity that could lead to traumatic events
- Deficits in attention and prefrontal cortical function resembling those in ADHD have been identified in PTSD

Meta-analysis of link between ADHD & PTSD

- Conducted a systematic review of the literature on the relationship between ADHD and PTSD and subjected the data to qualitative and quantitative analysis
- To examine the evidence linking ADHD to PTSD in adults and children, attending to the directionality of the association

PRISMA: Sources



Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

Risk for PTSD in Individuals with ADHD

Meta-analysis: Relative Risk for PTSD in ADHD

- 15 samples from 13 studies
- 9 Pediatric, 6 Adult
- **RR=2.9, p=0.0005**

Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

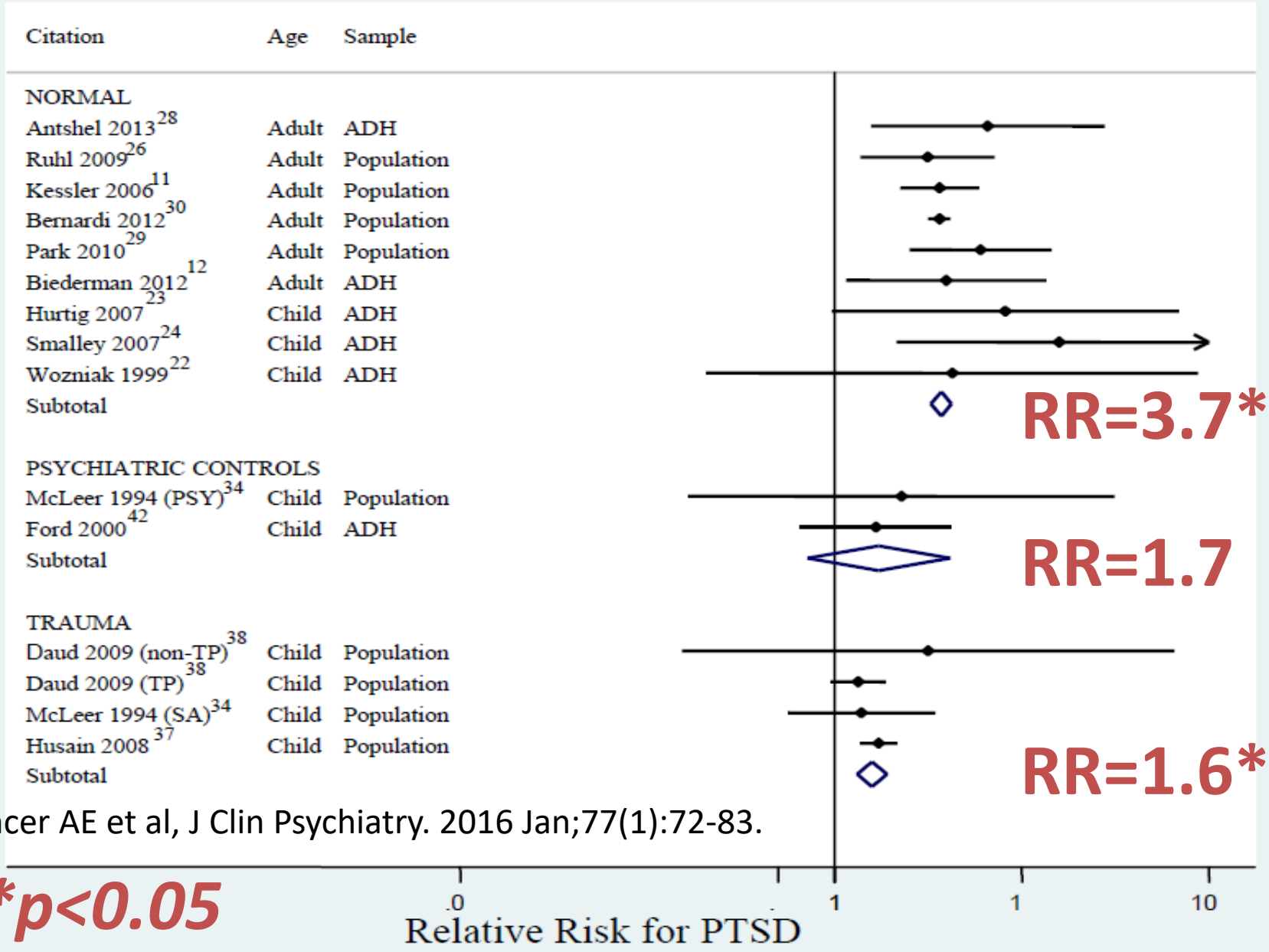
Meta-regression: PTSD in ADHD

Variable	P value
Referral Status	0.17
Age Group	0.20
Mean Age	0.001*
Control Group	0.006*
Study Sample	0.20

Mean age had a significant effect on relative risk, with studies of older patients showing greater relative risk

Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

Figure 2a. Meta-Analysis of the Relative Risk for PTSD in Individuals with ADHD



Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

*p<0.05

Meta-analysis: Relative Risk for PTSD in ADHD

Control Type	# Samples	Relative Risk	P value
Normal	9	3.7	0.001*
Traumatized	4	1.6	0.003*
Psychiatric	2	1.7	0.08

Significantly increased relative risk for PTSD in ADHD in samples using normal and traumatized controls

Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

Risk for ADHD in Individuals with PTSD

Meta-analysis: Relative Risk for ADHD in PTSD

- 16 samples from 13 studies
- 11 Pediatric, 5 Adult
- **RR=1.7, p<0.0005**

Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

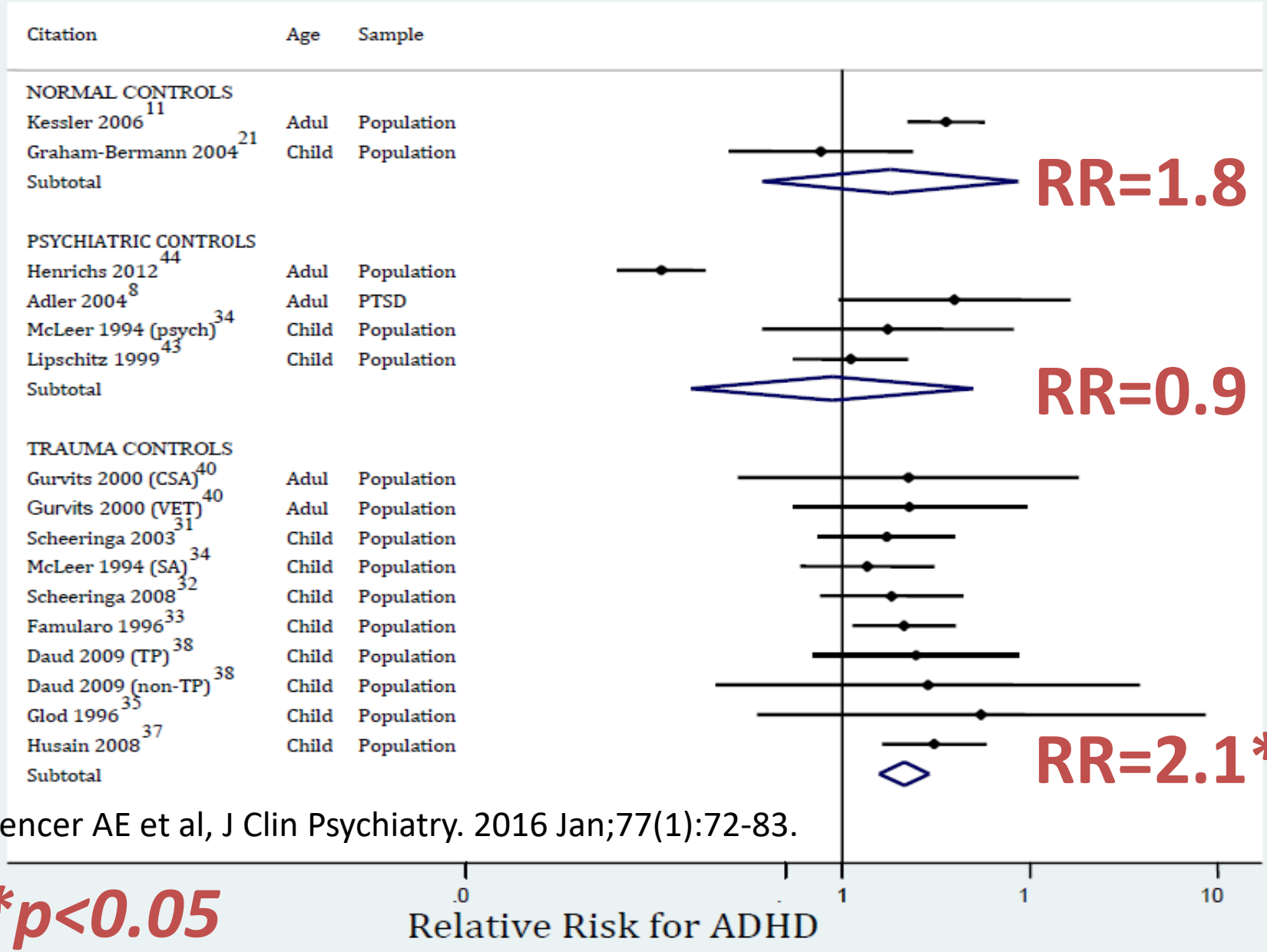
Meta-regression: ADHD in PTSD

Variable	P value
Referral Status	0.07
Age	0.69
Mean Age	0.9
Control Group	0.65
Study Sample	<0.00005*

Only Study sample significantly affected Relative Risk

Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

Figure 2b. Meta-Analysis of the Relative Risk for ADHD in Individuals with PTSD



Spencer AE et al, J Clin Psychiatry. 2016 Jan;77(1):72-83.

*$p<0.05$

Relative Risk for ADHD in PTSD By Control Type

Control Type	# Samples	Relative Risk	P value
Normal	2	1.8	0.32
Traumatized	10	2.1	<0.0005*
Psychiatric	4	0.9	0.16

Significantly increased relative risk for ADHD in PTSD in samples using traumatized controls

Spencer AE et al, *J Clin Psychiatry, Jan 2016*.

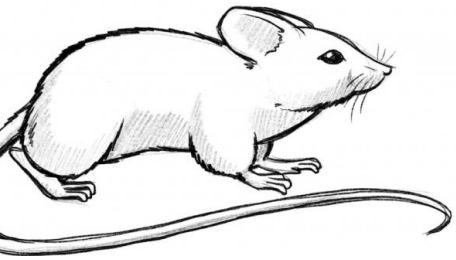
Additional Findings

- ADHD onset earlier than PTSD in all studies reporting temporality
- Significant, positive correlation between severity of symptoms when both disorders present

Conclusion:
ADHD may be a risk factor for PTSD

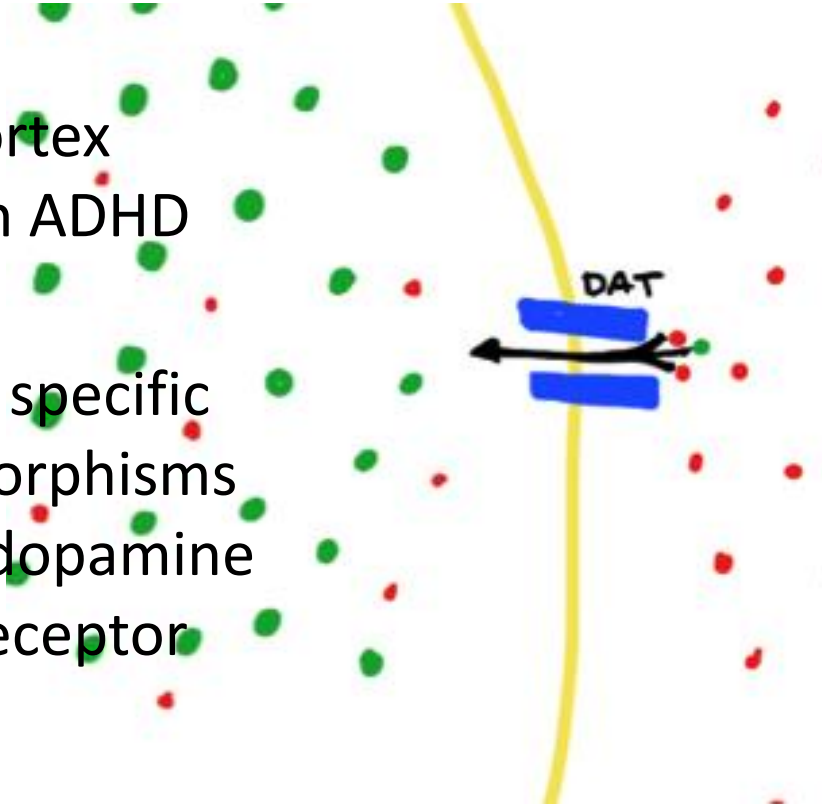
- Robust, bidirectional association between ADHD and PTSD in both community and clinical samples
- Compared to normal controls, individuals with ADHD had ***nearly 4x*** the risk of developing PTSD than those without ADHD
- Findings were not explained by trauma exposure

Neurobiological links between ADHD & PTSD



- In rodents, prenatal nicotine exposure leads to both an ADHD-like phenotype as well as to deficits in fear extinction (deficient in PTSD)

- Irregularities in dopaminergic neurotransmission and prefrontal cortex dysfunction have been found in both ADHD and PTSD
- Both ADHD and PTSD have common specific genetic risk factors, including polymorphisms in the 3'-untranslated region of the dopamine transporter gene and cannabinoid receptor gene



Neurobiology of PTSD

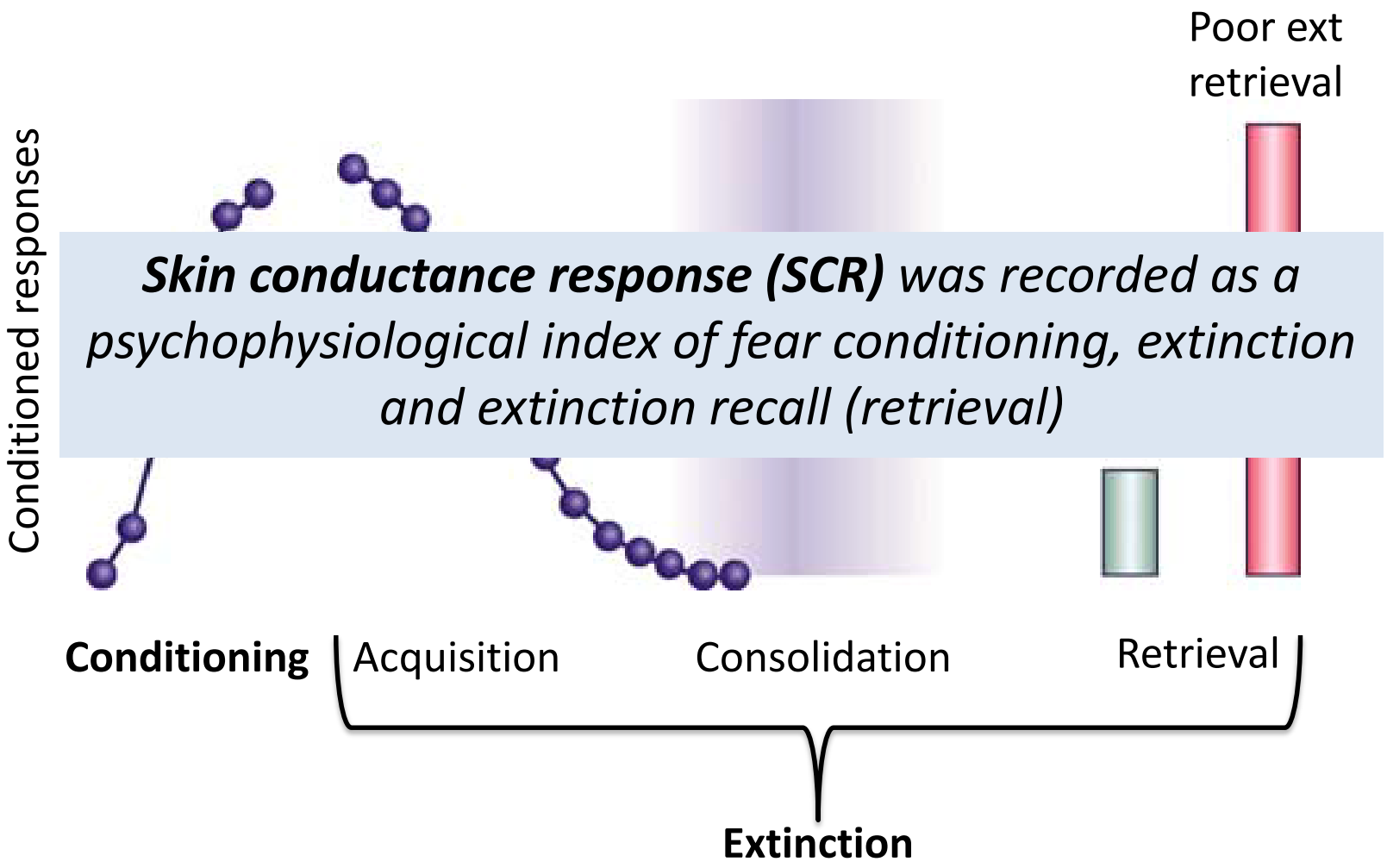
- Fear extinction learning and recall are impaired in PTSD ***vs.*** traumatized subjects without PTSD, as measured by Skin Conductance Response and fMRI
- Structural MRI studies also show reduced hippocampal volumes in PTSD ***and*** high-risk individuals

❖ *Might individuals with ADHD have dysfunctional activation in brain structures mediating fear extinction, explaining their high risk of developing PTSD?*

Examining Fear Circuitry in ADHD

- We studied **medication naïve young adults** with ADHD (N=27) and without ADHD (N=20) with ***no trauma history*** using the 2-day fear conditioning and extinction neuroimaging paradigm developed by Milad et al
- We **hypothesized** that ADHD subjects would demonstrate dysfunctional activation in brain structures that mediate fear extinction and learning

Fear Conditioning & Extinction



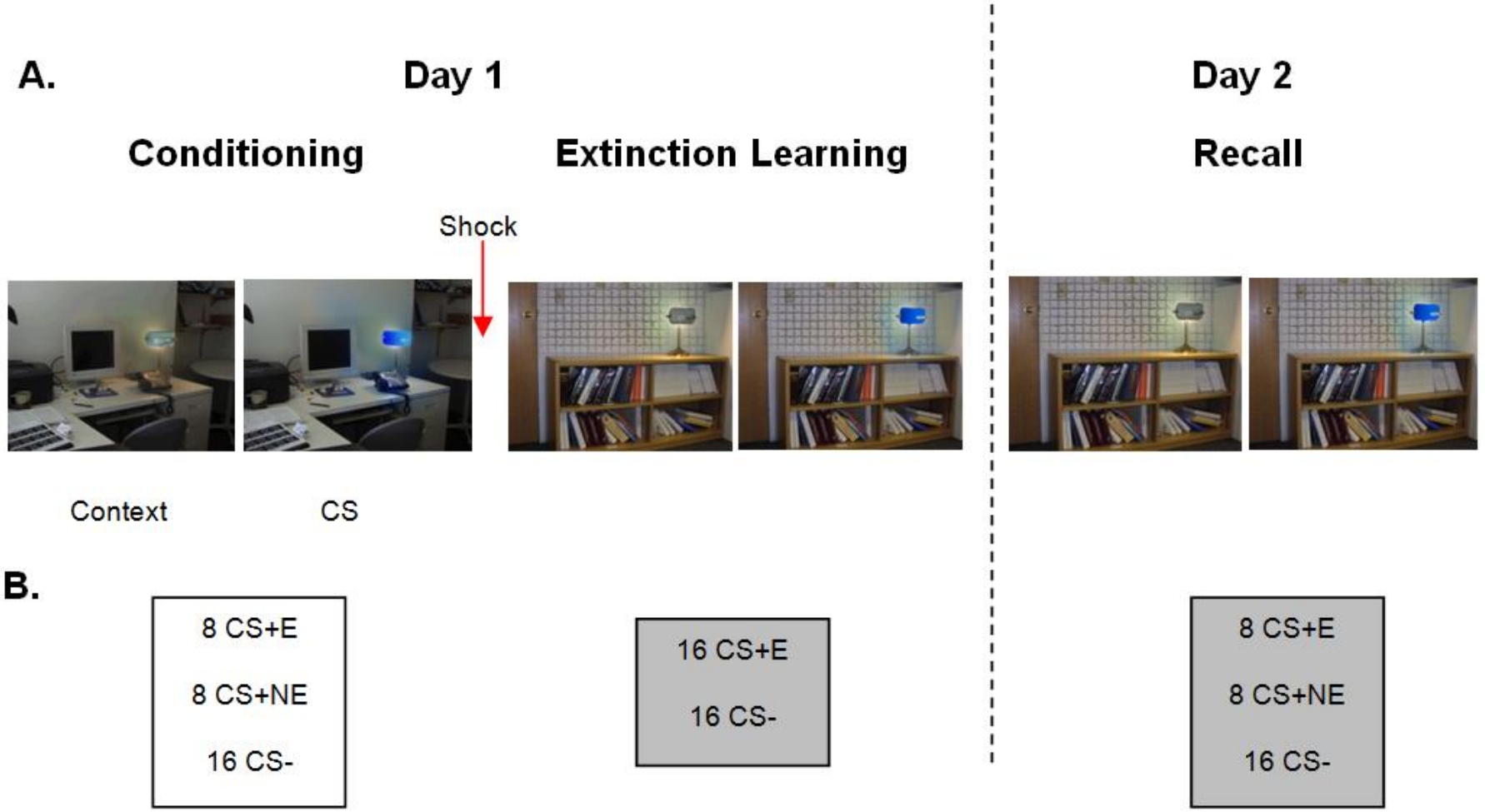
Neuropsychopharmacology (2007) **33,** 56-72. doi:10.1038/sj.npp.1301555

Fear conditioning and extinction paradigm

- Participants underwent a 2-day fear conditioning and extinction paradigm in a **3-T fMRI scanner**
- Two Ag/AgCl recording electrodes were attached to the palm of the participant's non-dominant hand to measure **skin conductance response (SCR)**

- **Electrical stimulation** was delivered through electrodes on the 2nd and 3rd fingers of the right hand
- **Shock intensity** was first calibrated for each participant to reach a highly annoying, but not painful, stimulation

Experimental Protocol



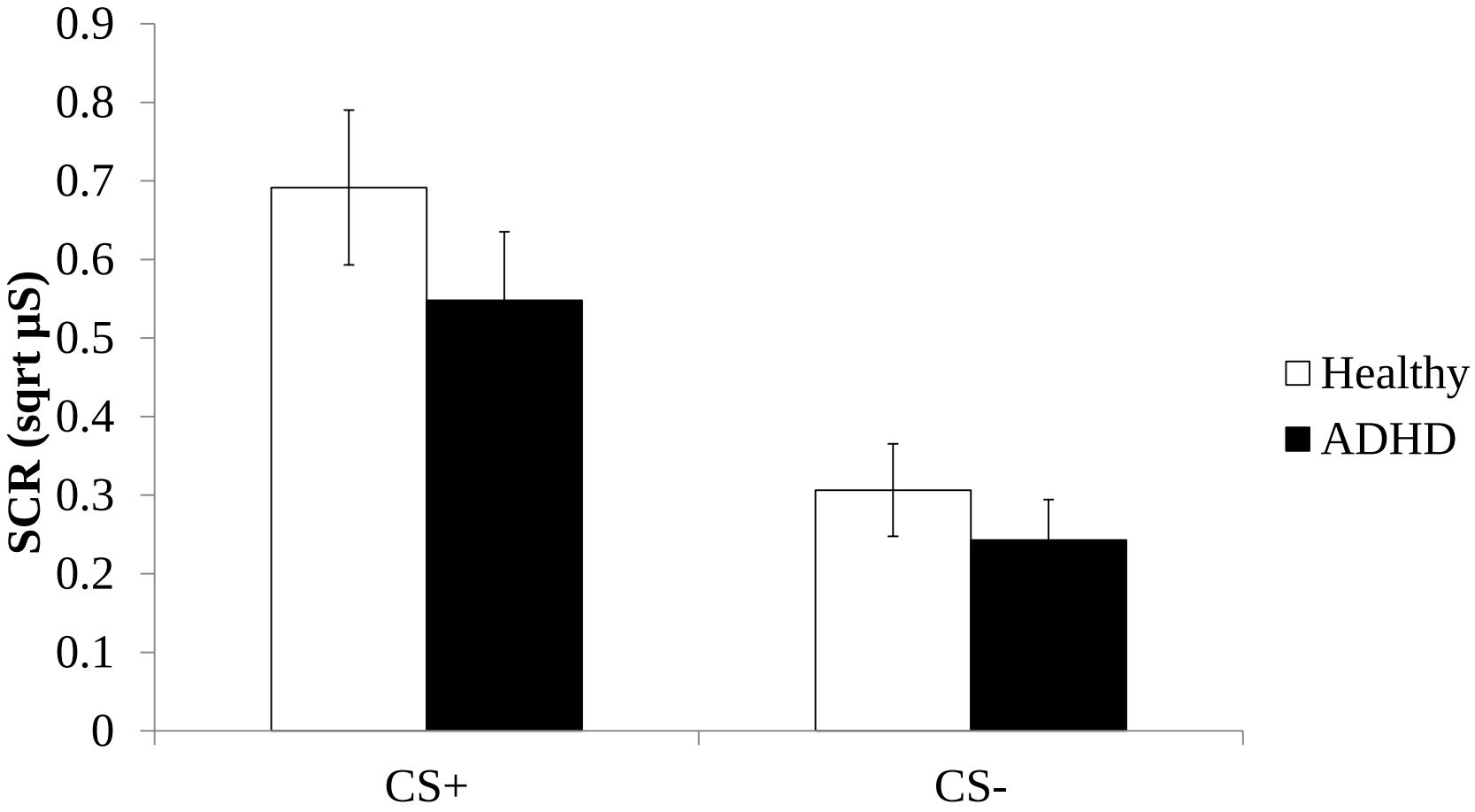
Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

Demographics and Clinical Scores

	ADHD n=27	HC n= 20	Statistic	p-value
Age (years)	23.3 ± 1.0	25.1 ± 0.8	z = 1.70	0.09
Sex (female)	14	10	$X^2 = 0.02$	0.90
Education (years)	15.4 ± 1.4	17.3 ± 0.4	T = 3.43	<0.001*
Shock Level (mA)	2.1	2.1	T = -0.37	0.71
AISRS Score	39.0 ± 1.6	---	----	----

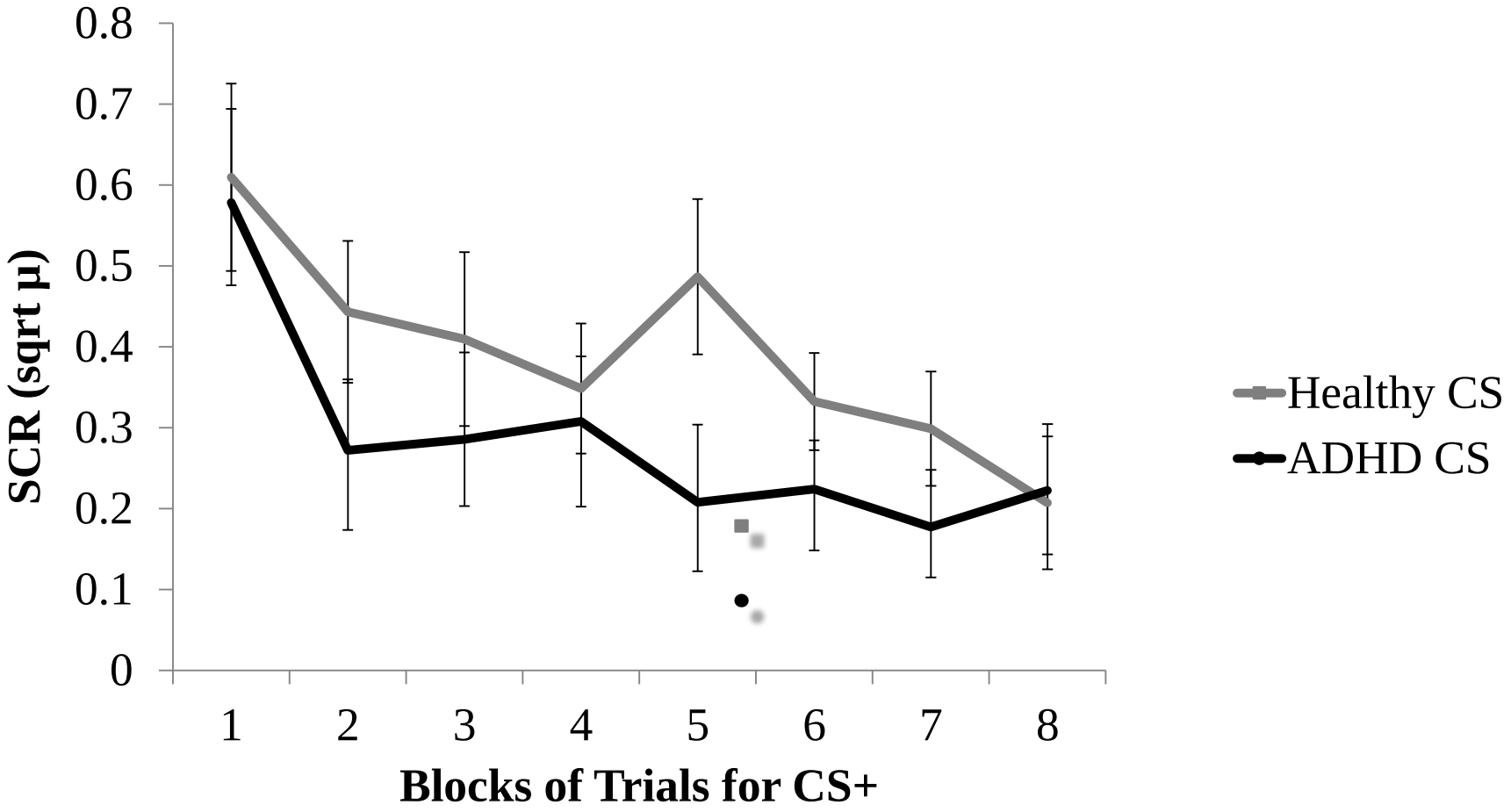
Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

Equivalent Skin Conductance Response Between Groups during Conditioning



Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

Comparable Skin Conductance Response in Both Groups During Extinction Learning



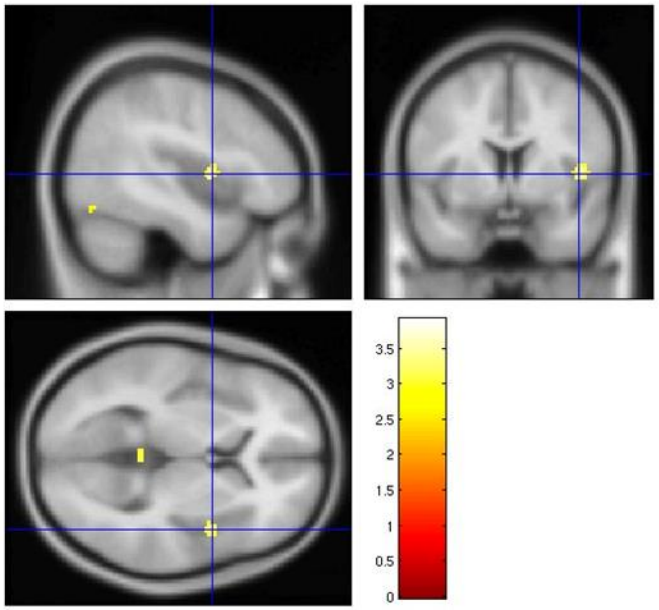
Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

fMRI Early Extinction Contrast

eCS+E vs. eCS- (early extinction)

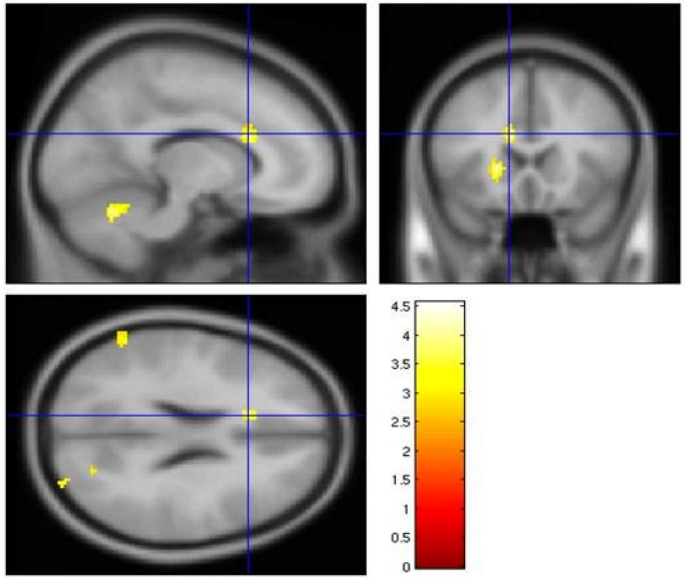
R Insular Cortex

ADHD > HC



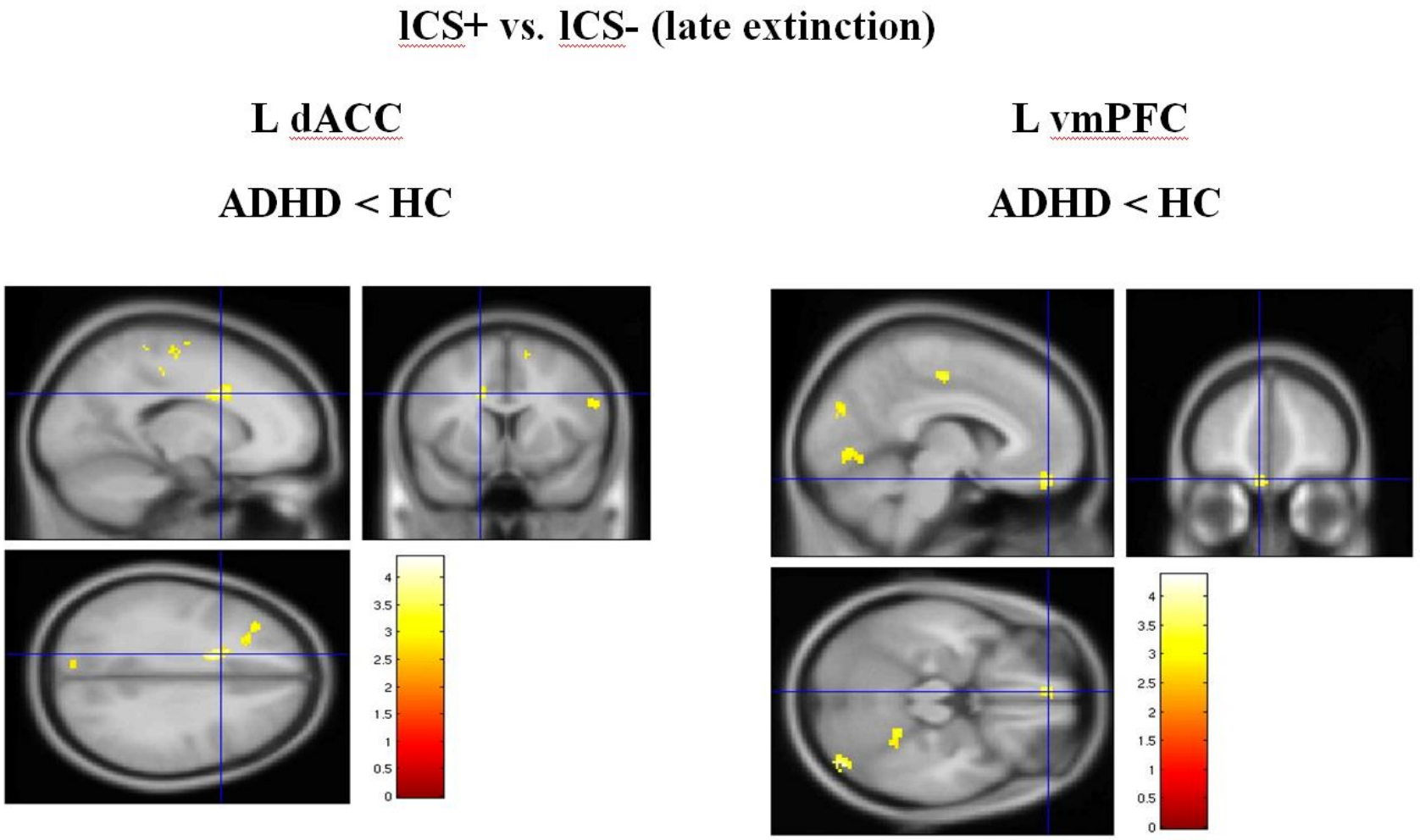
L dACC

ADHD < HC



Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

fMRI Late Extinction Contrast



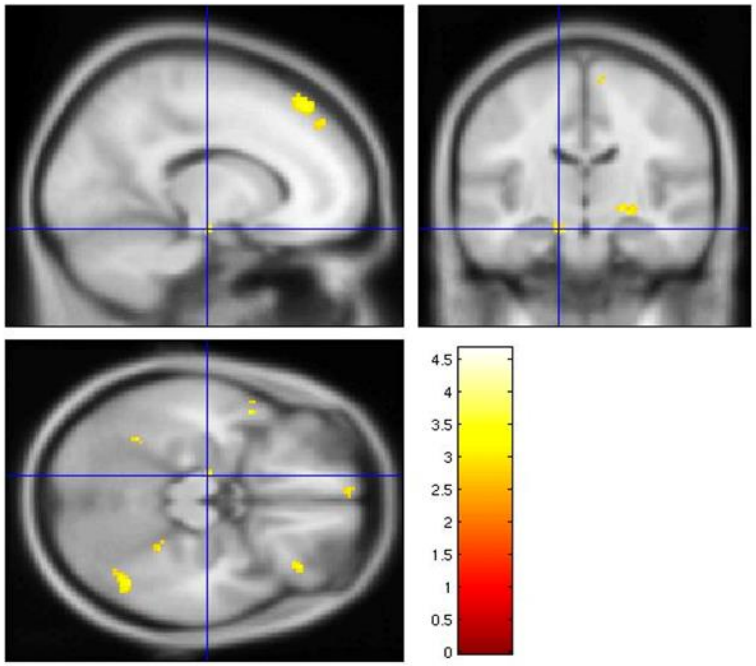
Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

fMRI Extinction Recall Contrast

eCS+E vs . eCS- (extinction recall)

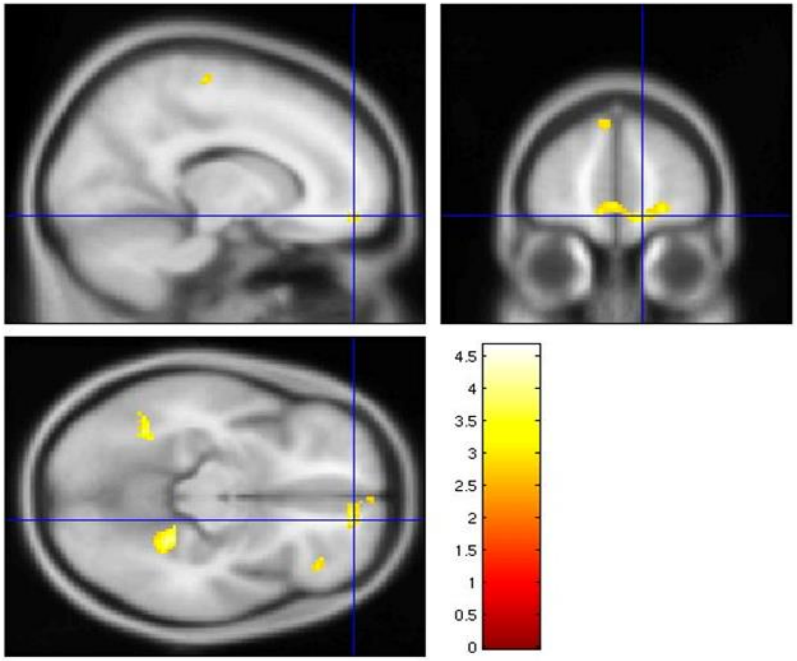
L Hippocampus

ADHD < HC



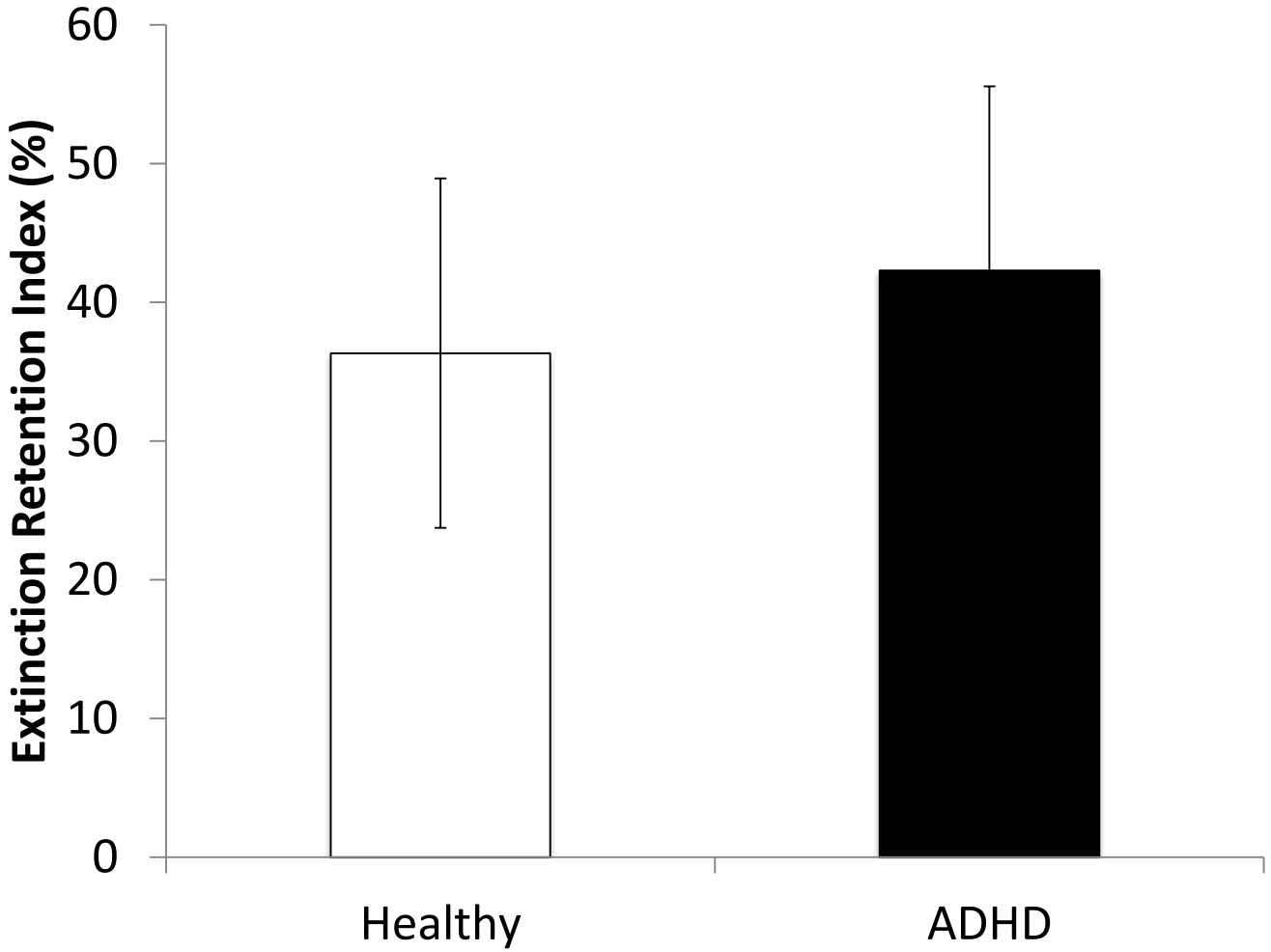
R vmPFC

ADHD < HC



Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

No difference in the Extinction Retention Index Between Groups during Extinction Recall



Spencer AE et al, *Psychiatry Res*. 2017 Feb 10;262:55-62.

Deficient fear circuitry in ADHD

- ✓ Medication-naive, non-traumatized subjects with ADHD have dysfunctional activation in brain structures that mediate fear extinction learning and extinction recall
  - ➔ including in **vmPFC, hippocampus, dACC and insula**
- ✓ First time that deficits in fear circuitry during late extinction learning and recall have been demonstrated in ADHD

Some similar deficits as in PTSD

- **Deficient activation of vmPFC and hippocampus during extinction recall** in ADHD is consistent with previous findings in PTSD (vs. traumatized controls without PTSD)
- May begin to explain the strong statistical association between the disorders

Neurobiological vulnerability to PTSD?

- Multiple investigators documented impaired activation in vmPFC and hippocampus during extinction recall in PTSD
- Our study suggests that these abnormalities may actually precede PTSD, representing **pre-trauma vulnerability**

Finding May Not Be Specific to ADHD

- Structural imaging studies have also shown that diminished hippocampal volumes are an antecedent, pre-trauma risk factor for PTSD
- Early studies have identified impaired fear circuitry in other psychiatric disorders including OCD and schizophrenia
- Our meta-analysis showed that subjects with other psychiatric disorders had similar vulnerability to PTSD as subjects with ADHD

Clinical Implications

- Patients with ADHD may be vulnerable to developing PTSD
- Consider screening for trauma and PTSD in patients with ADHD
- Consider screening patients with PTSD for ADHD
- When both disorders present, consider functional impairment from and treatment of both
- Not known how medications for ADHD affect fear circuitry

Future Work

- Further work is needed to:
  - **Replicate** these findings in subjects with ADHD and other psychiatric populations
  - **Study** how widely used medications for ADHD affect fear circuitry and subsequent development of PTSD