Blunted Ventral Striatum Development in Adolescence Reflects Emotional Neglect and Predicts Depressive Symptoms

Hanson J. L., Hariri, A. R., & Williamson, D. E. (2015)

2020.10.05

Computational Clinical Science Lab

Jihyun Hur

Authors

Jamie L. Hanson

- Postdoc Fellow at Duke University (~2016)

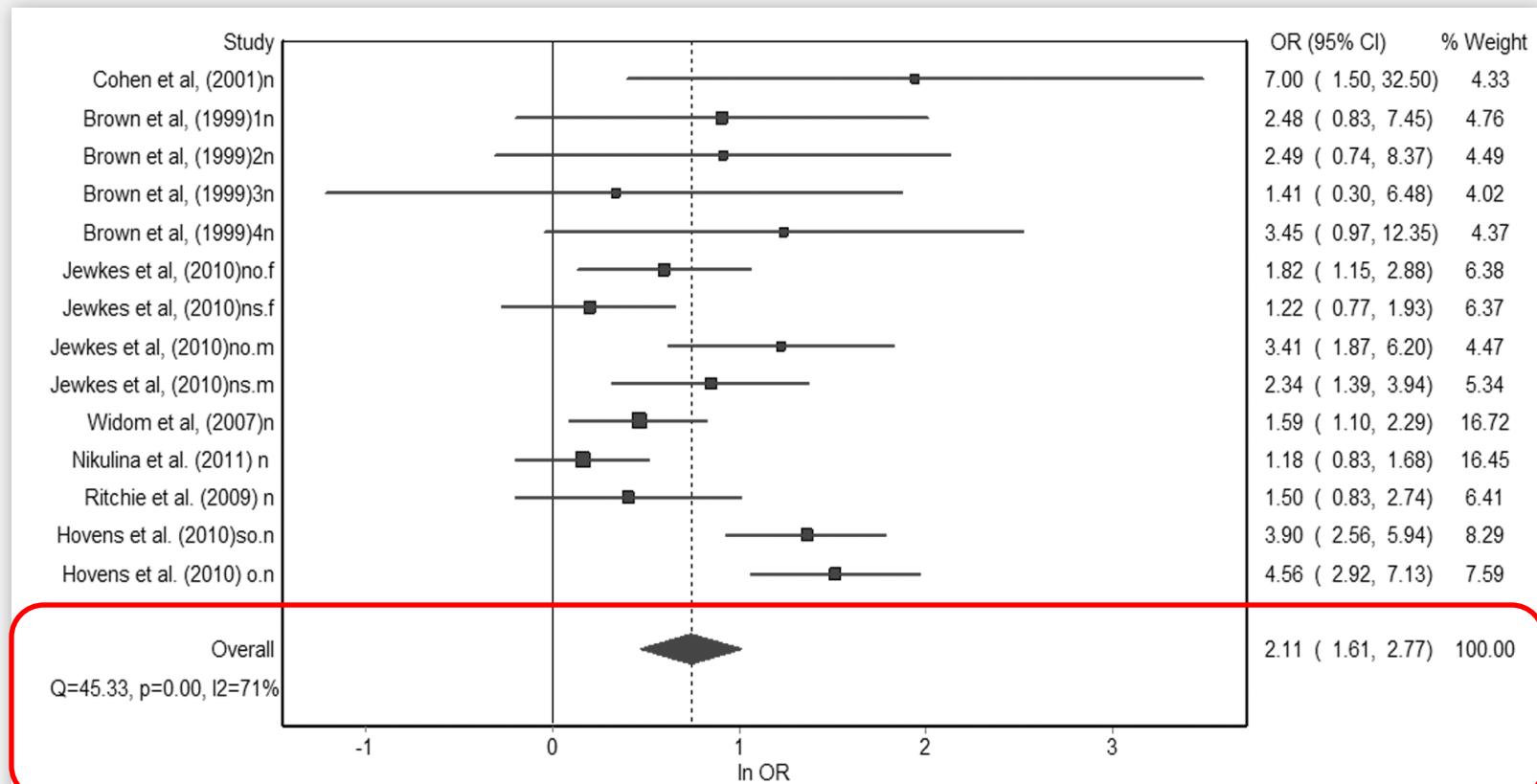- Assistant Professor at the University of Pittsburg

Ahmad R. Hariri

- Professor of Psychology & Neuroscience at Duke University

- Principal Investigator of the Lab of Neurogenetics

Douglas E. Williamson

- Professor in Psychiatry and Behavioral Sciences at Duke University School of Medicine

Early Life Stress (ELS) & Depression

Plot for meta-analysis of the <u>neglect-depressive disorders association</u>
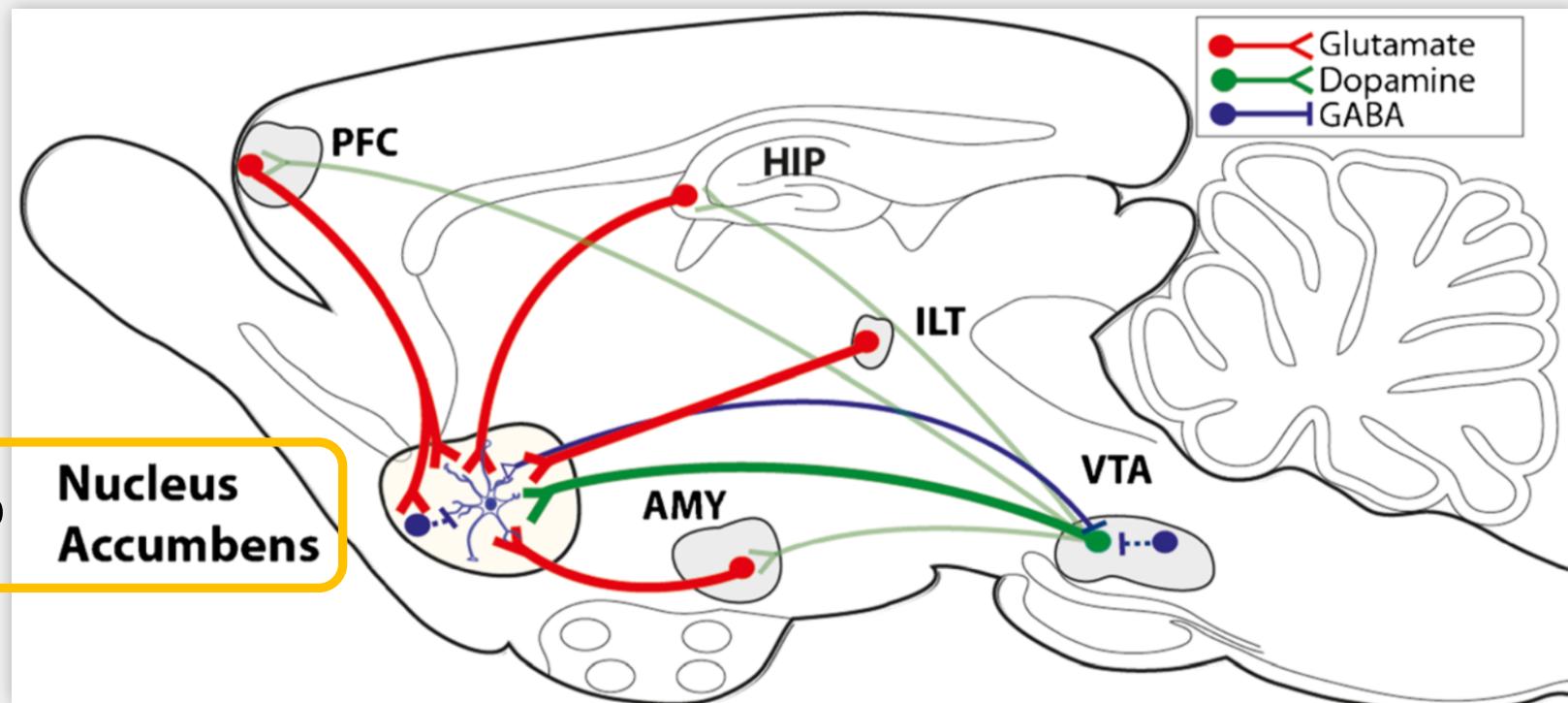

*OR: Odd Ratio

*CI: Confidence Inveral

Norman et al. (2012)

Emotional Neglect (EN)

Emotional Abuse

"**Emotional unresponsiveness**, **unavailability**, and **limited emotional interactions** between parent and child"

Hanson et al. (2015)

Neural Mechanisms of Depression

<u>Blunted Mesolimbic Reward Pathway</u> → Decreased Reward Encoding

Ventral Striatum (VS) ⊃ Nucleus Accumbens

Glutamate
Dopamine
GABA

PFC
HIP
ILT
VTA
AMY

*VTA: Ventral Tegmental Area
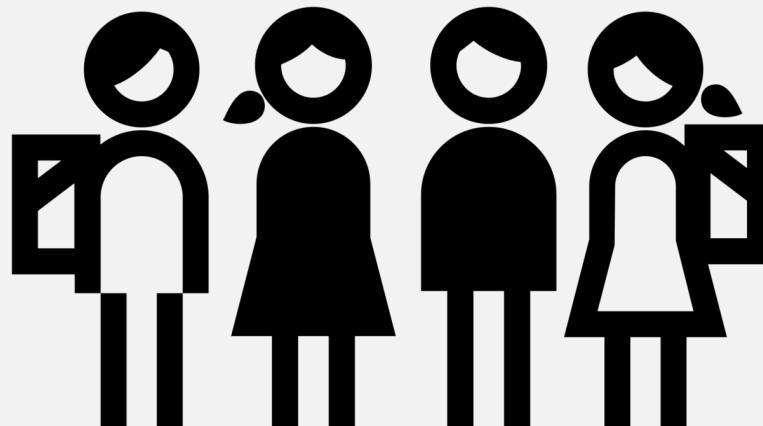
*ILT: Intralaminar Thalamus

*HIP: Hippocampus

*AMY: Amygdala

*PFC: Prefrontal Cortex

Heshmati & Russo (2015)

EN, VS Dysfunction, and Depression?

Initial Episodes of Depression mostly during **Adolscence**

| EN | → | VS Dysfunction | → | Depression |

Hypotheses

I. Association & Mediation

EN ↑ → VS Dysfunction ↑ → Depression ↑

II. Outcome Valence

EN ↑ → VS Dysfunction in Reward ↑
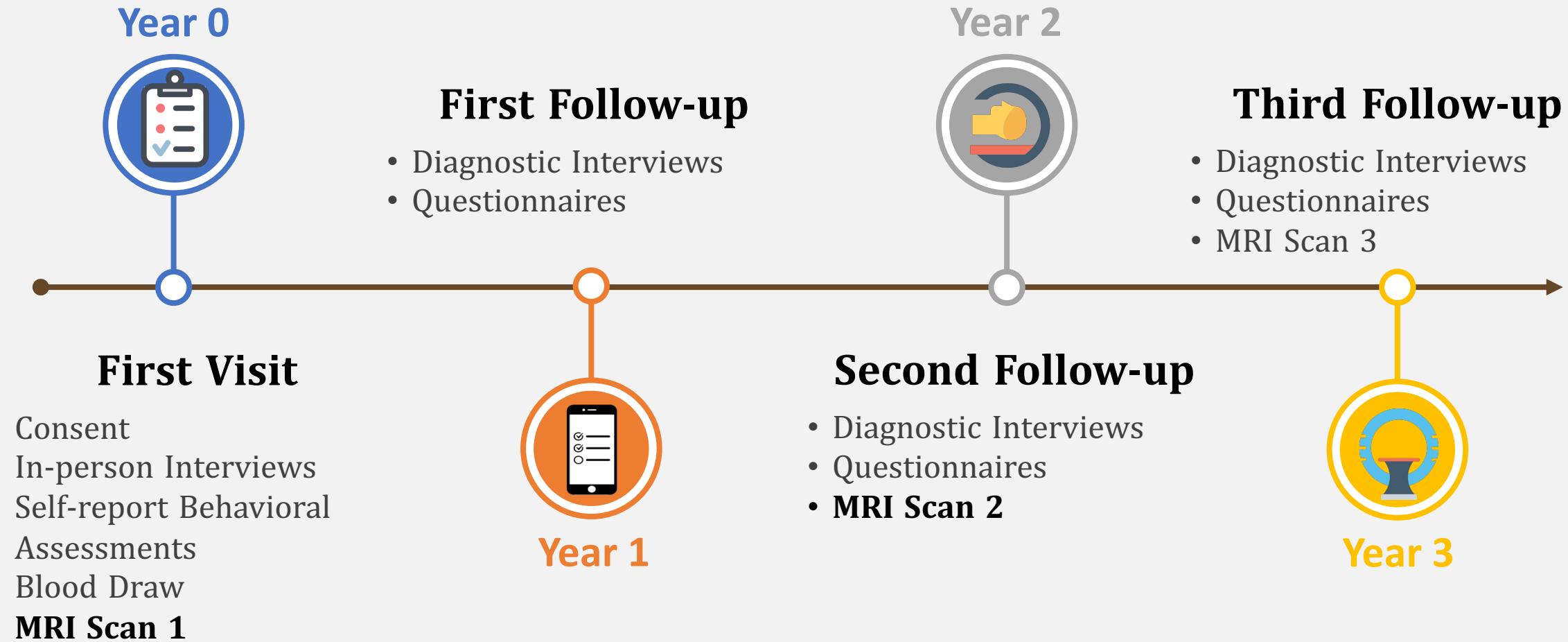
Participants

Teen Alcohol Outcomes Study

- <u>331</u> adolescents (ages: 11-15)

- Emphasis on <u>depression & alcohol use disorders</u>

- Families within 30-mile radius of University of Texas Health Science Center at San Antonio (White et al., 2012)

Study Design

Year 0

First Follow-up
- Diagnostic Interviews
- Questionnaires

Year 2

Third Follow-up
- Diagnostic Interviews
- Questionnaires
- MRI Scan 3

First Visit
- Consent
- In-person Interviews
- Self-report Behavioral Assessments
- Blood Draw
- **MRI Scan 1**

Year 1

Second Follow-up
- Diagnostic Interviews
- Questionnaires
- **MRI Scan 2**

Year 3

Participants

Data Exclusion Criteria

1. Task Performance (-59)

- Mean % of feedback < 60%

2. fMRI Artficact (-111)

- Head motion
- Extreme Signal Intensity Values

Demographic Information

	High Risk* (N = 59)	Low Risk (n = 47)
Sex (male)	28	27
Race (non-white)	25	16
Age in Scan 1 (mean)	13.77	13.55
Age in Scan 2 (mean)	15.87	15.62
Between-scan Years	2.1	2.07

*High Risk: Family History with Depressive Disorders

Self-Report Behavioral Assessments

Depression

Child-report Version of the Mood and Feelings Quesionnaire

Anxiety

Child Version of Screen for Child Anxiety Related Disorders

EN (Child Trauma Questionnaire-Short Form)

When I was growing up, …

2. I knew there was <u>someone</u> to take care of me and protect me

5. There was <u>someone</u> in my family who helped me feel important or special.

7. <u>I felt loved.</u>

13. <u>People</u> in my family <u>looked out for each other.</u>

19. <u>People</u> in my family felt close to each other.

26. There was <u>someone</u> to <u>take me to the doctor</u> if I needed it.

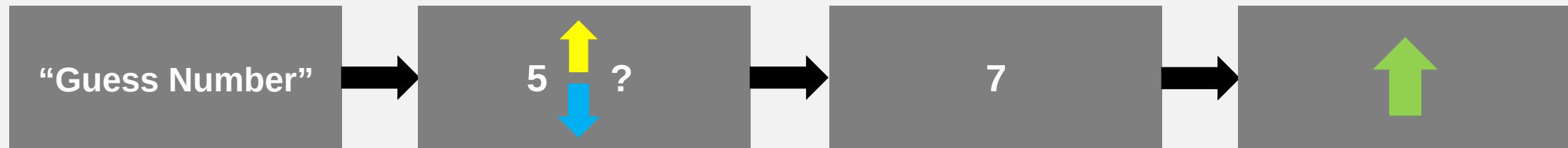28. My family was <u>a source of strength and support.</u>

Final EN Score: Mean EN Score of Scan 1 & Scan 2

Bernstein et al. (2003)
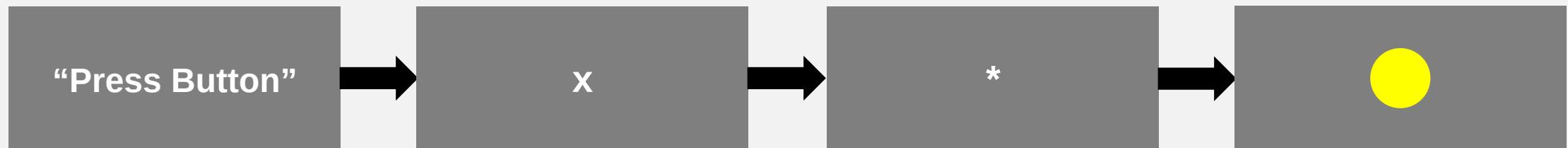
VS Activity: Card-Guessing Task

Positive/Negative Condition : 5 trials/block X 3 blocks/cond. = **15 trials/cond.**

"Guess Number"	5 ↑↓ ?	7	↑

- Positive: 80% Correct Guess
- Negative: 20% Correct Guess

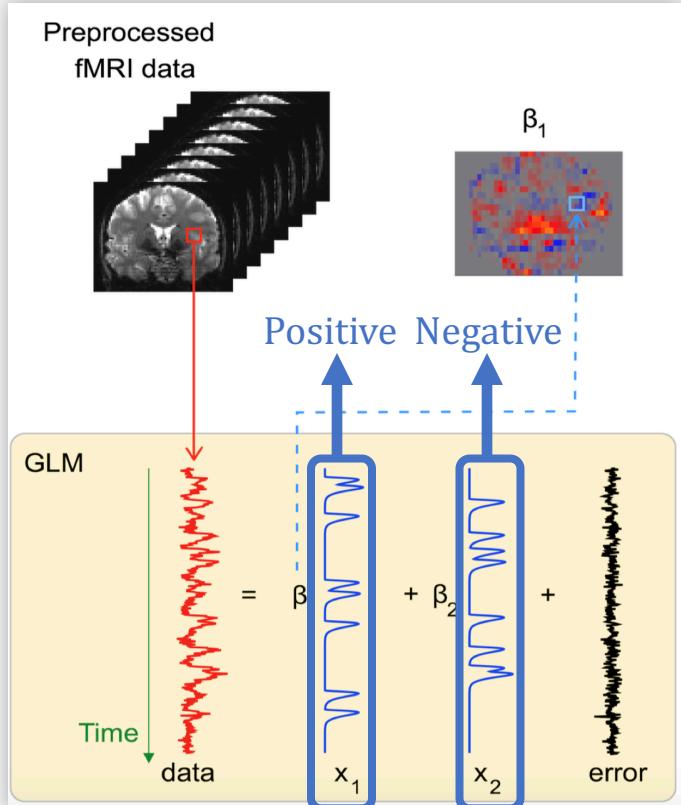**No Feedback Condition**

"Press Button"	x	*	●

+ One incongruent trial in each block: "to maintain participants' motivation to perform well" (Nikolova et al., 2012)

VS Activity

fMRI Data Processing

Preprocessed fMRI data

β_1

Positive Negative

GLM

$= \beta$ $+ \beta_2$ $+$

Time

data x_1 x_2 error

Jenkinson et al. (2018)

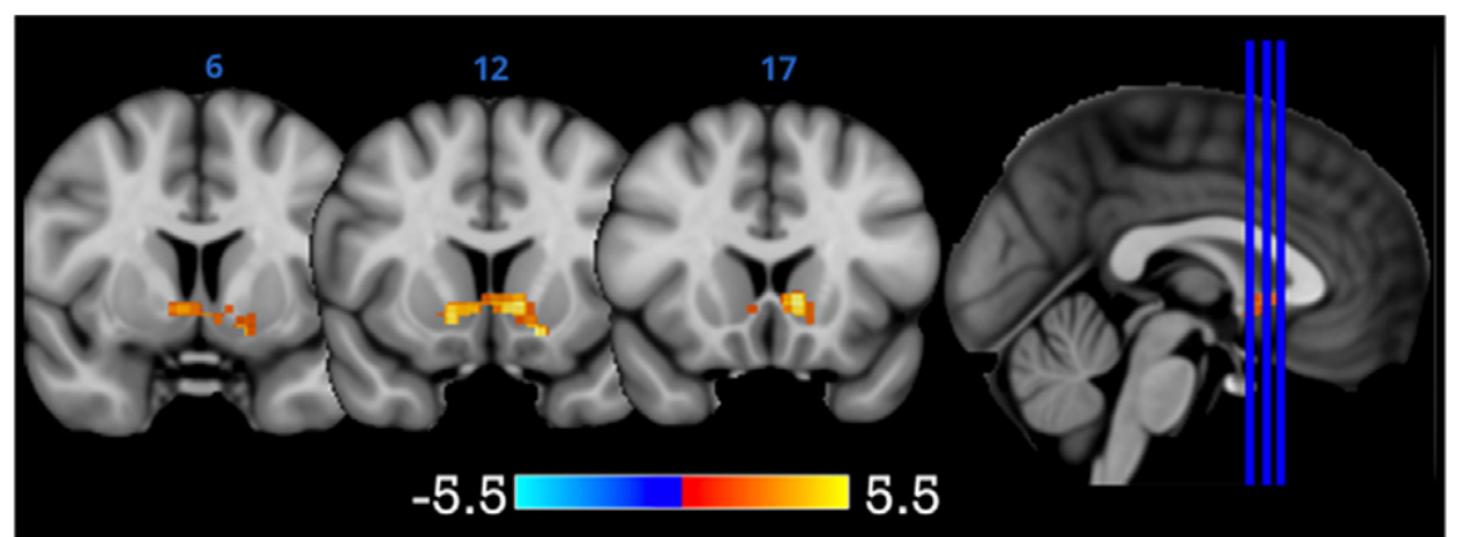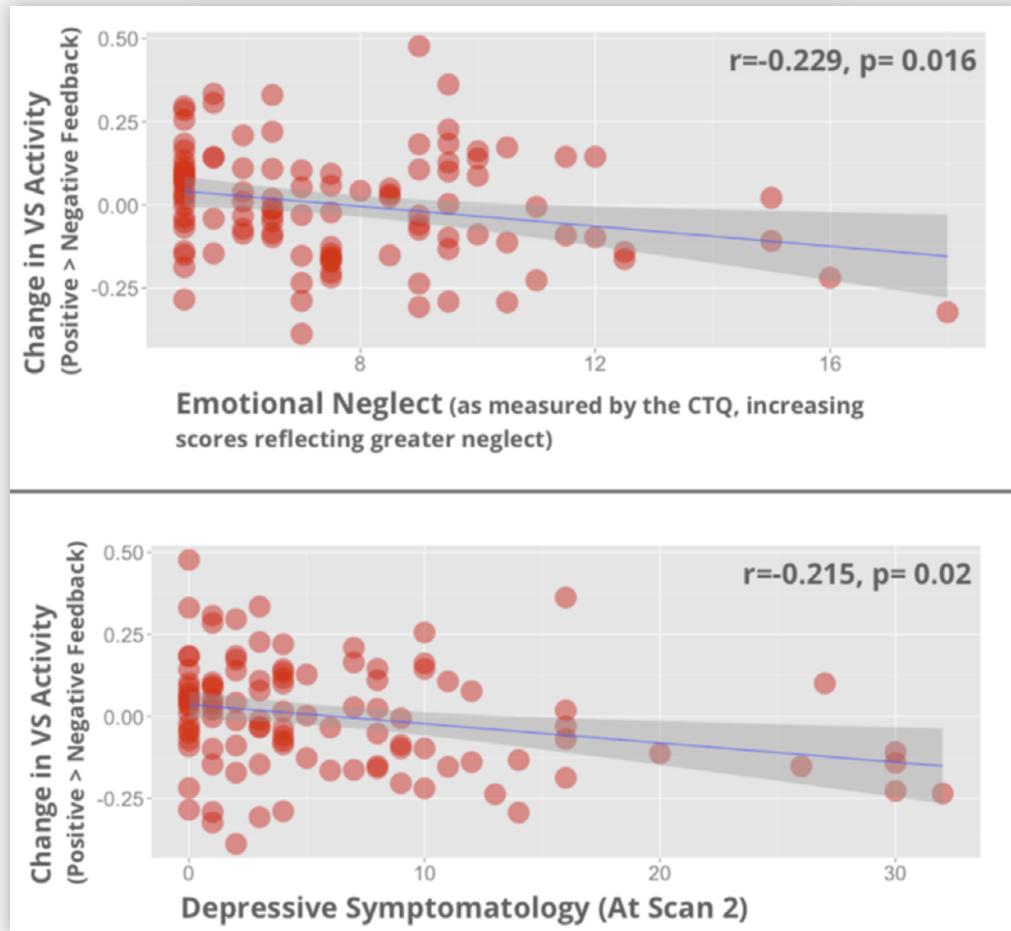**fMRI Analysis Result**

6   12   17

-5.5   5.5

Figure 1. Ventral striatum activity for the contrast of positive > negative feedback, controlling for multiple comparisons; $p = .05$ corrected.
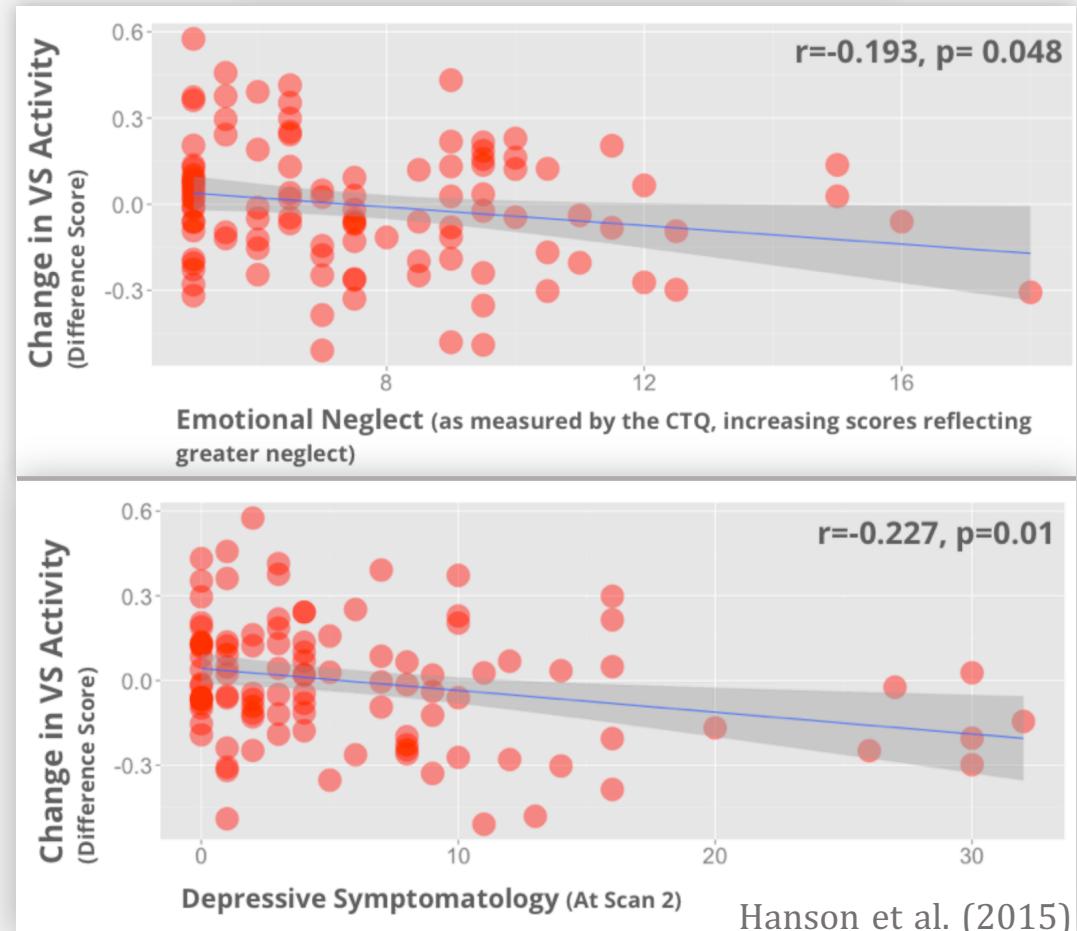
Hanson et al. (2015)

Result I: Association

Main Results

Supp. Results

Change in VS: Residuals

r=-0.229, p= 0.016

Change in VS Activity (Positive > Negative Feedback)

Emotional Neglect (as measured by the CTQ, increasing scores reflecting greater neglect)

r=-0.215, p= 0.02

Change in VS Activity (Positive > Negative Feedback)

Depressive Symptomatology (At Scan 2)

Change in VS: Difference

r=-0.193, p= 0.048

Change in VS Activity (Difference Score)

Emotional Neglect (as measured by the CTQ, increasing scores reflecting greater neglect)

r=-0.227, p=0.01

Change in VS Activity (Difference Score)

Depressive Symptomatology (At Scan 2)

Hanson et al. (2015)
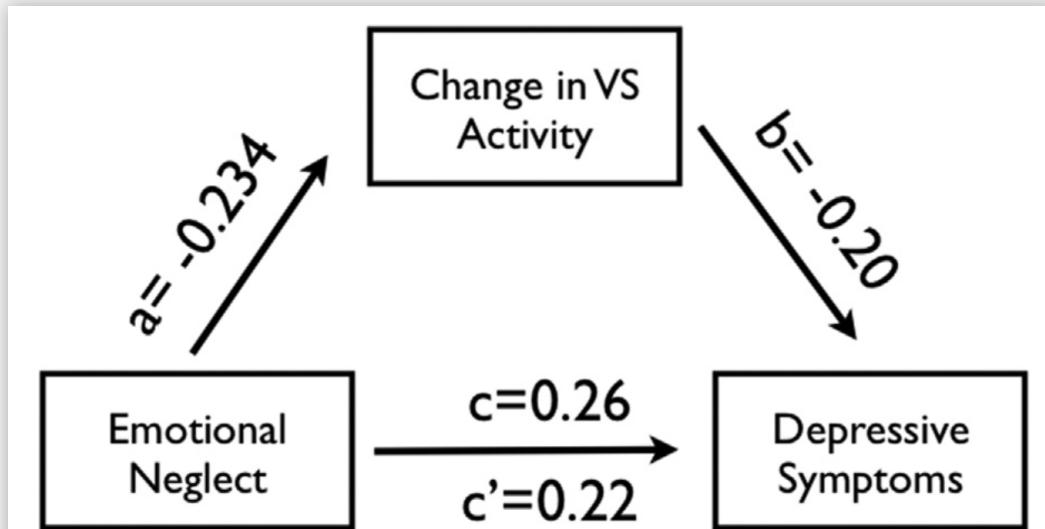
Result I: Association (Others)

Sex Difference

I. Interaction of sex and emotional neglect was not related to VS change.

II. Interaction of sex and VS change was not related to depressive symptoms.

Puberty

I. Pubertal stage was not significantly associated with VS change and depressive symptoms.

Hanson et al. (2015), Supplimentary pg. 7, 12

Result II: Mediation

Main Result

Proportion mediated= 0.18; 95% CI=0.002-0.83, p=0.04
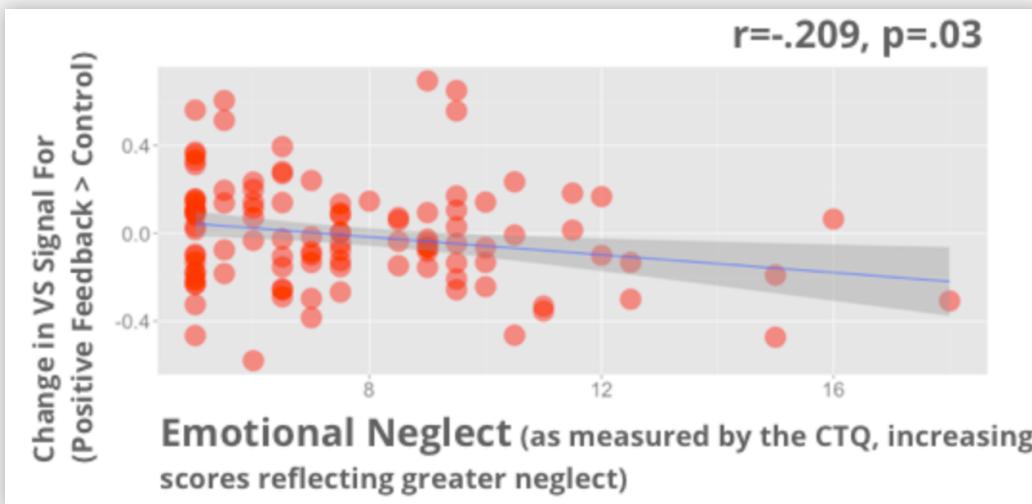
C = without change in VS activity
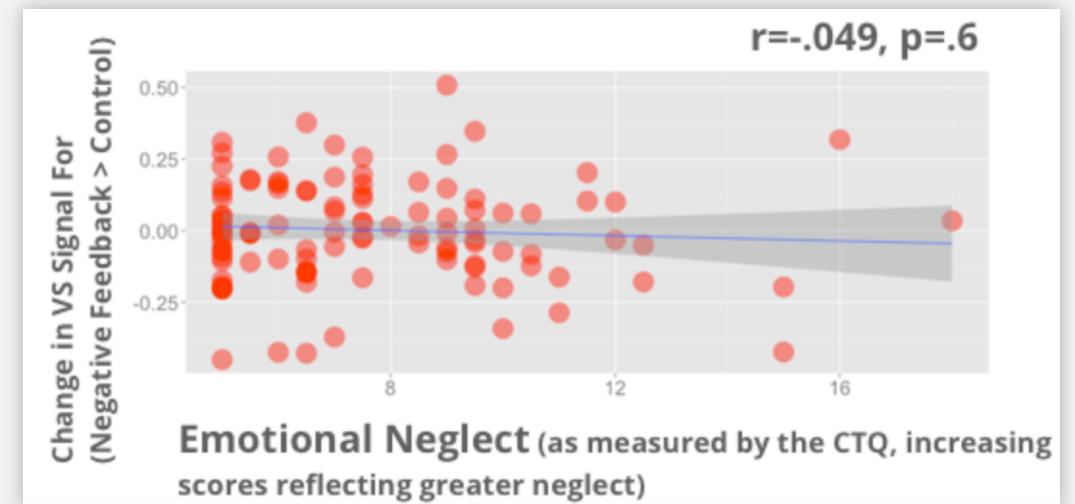C' = with change in VS activity

Supp. Result

- Similar result with change in VS activity indexed by a difference score

- Non-significant result when reversed

Hanson et al. (2015)

Result III: Outcome Valence

Postive Feedback-EN

r=-.209, p=.03

Change in VS Signal For (Positive Feedback > Control)

Emotional Neglect (as measured by the CTQ, increasing scores reflecting greater neglect)

Negative Feedback-EN

r=-.049, p=.6

Change in VS Signal For (Negative Feedback > Control)

Emotional Neglect (as measured by the CTQ, increasing scores reflecting greater neglect)

Hanson et al. (2015)

Limitations & Discussion

Limitations

- No timing information available for EN
- Used one summed score for depressive symptoms
- Too many excluded participants

Discussion

- Clear association between childhood experiences, neural activity, and related outcome symptoms
- First empirical study showing changes in VS activity as a function of EN predict depressive symptoms in 2 years
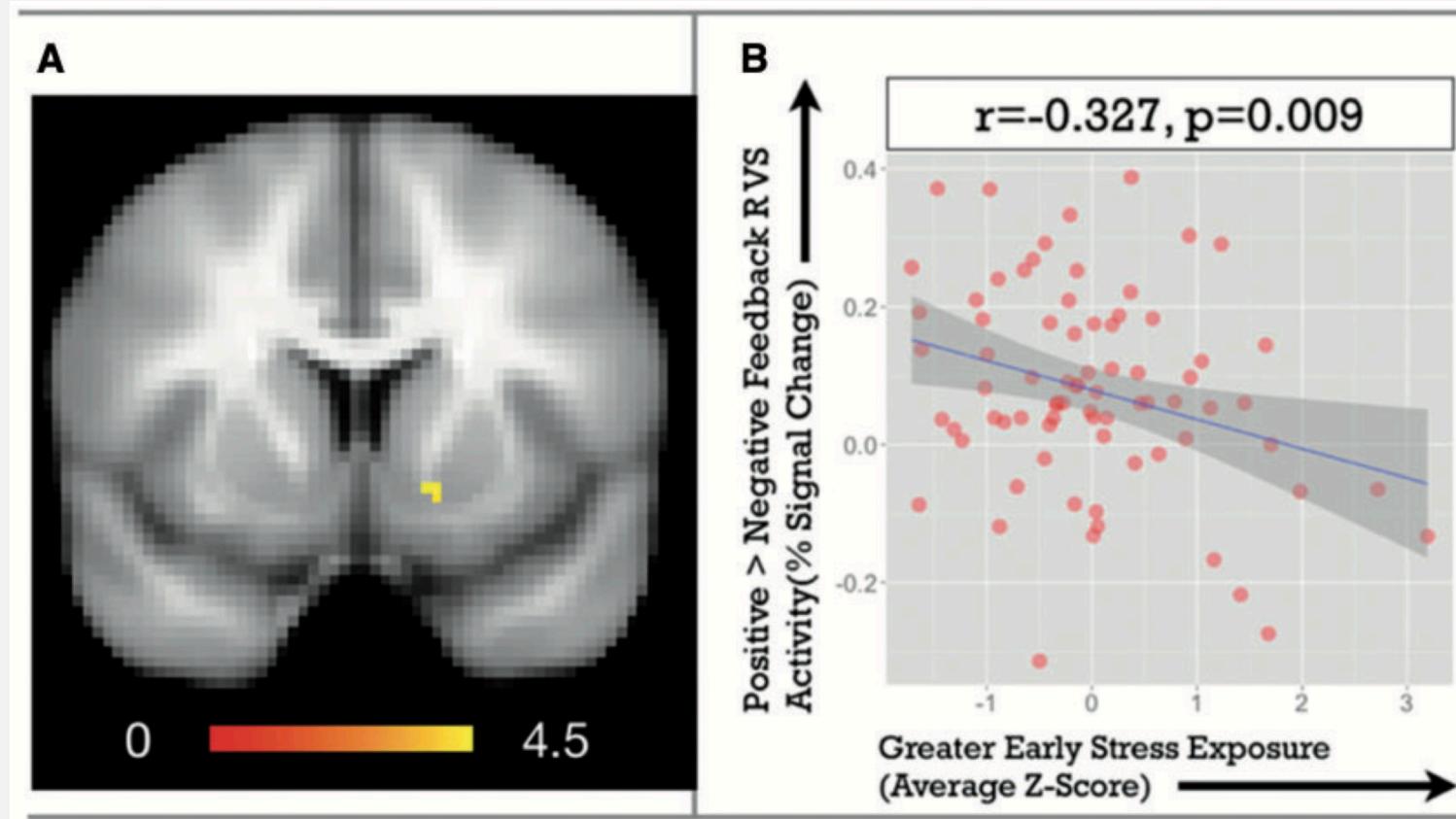
Follow-up Study

Cumulative stress in childhood is associated with blunted reward-related brain activity in adulthood

Jamie L. Hanson,[1,2,3] Dustin Albert,[4] Anne-Marie R. Iselin,[5] Justin M. Carré,[6] Kenneth A. Dodge,[3,7] and Ahmad R. Hariri[1]

- Cumulative Stress:
  - Self-report
  - Major Life Stressors experienced by the child during previous year
  - Sum Scores by time period:
    - Early: Kindergarten-Grade 3
    - Middle: Grade 4-7
    - Late: Grade 8-12

Follow-up Study

Results

- **Only Early Childhood Stressors** were associated with blunted VS activity in adulthood.

- **Neither middle nor later developmental epoch stress score** was associated with blunted VS activity in adulthood.

Hanson et al. (2016), Social Cognitive and Affective Neuroscience

Discussion Question

"If you were a reviewer, would you accept this paper?"

Discussion Question (Results)

- 결과
  - 매개효과 분석의 유의미성이 높지 않았다. 우울증상에 여러 하위 증상이 포함되어 있다는 점을 고려할 때, 하위증상 별로 점수를 계산하여 분석했을 때 통계적 유의미성이 증가할 수 있을까? 혹은 다른 개선 방법이 있을까?

Discussion Question (Methodology)

- 정서적 방임(EN) 측정
  - 본 연구에서는 EN을 설문지를 통해 회고적으로 보고하도록 했다. 또한 두 번 측정한 뒤 두 점수의 평균 합산 점수를 사용하였다. 이러한 측정 방식이 타당하다고 할 수 있는가?

- 참여자 연령 및 모집 기준
  - 청소년기 참여자를 모집하였으나 발달적 수준을 따로 고려하지 않았다. 또한 청소년기 정신장애 유병률에는 성차가 뚜렷한데 본 연구에서는 따로 구분하여 살펴보지 않았다. 본 연구의 결과가 다른 청소년 집단에게도 적용될 수 있을까?

References

- Bernstein, D.P., Stein, J.A., Newcomb, M.D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D. & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Neglect* 27, 169–190.

- Hanson, J., Hariri, A., Williamson, D. (2015). Blunted Ventral Striatum Development in Adolescence Reflects Emotional Neglect and Predicts Depressive Symptoms. *Biological Psychiatry* 78(9), 598-605. https://dx.doi.org/10.1016/j.biopsych.2015.05.010

- Hanson, J., Albert, D., Iselin, A., Carré, J., Dodge, K., Hariri, A. (2016). Cumulative stress in childhood is associated with blunted reward-related brain activity in adulthood. Social Cognitive and Affective Neuroscience 11(3), 405-412. https://dx.doi.org/10.1093/scan/nsv124

- Heshmati, M., Russo, S.J. (2015). Anhedonia and the Brain Reward Circuitry in Depression. *Curr Behav Neurosci Rep* 2, 146–153.https://doi.org/10.1007/s40473-015-0044-3

- White, M. G., Bogdan, R., Fisher, P. M., Muñoz, K. E., Williamson, D. E., Hariri, A. R. (2012). FKBP5 and emotional neglect interact to predict individual differences in amygdala reactivity. *Genes Brain Behav* 11, 869–878.

- Nikolova, Y., Bogdan, R., Brigidi, B., Hariri, A. (2012). Ventral Striatum Reactivity to Reward and Recent Life Stress Interact to Predict Positive Affect. *Biological Psychiatry* 72(2), 157-163. https://dx.doi.org/10.1016/j.biopsych.2012.03.014

- Norman, R. E., Byambaa, M., De, R., Butchart, A., Scott, J., Vos, T. (2012). The long-term health consequences of child physical abuse, emotional abuse, and neglect: A systematic review and meta-analysis. *PLoS Med* 9:e1001349.3.