Environmental enrichment enhances resilience: Implications for public health policy?

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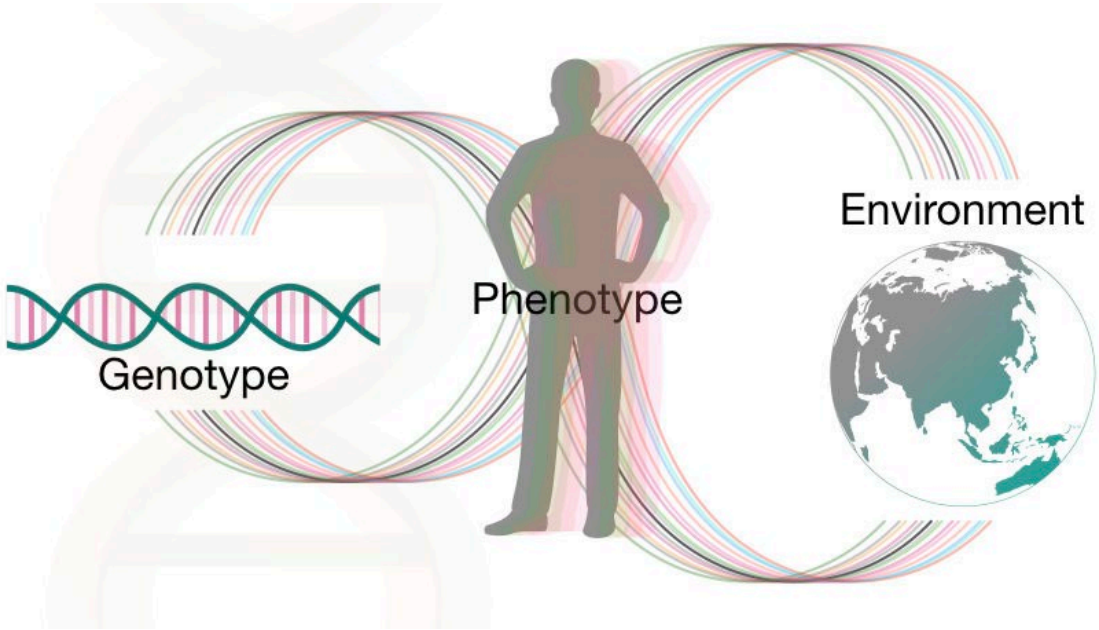
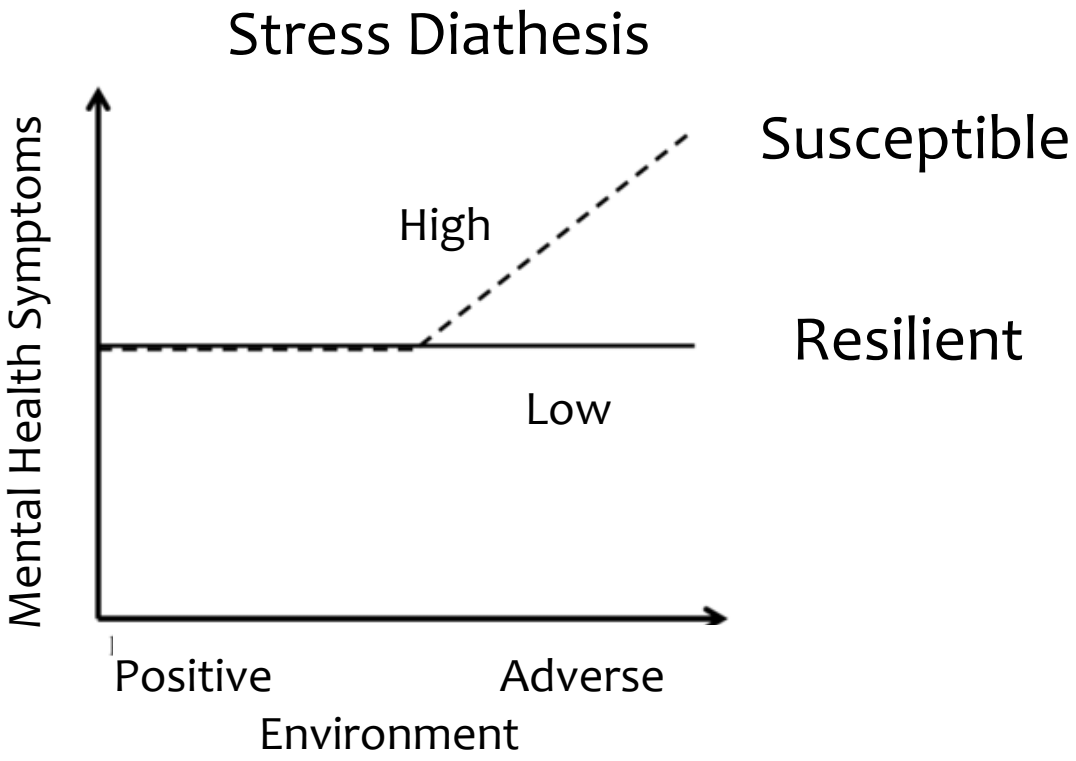
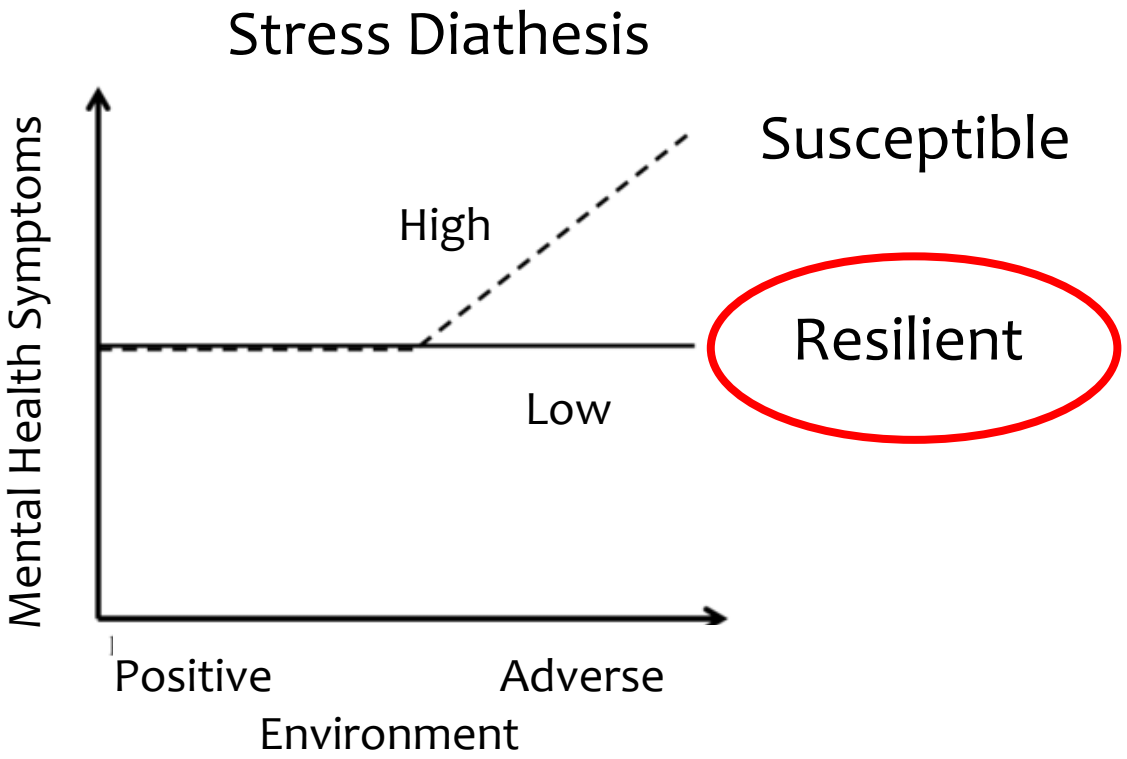
The ePGS approach provides a method by which to identify mechanisms underlying gene x environment interactions



Models for gene x environment interaction



Models for gene x environment interaction

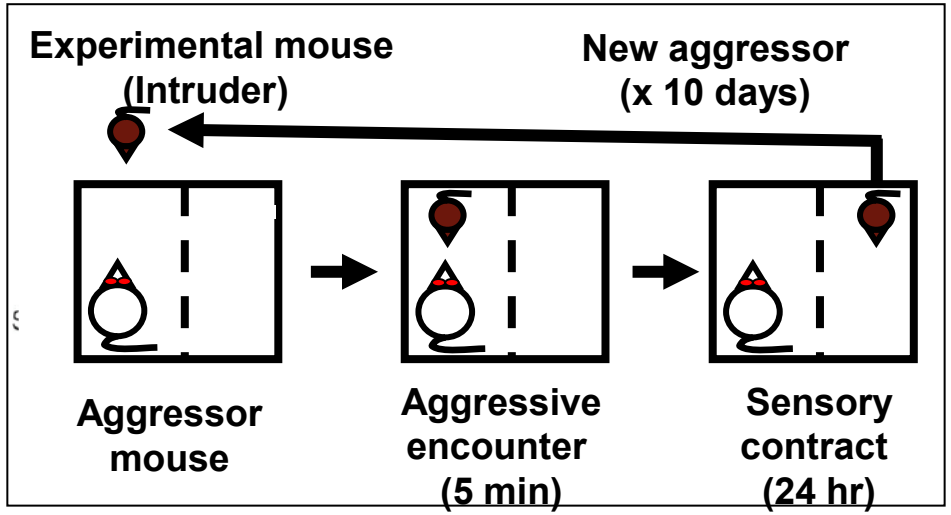


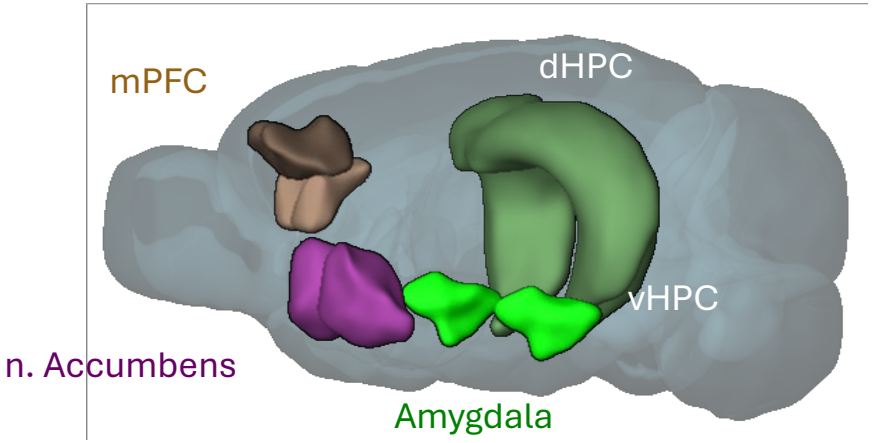
Mouse model of “resilience”

Environmental Enrichment

Dampens stress reactivity
Enhances ‘recovery’ post-stress
Decreases anxiety/depression
Reduces inflammation
Enhances metabolic health

Brain-wide structural correlates of susceptibility and resilience to chronic stress





Rose Bagot
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LETTER

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Hippocampal neurogenesis confers stress resilience by inhibiting the ventral dentate gyrus

Christoph Anacker[1*], Victor M. Luna[1], Gregory S. Stevens[1], Amira Millette[1], Ryan Shores[1], Jessica C. Jimenez[1], Briana Chen[1] & René Hen[1,2,3*]

Christoph Anacker
Columbia University

Environmental enrichment activates molecular signals that drive neuronal differentiation and neurogenesis

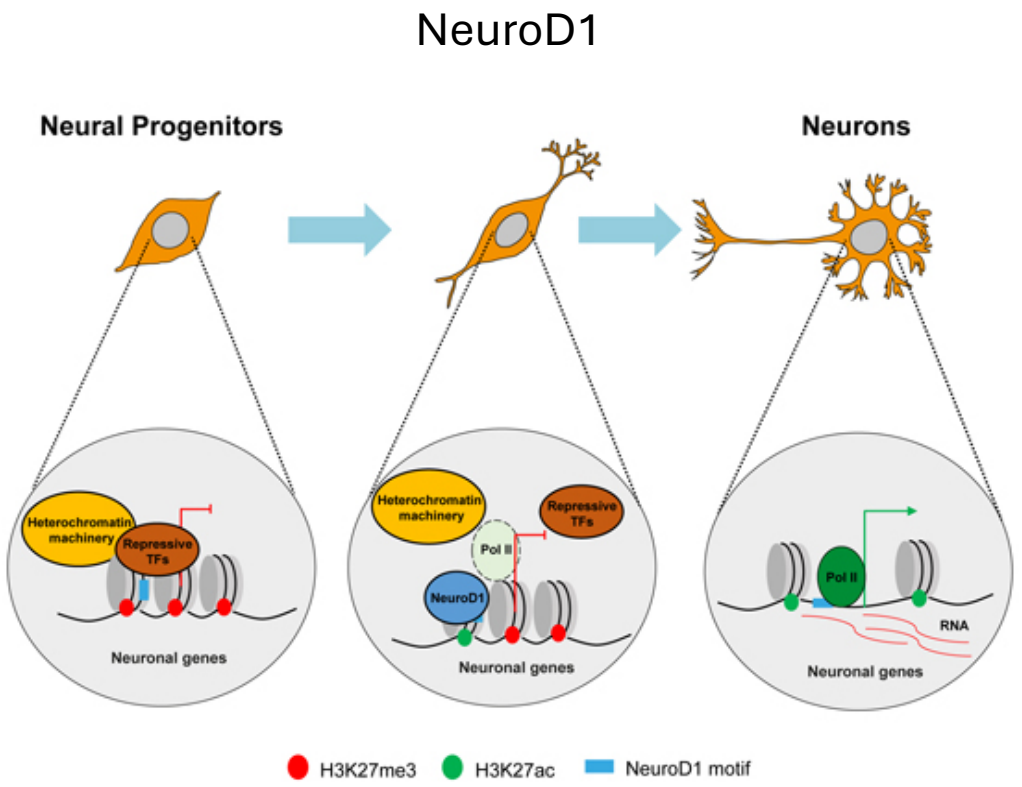
nature COMMUNICATIONS

ARTICLE

DOI: 10.1038/s41467-017-02748-x OPEN

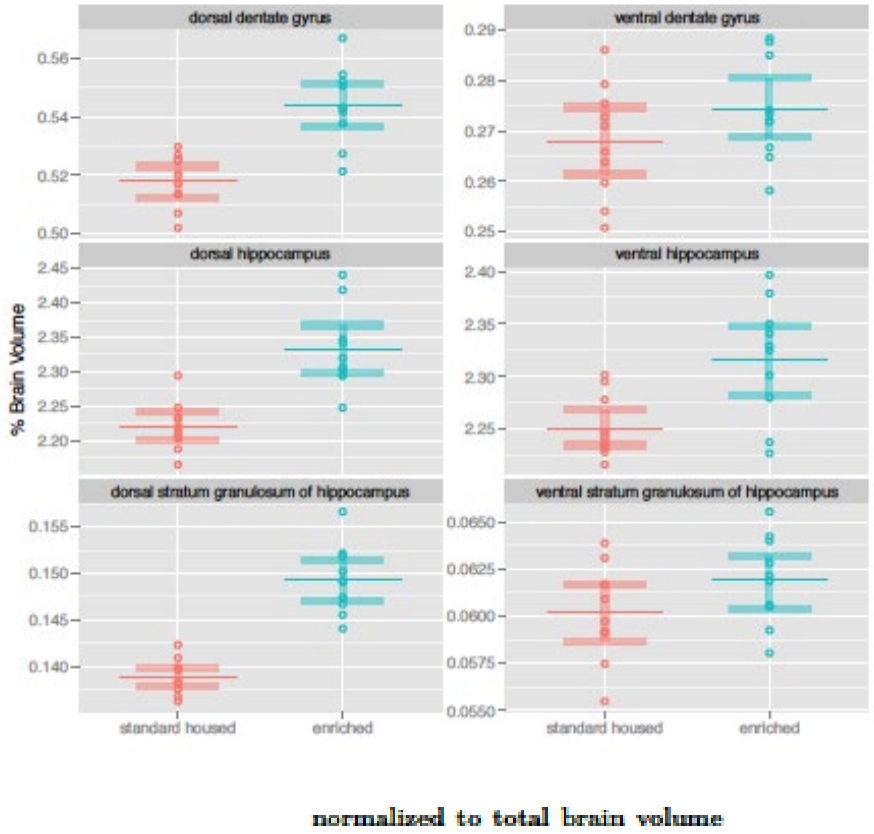
Environmental enrichment increases transcriptional and epigenetic differentiation between mouse dorsal and ventral dentate gyrus

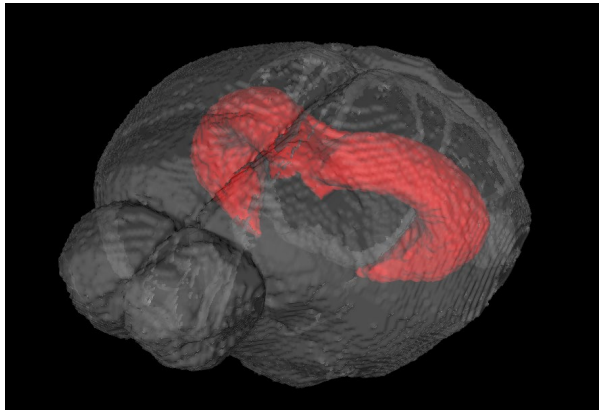
Tie-Yuan Zhang[1,2,3], Christopher L. Keown[4], Xianglan Wen[1,2,3], Junhao Li[4], Dulcie A. Vousden[5], Christoph Anacker[1,2,3], Urvashi Bhattacharyya[4], Richard Ryan[1,2,3], Josie Diorio[1,2,3], Nicholas O'Toole[1,2,3], Jason P. Lerch[5], Eran A. Mukamel[4] & Michael J. Meaney[1,2,3,6]



Pataskar et al. EMBO J (2015) 35: 24 - 45

Enrichment increases hippocampal volume (MRI)

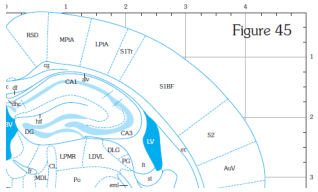


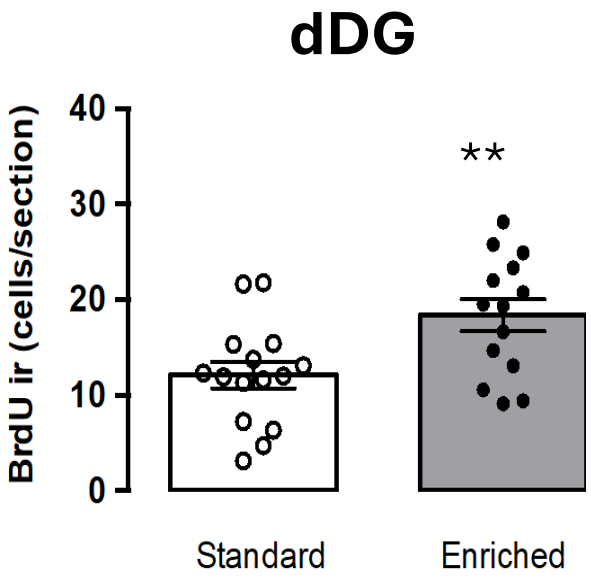


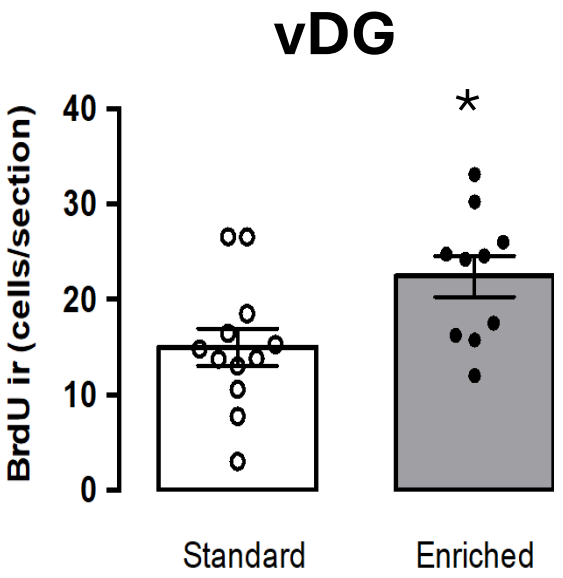
Structure	Effect Size	p value (effect of enrichment)
ventral DG	0.95	0.048
ventral stratum granulosum	1.04	0.037
ventral hippocampus	1.54	0.004
dorsal DG	1.67	0.003
dorsal hippocampus	1.75	0.003
dorsal stratum granulosum	2.43	0.0003

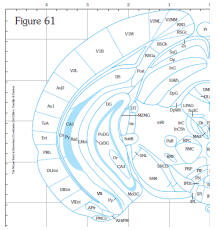
Zhang et al *Nature Comm* 2019

Enrichment promotes increases hippocampal neurogenesis

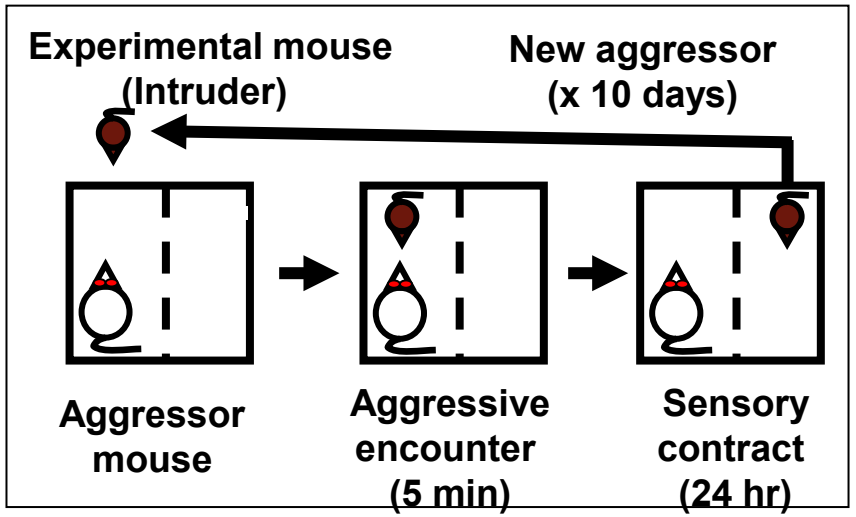








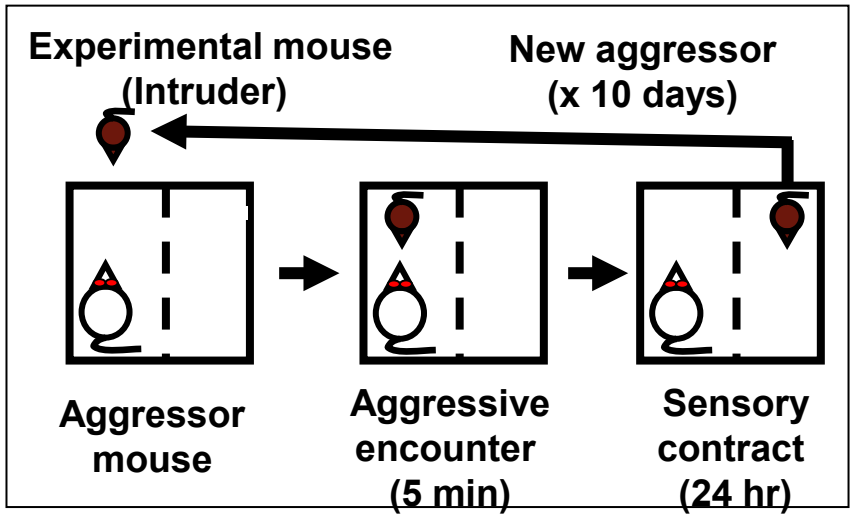
Enrichment promotes ‘resilience’ to effects of chronic social defeat



Chronic Social Defeat

Increases anxiety/depression
Increases inflammation
Impairs metabolic health

Enrichment promotes ‘resilience’ to effects of chronic social defeat



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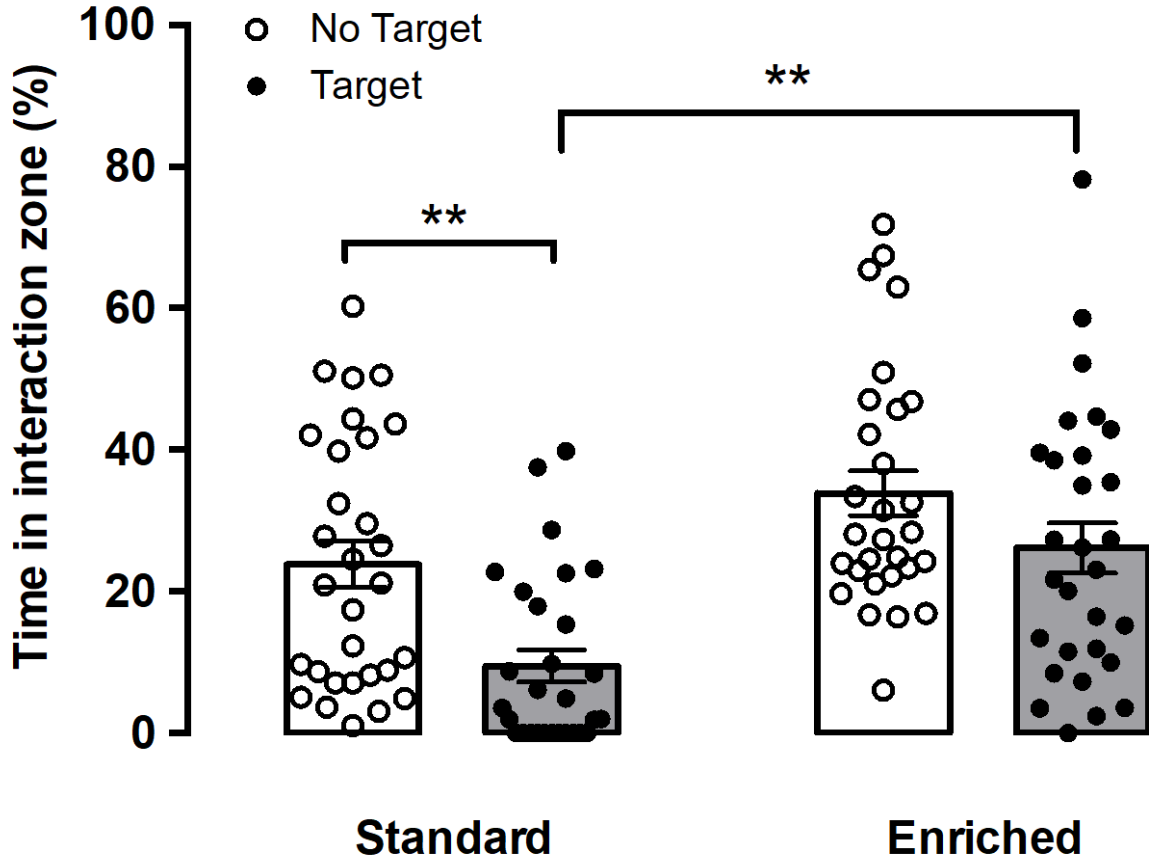


$^{**}p < 0.01$

Mouse model of “resilience”

Environmental Enrichment vs Standard housing

(Post-Weaning to Day 70)

↓

RNAseq ventral hippocampal dentate gyrus (Day 90)

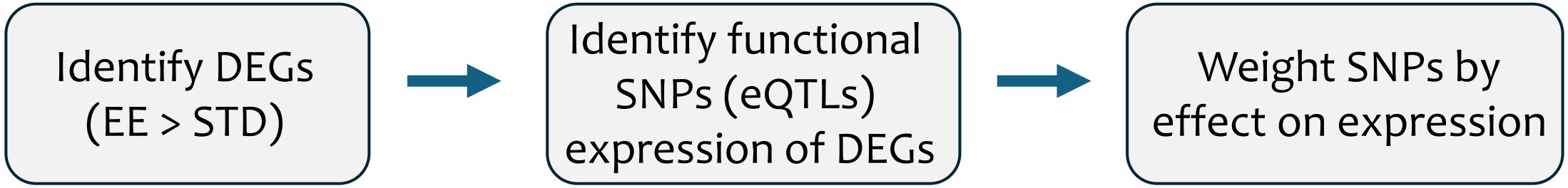
↓

Differentially Expressed Genes (FDR <0.1)

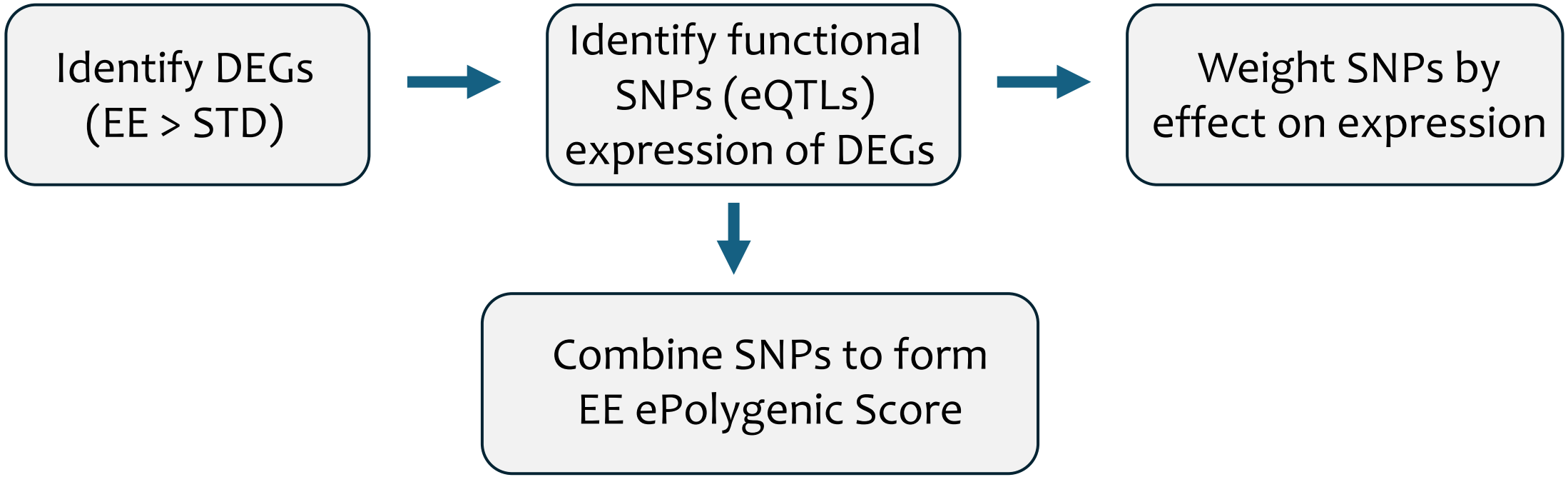
↓

Calculate EE ePGS

Calculation of an Environmental Enrichment polygenic score for human data sets



Calculation of an Environmental Enrichment polygenic score for human data sets



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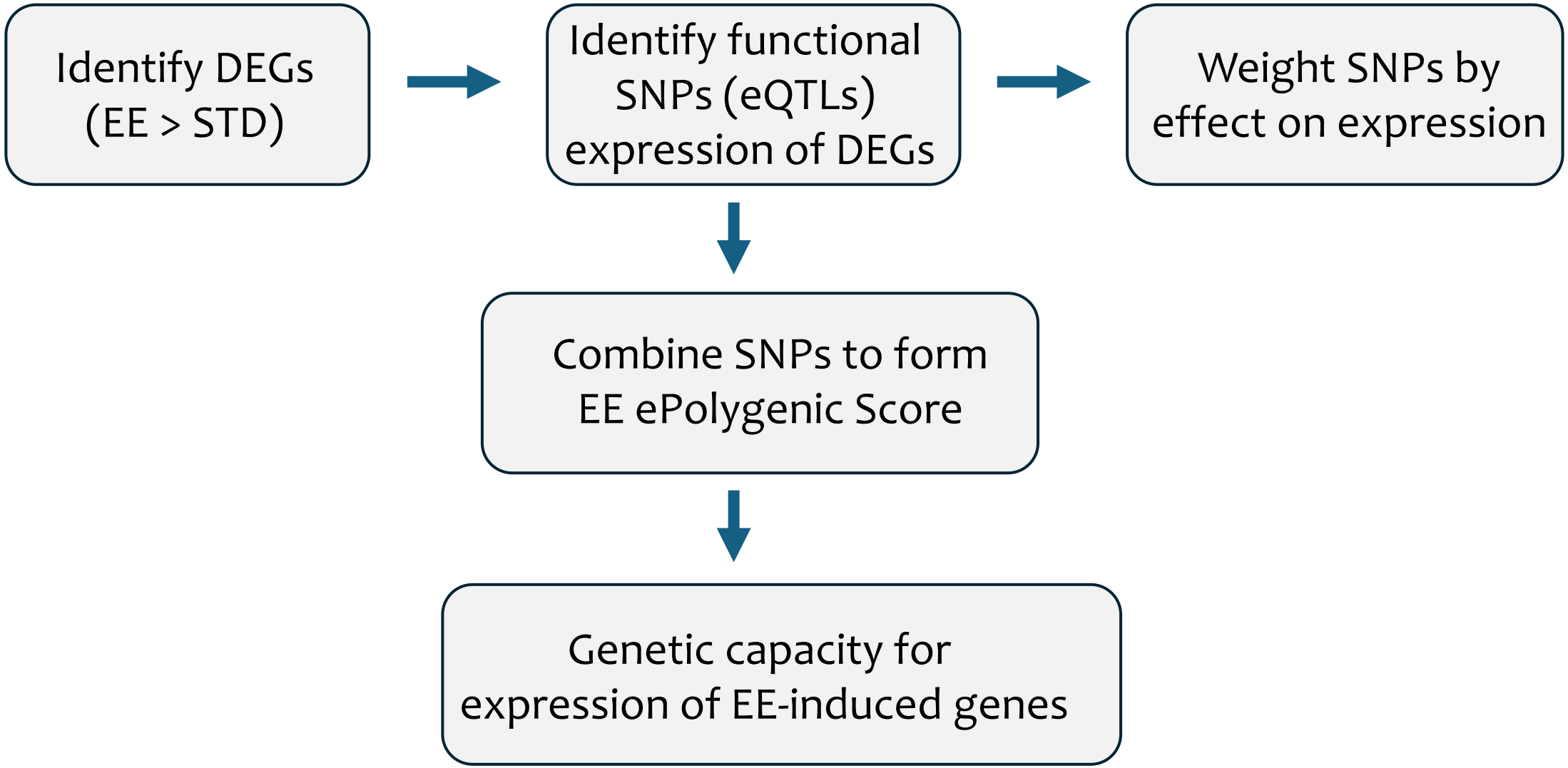
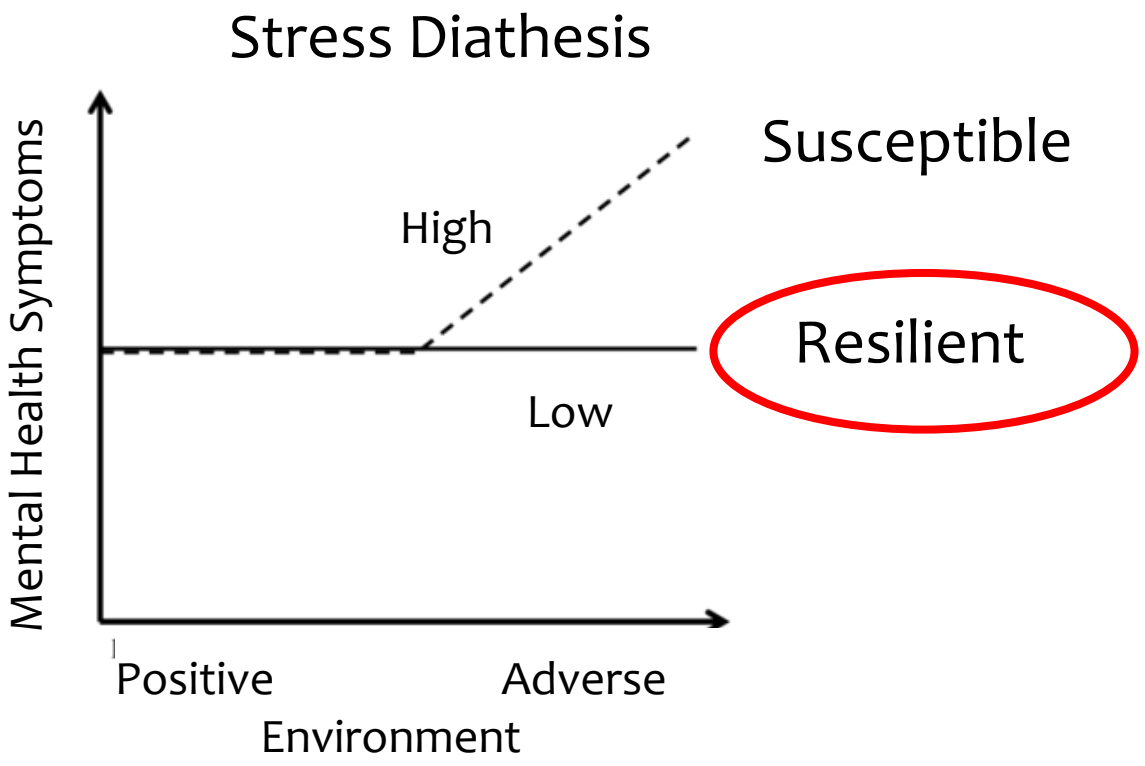


Does an environmental enrichment ePGS confer resilience among highly stressed humans?



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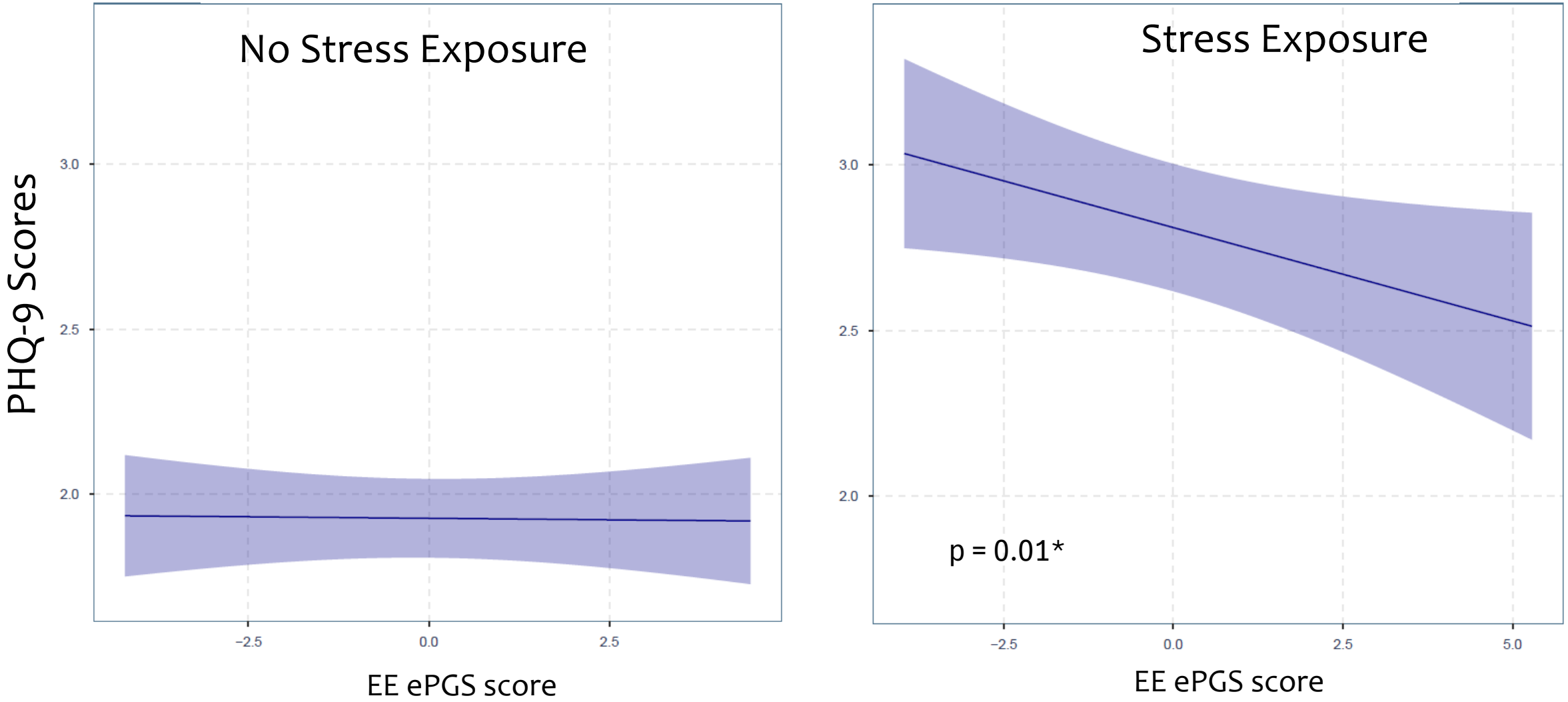
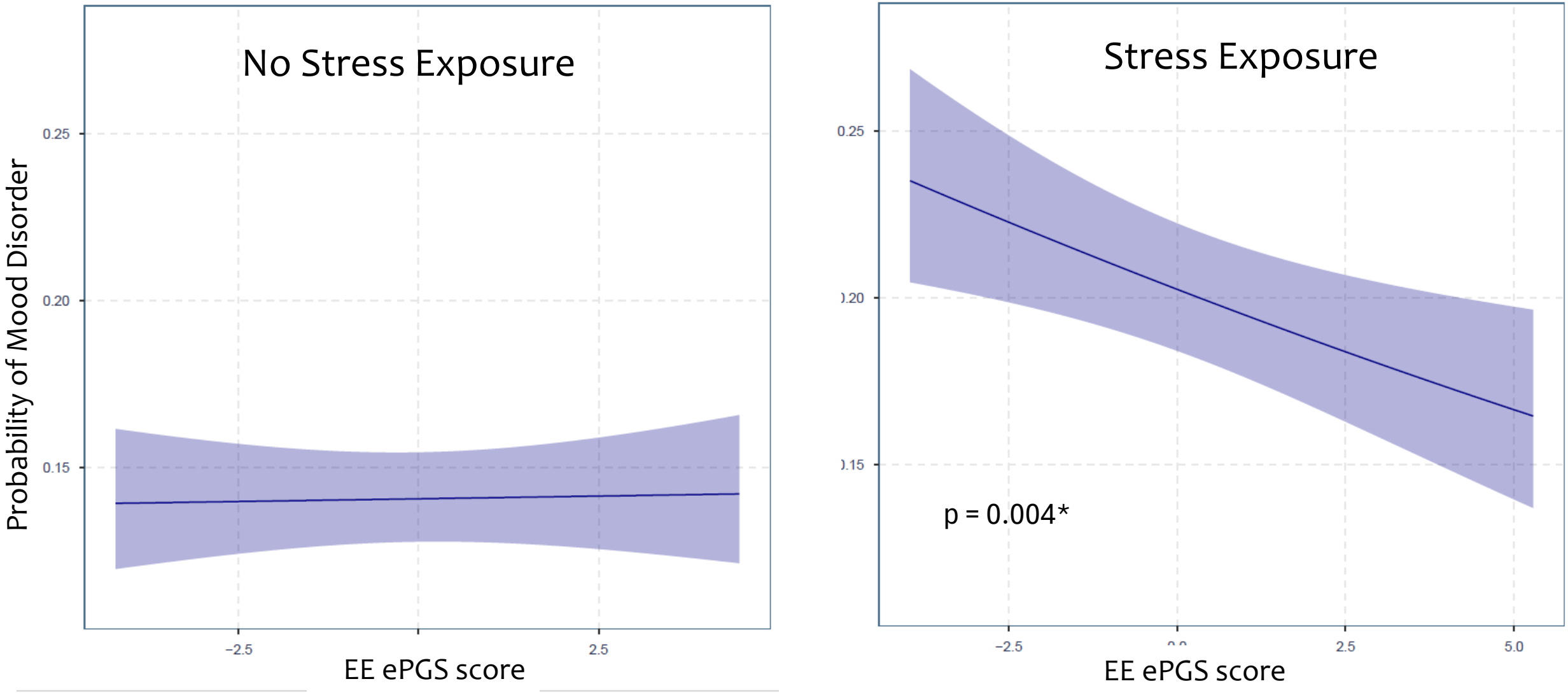
Stress vs no stress (past 2 years)

Depression

Enrichment ePGS (vHipp) moderates the effect of stress on depressive symptoms (PHQ-9)



Enrichment ePGS (vHipp) moderates the effect of stress on probability of Mood Disorder



Does Experience Enhance Cognitive Flexibility? An Overview of the Evidence Provided by the Environmental Enrichment Studies

Francesca Gelfo [1,2]*

frontiers in Behavioral Neuroscience

Brockett, A. T., LaMarca, E. A., and Gould, E. (2015). Physical exercise enhances cognitive flexibility as well as astrocytic and synaptic markers in the medial prefrontal cortex. PLoS One 10:e0124859.

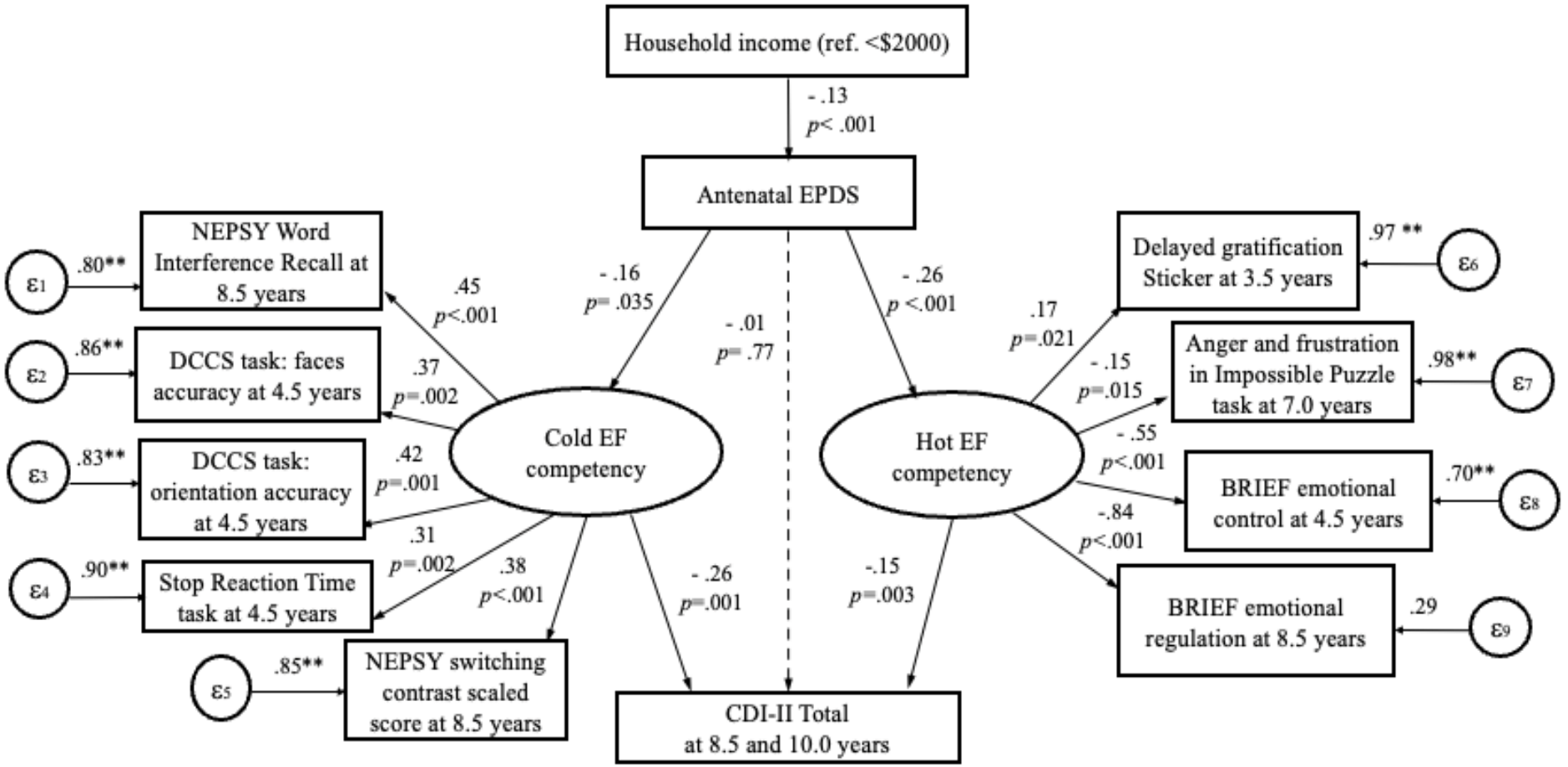
Rountree-Harrison, D., Burton, T. J., Leamey, C. A., and Sawatari, A. (2018). Environmental enrichment expedites acquisition and improves flexibility on a temporal sequencing task in mice. Front. Behav. Neurosci. 12:51.

Sampedro-Piquero, P., Zancada-Menendez, C., and Begega, A. (2015). Housing condition-related changes involved in reversal learning and its c-Fos associated activity in the prefrontal cortex. Neuroscience 307, 14–25.

Schrijver, N. C., Pallier, P. N., Brown, V. J., and Würbel, H. (2004). Double dissociation of social and environmental stimulation on spatial learning and reversal learning in rats. Behav. Brain Res. 152, 307–314.

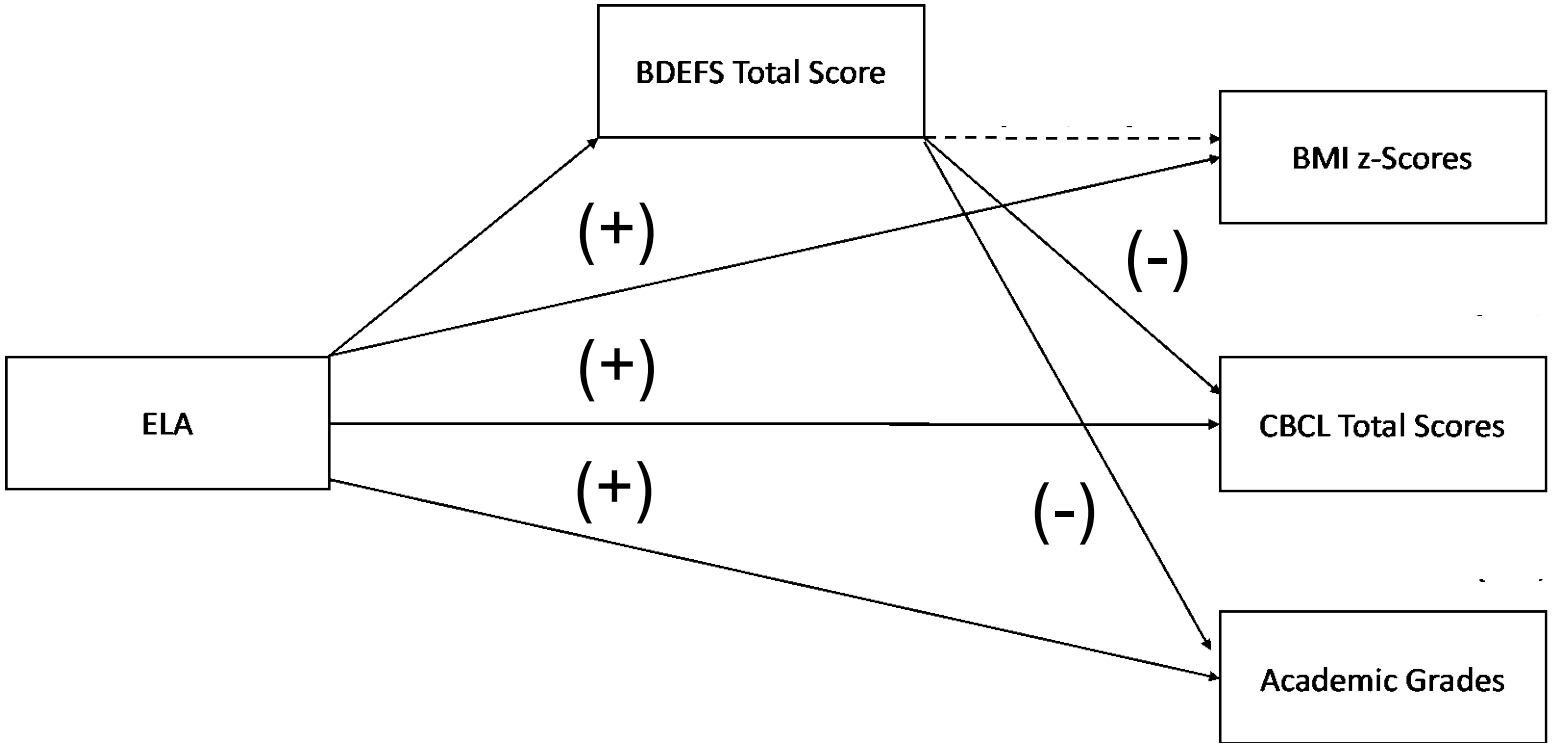
Zeleznikow-Johnston, A., Burrows, E. L., Renoir, T., and Hannan, A. J. (2017). Environmental enrichment enhances cognitive flexibility in C57BL/6 mice on a touchscreen reversal learning task. Neuropharmacology 117, 219–226.

Maternal Depressive Symptoms and Risk for Childhood Depression: Role of Executive Functions



Han et al. *J Am Acad Child & Adol Psychiatry* 2025

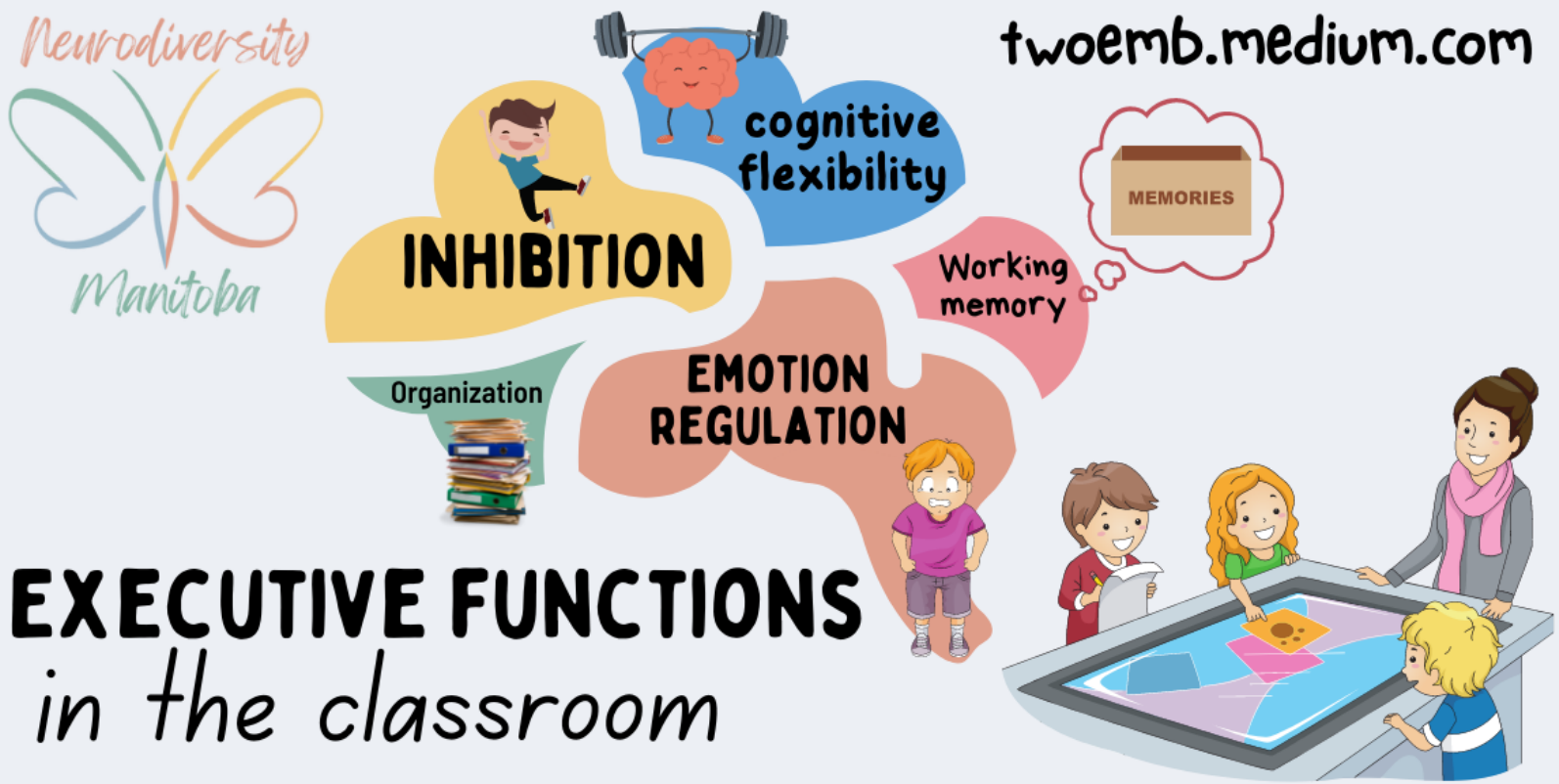
Executive function serves as a source of resilience to effects of Early Life Adversity (ELA)



High-Risk sample: Penn State Child Maltreatment Cohort
Population sample: Adolescent Brain Cognitive Development (ABCD) cohort

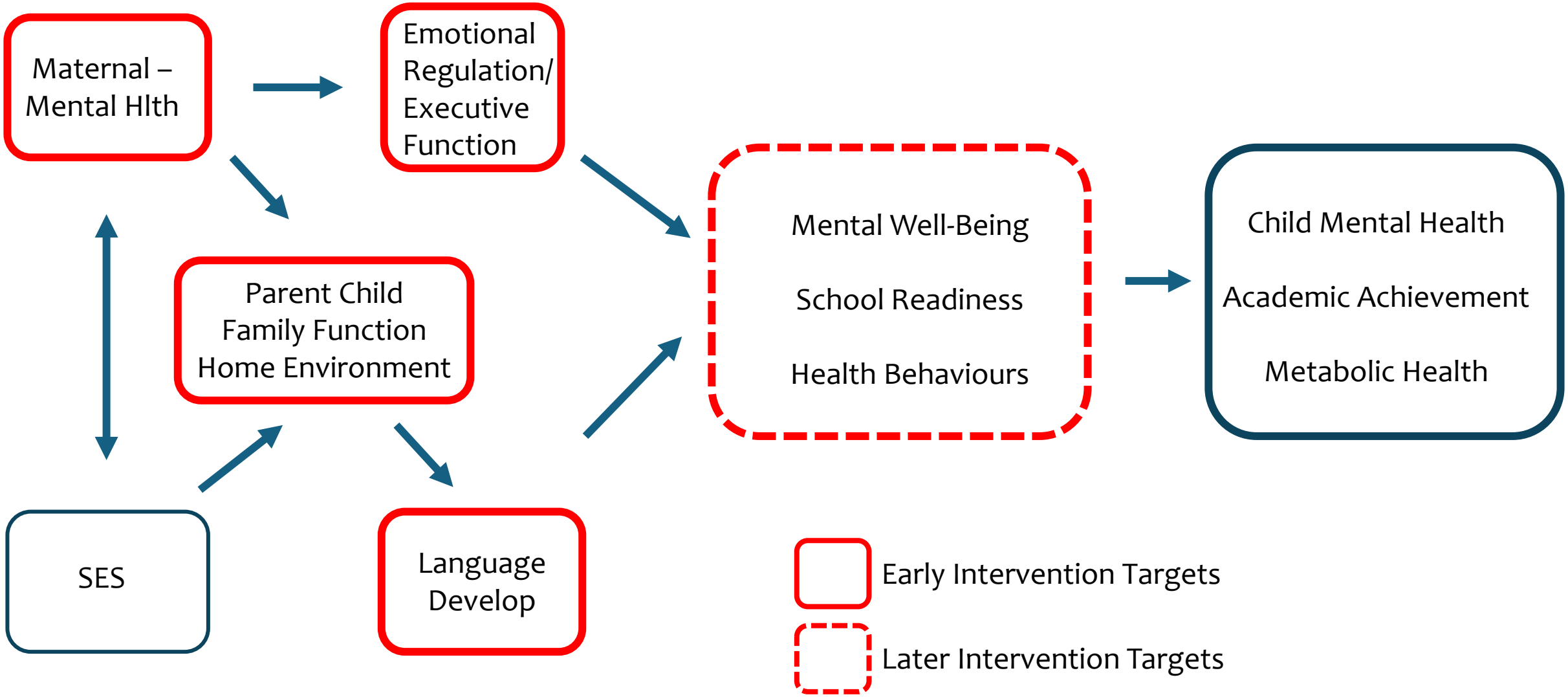
Neurodiversity Manitoba

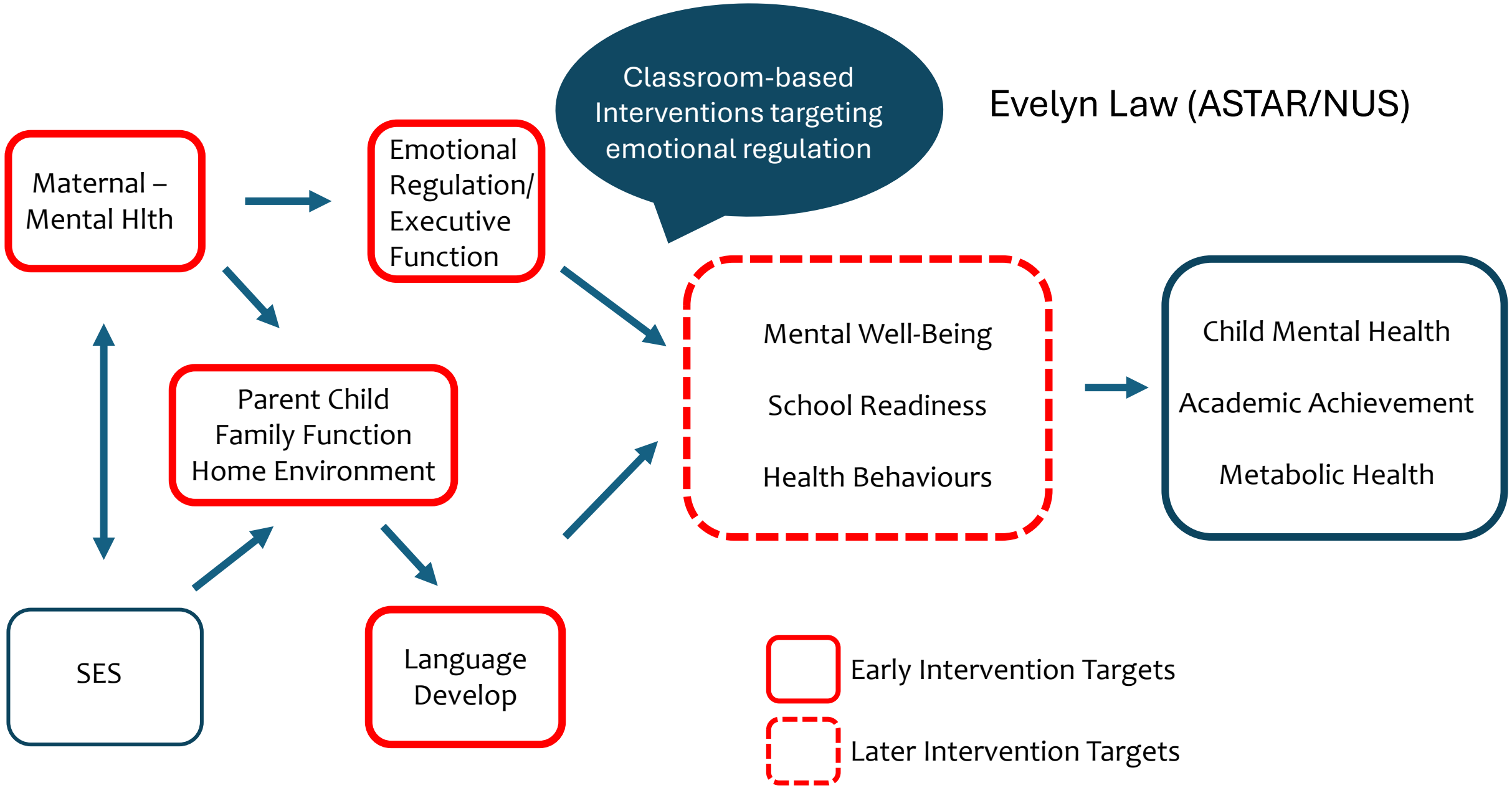
twoemb.medium.com



EXECUTIVE FUNCTIONS

in the classroom


Maternal – Mental Hlth
Emotional Regulation/ Executive Function
Parent Child Family Function Home Environment
SES
Language Develop
Mental Well-Being
School Readiness
Health Behaviours
Child Mental Health
Academic Achievement
Metabolic Health
Early Intervention Targets
Later Intervention Targets


Classroom-based Interventions targeting emotional regulation
Evelyn Law (ASTAR/NUS)
Maternal – Mental Hlth
Emotional Regulation/ Executive Function
Parent Child Family Function Home Environment
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Language Develop
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Early Intervention Targets
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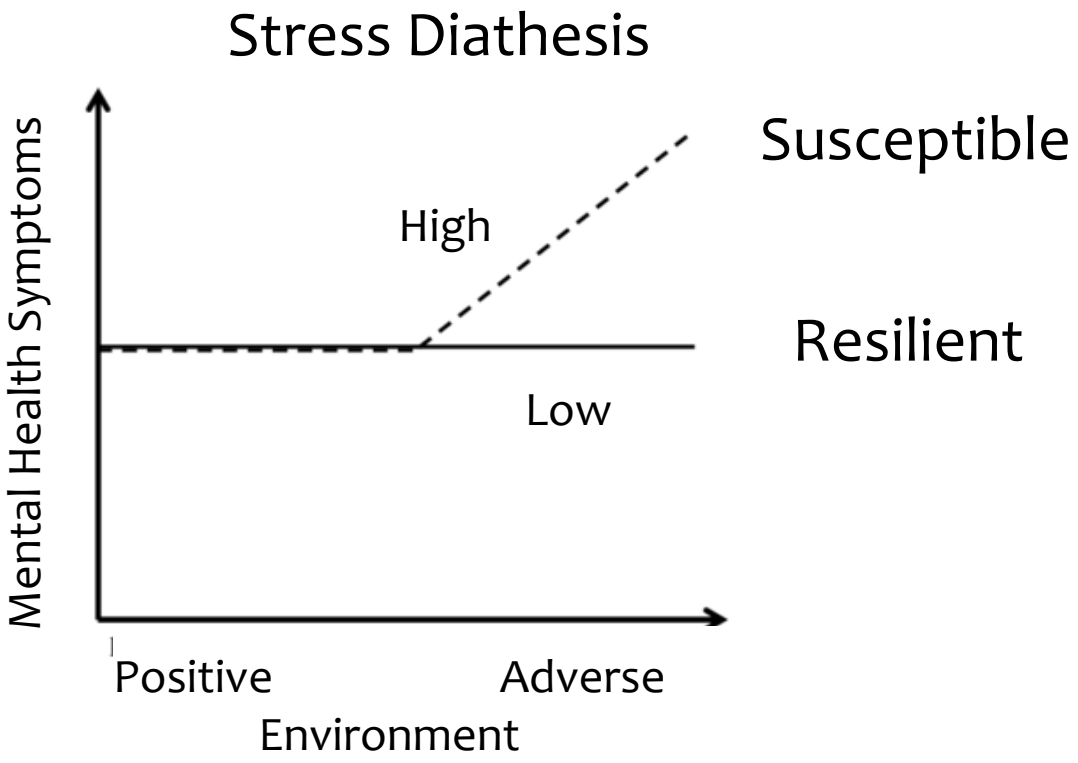
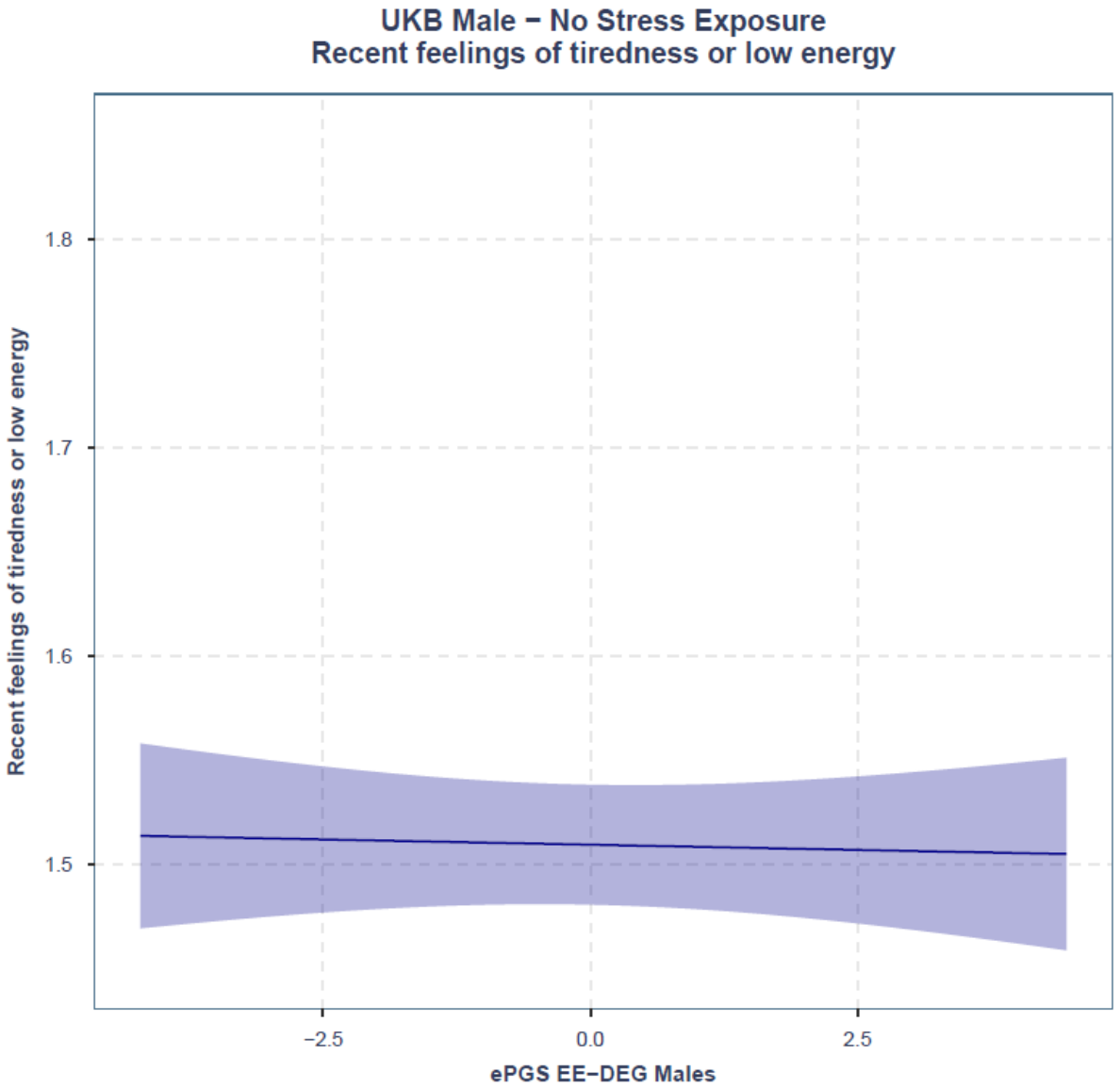
Model for gene x environment interaction

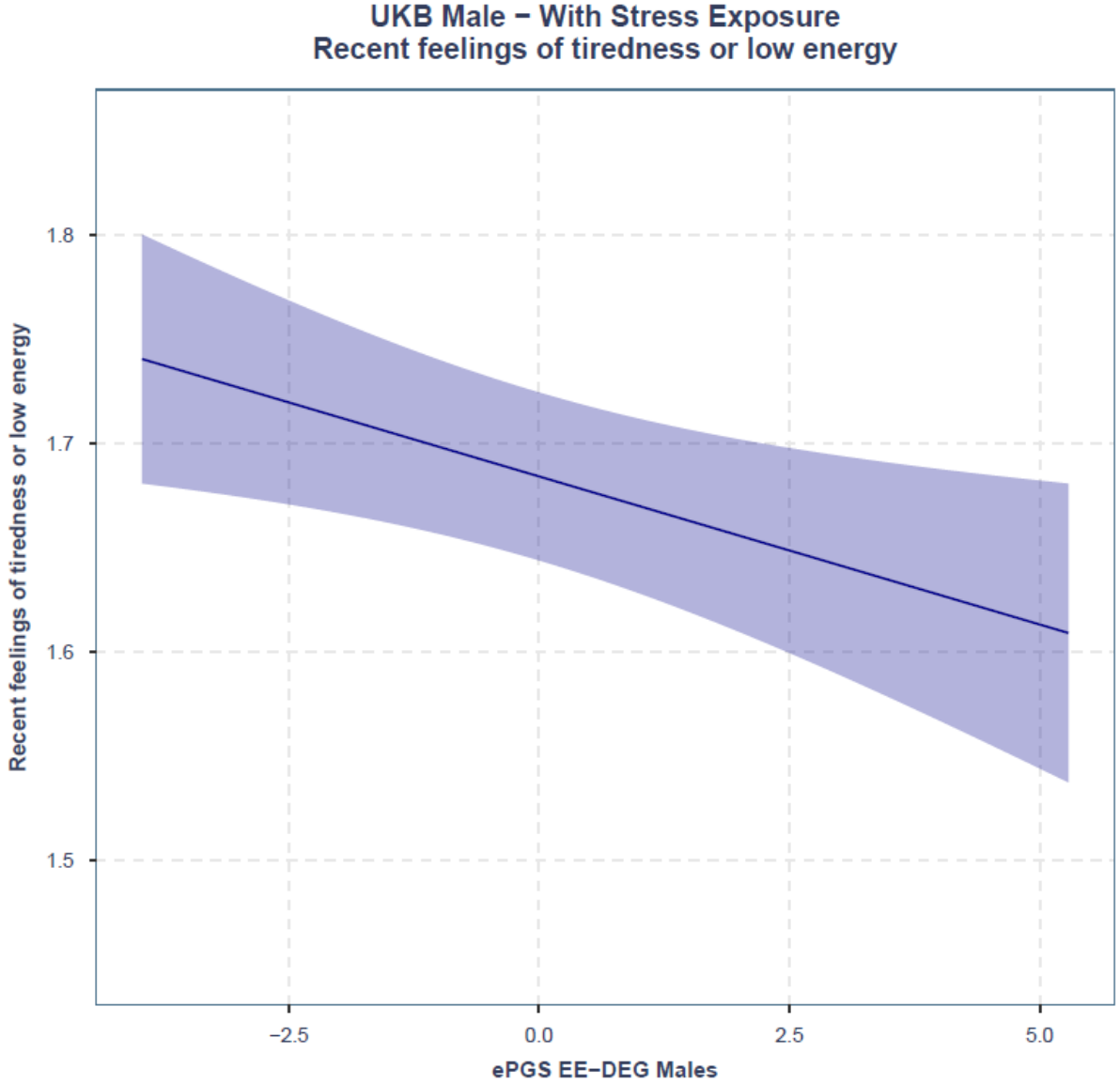


Stress vs no stress (past 2 years)

Depression

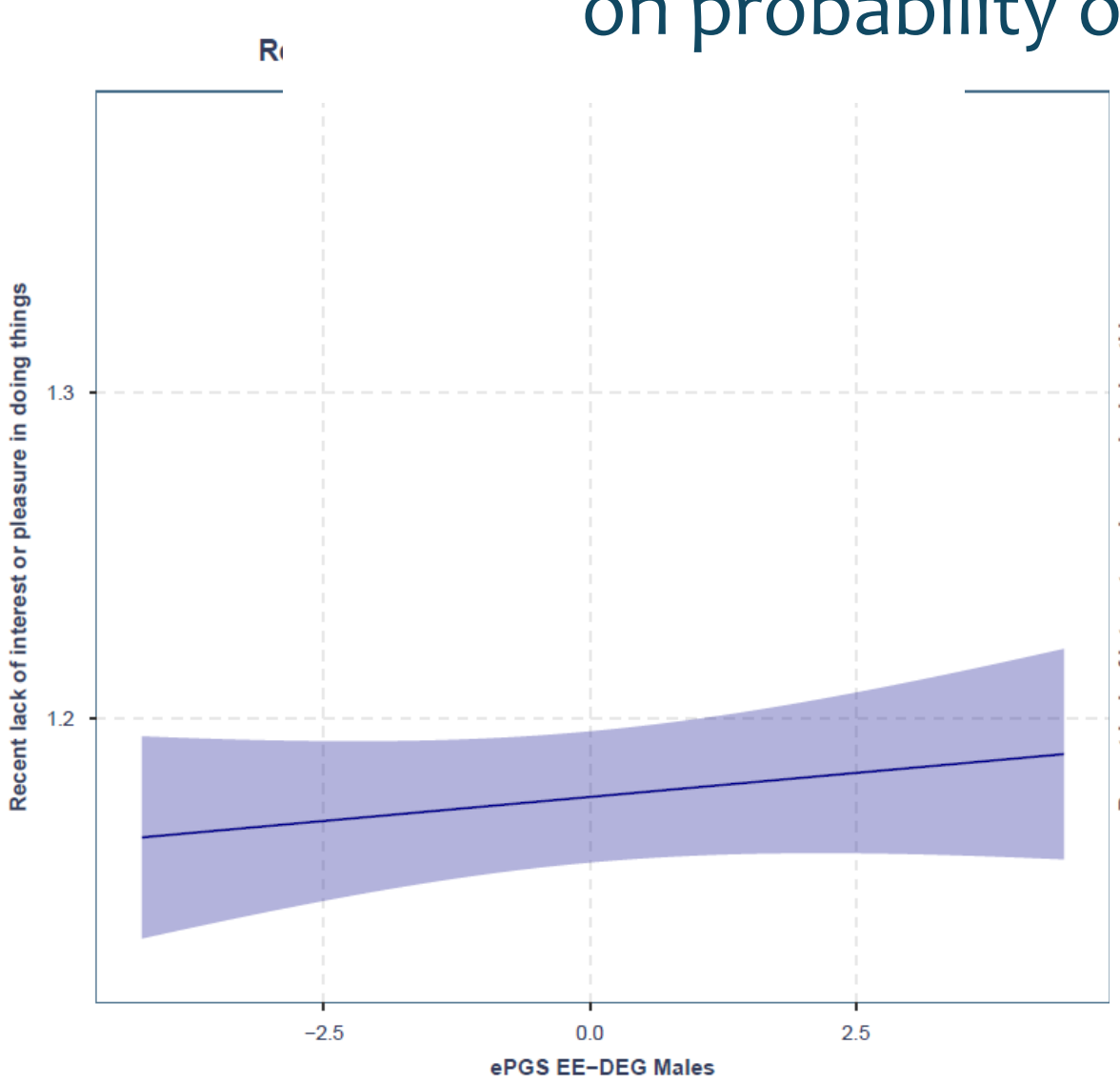


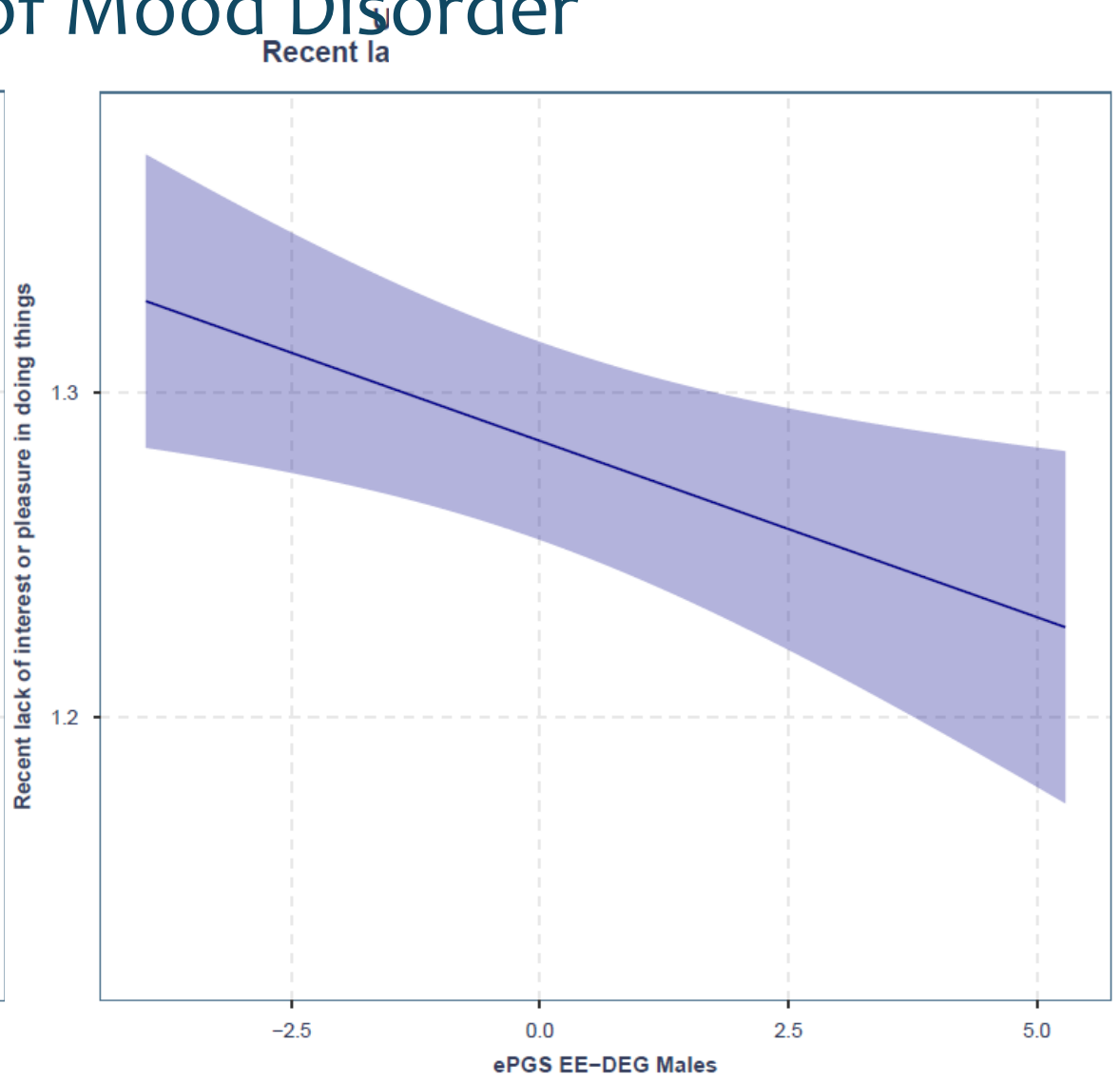
P= 0.80; B= -0.001



P= 0.012; B= -0.014; FDR= 0.04*

Enrichment ePGS (vHipp) moderates the effect of stress on probability of Mood Disorder





P= 0.012; B= -0.010; FDR= 0.04*

Expression-Based Polygenic Scores (ePGS)