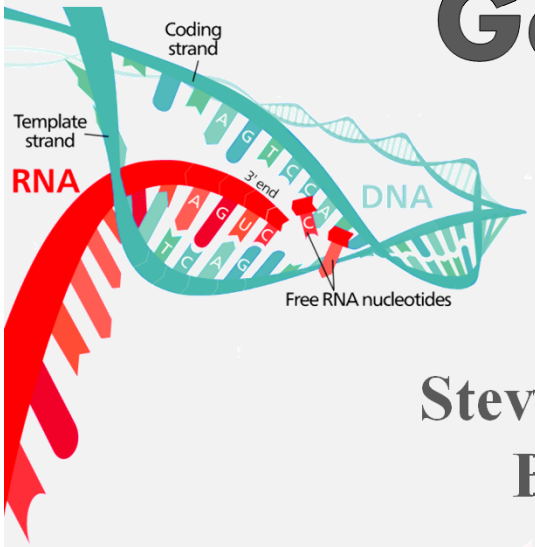
Childhood & Later Life Stressors & Increased Inflammatory Gene Expression in Old Age



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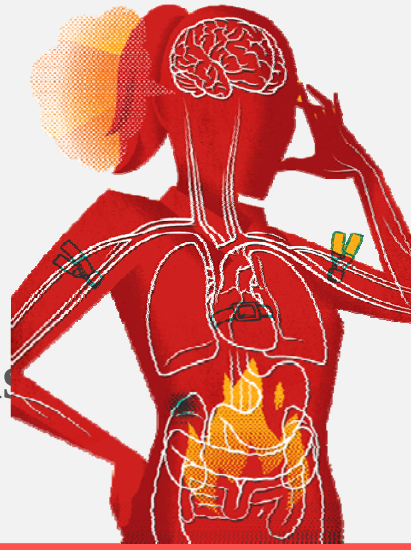
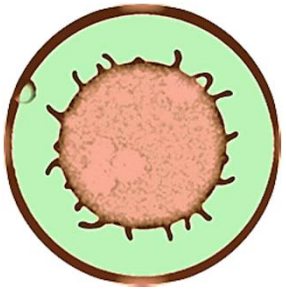
Biomarker Network Meeting 2014

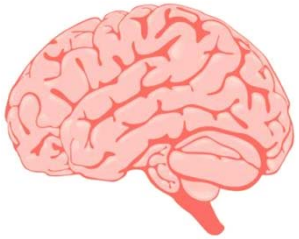


BACKGROUND

Adverse life experiences are linked to poorer health and an increased risk of death and disease.



Stress has been shown to elicit increases in circulating levels of pro-inflammatory cytokines.



Stress during "critical periods" may sensitive the brain to be hyper-responsive to subsequent adversities

However…

- **It is often difficult to disentangle the influences of adversity in childhood vs. adulthood.**
- **We don't know whether these differences persist into old age.**

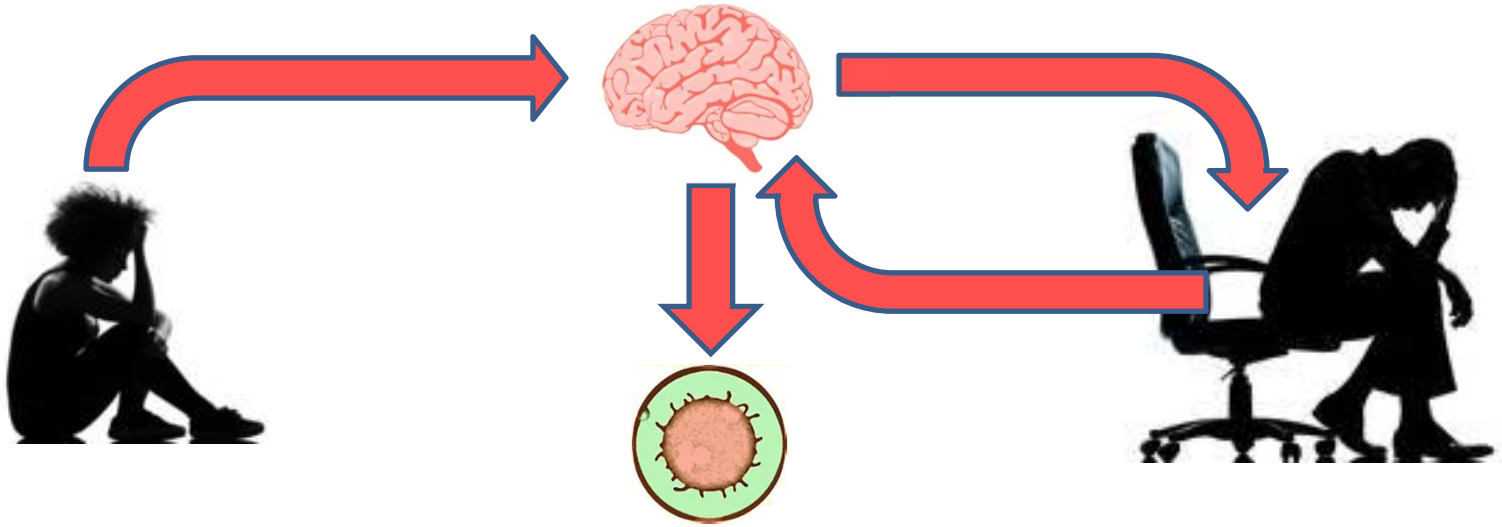
AIMS

Examine the associations between stressors experienced in childhood and adulthood, and the quantitative expression level of three cardinal pro-inflammatory genes:

- COX2, also known as prostaglandin-endoperoxide synthase 2, *PTGS2*
- *ILIB*
- *IL8*

We hypothesize that:

- **Childhood exposure to adversity will be associated with more pronounced increase in inflammatory gene expression than later life exposures.**
- **Early life adversity will sensitize inflammatory gene expression to the effects of stress encountered later in life.**



DATA

HRS Pilot Sample, 2010

- **Randomly selected sample of N=122 participants who had participated in the interview in 2006 or 2008**

- **Blood samples collected into PAXgene RNA tubes.**

- **Six mRNA species were assayed by quantitative RT-PCR, including *ILIB*, *IL8*, *PTGS2* and a housekeeping / normalization marker—ACTB.**

- **A composite RNA score was calculated as the mean between *ILIB*, *IL8*, *PTGS2* after subtracting ACTB from each.**

- **Five adversity variables.**
  1. **Childhood SES**
  2. **Childhood Trauma**
  3. **Childhood Health**
  4. **Adulthood SES**
  5. **Adulthood Trauma**

SAMPLE

Sample Characteristics (N=114)

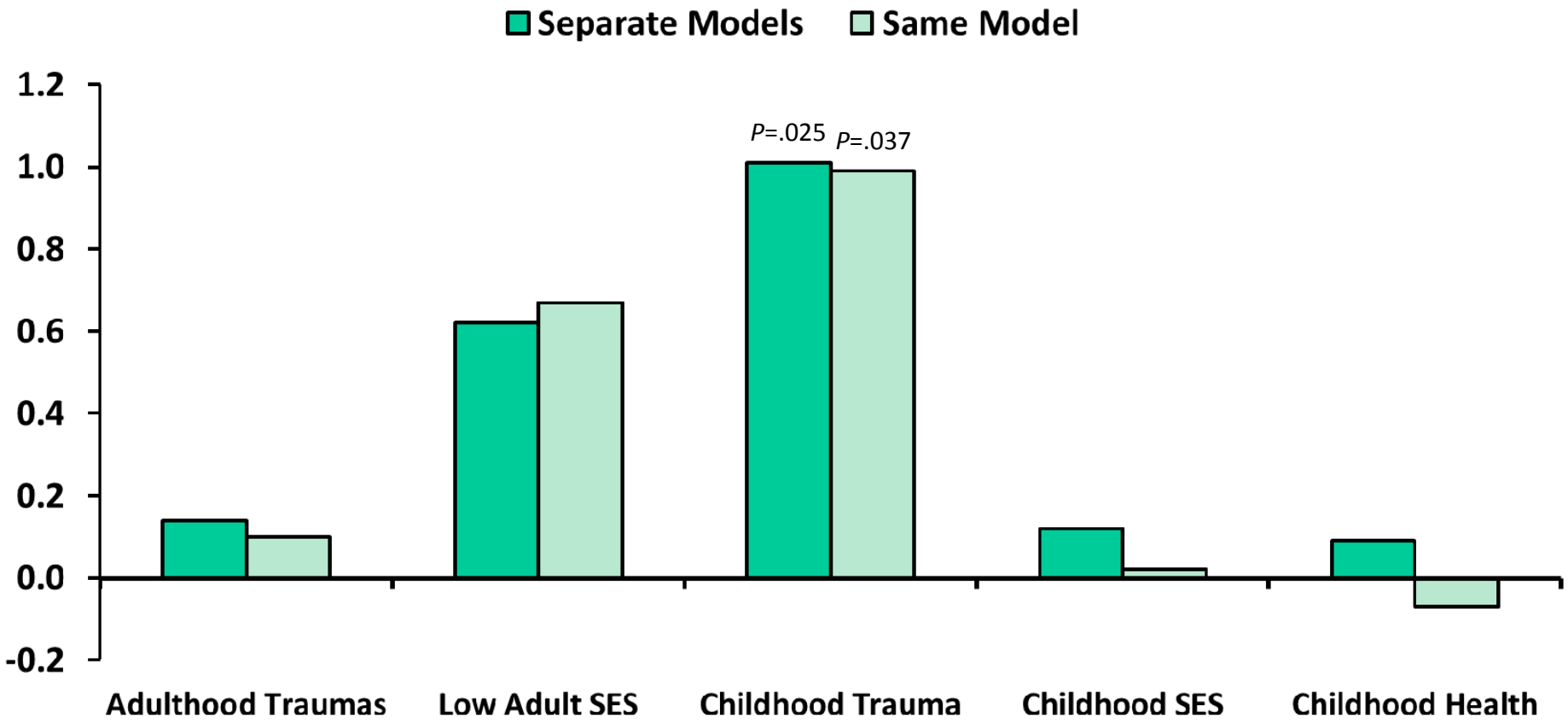
Characteristics	Values
Age (years), mean (sd)	73.22 (9.55)
Sex (Female=1), (%)	55.26%
Race (White=1), (%)	92.16%
Former Smoker, (%)	54.39%
Current Smoker, (%)	10.53%
Obesity, (%)	29.82%
Drinks per Day, mean (sd)	2.12 (4.51)
Childhood Trauma, mean (sd)	0.19 (0.44)
Childhood SES, mean (sd)	1.57 (1.35)
Childhood Health Conditions, mean (sd)	0.29 (0.62)
Adulthood Traumas (count), mean (sd)	1.21 (1.08)
Low Adult SES, (%)	7.02%
Centered RNA Composite Score, mean (sd)	0 (1.97)

RESULTS

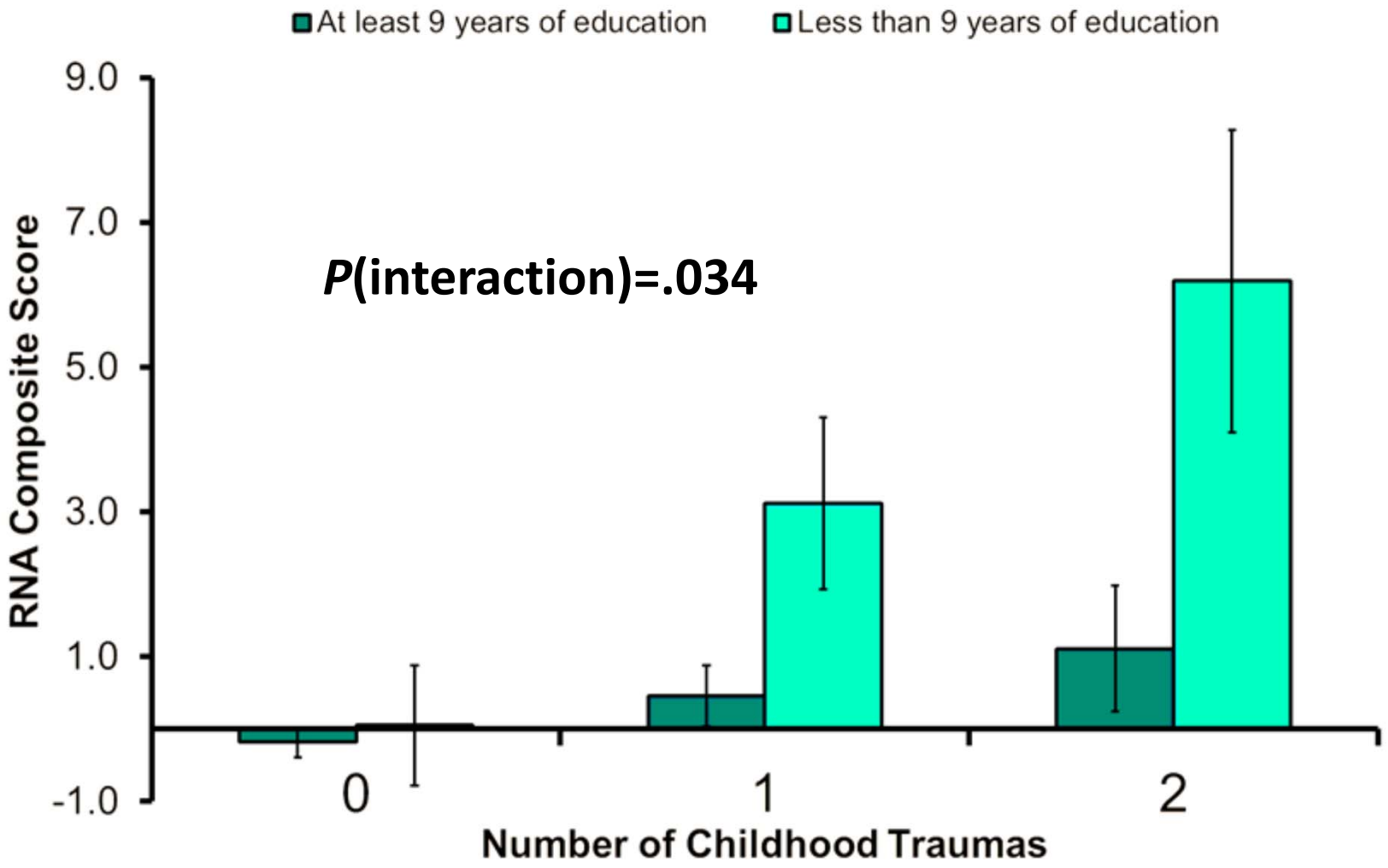
Pearson Correlations Between Childhood and Adulthood Adversity

	Adulthood Traumas	Low Adult SES	Childhood Trauma	Childhood SES
Adulthood Traumas				
Low Adult SES	-0.054			
Childhood Trauma	0.156	0.036		
Childhood SES	0.183	0.369	0.141	
Childhood Health Conditions	0.040	-0.073	0.183	0.076

RESULTS


Separate Models
Same Model
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
P=.025
P=.037
Adulthood Traumas
Low Adult SES
Childhood Trauma
Childhood SES
Childhood Health

RESULTS


At least 9 years of education
Less than 9 years of education
9.0
7.0
5.0
3.0
1.0
-1.0
RNA Composite Score
P(interaction)=.034
0
1
2
Number of Childhood Traumas

CONCLUSIONS

Childhood exposure to traumatic events is associated with elevated expression of pro-inflammatory genes in late adulthood.

Childhood trauma may exacerbate the association between gene expression and low SES in adulthood.

- **Early life adversity may increase later life reactivity to stress.**

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Self-reported items used to measure adversity
Childhood SES (Possible Range 0-5)
Before age 16, would you say your family during that time was pretty well off financially, about average, or poor? (poor=1)
Before age 16, was there a time when you or your family received help from relatives because of financial difficulties?
While you were growing up, before age 16, did financial difficulties ever cause you or your family to move to a different place?
Mother had less than 9 years of education
Father had less than 9 years of education
Childhood Traumas (Possible Range 0-2)
Before you were 18 years old, did either of your parents drink or use drugs so often that it caused problems in the family?
Before you were 18 years old, were you ever physically abused by either of your parents?
Childhood Health (Possible Range 0-8)
Before you were 16 years old, did you have asthma?
Before you were 16 years old, did you have diabetes?
Before you were 16 years old, did you have heart problems?
Before you were 16 years old, did you have ear problems?
Before you were 16 years old, did you have severe headaches/migraines?
Before you were 16 years old, did you have epilepsy/seizures?
Before you were 16 years old, did you have respiratory problems?
Before you were 16 years old, did you have hypertension?
Adulthood Traumas (Possible Range 0-7)
Has a child of yours ever died?
Have you ever been in a major fire, flood, earthquake, or other natural disaster?
Have you ever fired a weapon in combat or been fired upon in combat?
Has your spouse, partner, or child ever been addicted to drugs or alcohol?
Were you the victim of a serious physical attack or assault in your life?
Did you ever have a life-threatening illness or accident?
Did your spouse or a child of yours ever have a life-threatening illness or accident?
Adulthood Low SES (0, 1)
Participant had less than 9 years of education