

Early Life Stress, Neurodevelopment, and Psychopathology in Adolescents: The Impact of the COVID-19 Pandemic

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Prevalence and Burden of Depression and Suicidal Behaviors

- ◆ Depression is *the* leading cause of disability worldwide and a significant risk factor for suicide
- ◆ Adolescence is a particular period of risk for depression and other forms of psychopathology

How Can We Understand the Emergence of Depression in Adolescence?



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Importance of Early Life Stress



Early Life Stress and Major Depressive Disorder

- ELS is a potent risk factor for the development and persistence of MDD in adolescence^{1,2}
 - Adolescents who have experienced ELS have an increased risk of developing MDD (OR=2.58)³

¹McLaughlin et al. (2012) *JAMA Psych*

²Nanni et al. (2012) *AJP*

³LeMoult et al. (2020) *JAACAP*

Our Early Life Stress Project

- ◆ We initiated a multi-domain longitudinal study designed to examine the relation between ELS and the emergence of various forms of psychopathology in adolescence
- ◆ We recruited 220 healthy boys and girls who were exposed to a range of early life stressors
- ◆ We are conducting comprehensive assessments of these children, two years apart. When the COVID-19 shut-down was mandated in March, 2020, we were 2/3 of the way through the third assessment and were starting the fourth wave of assessments

T1

9-12 years

T2

11-14 years

T3

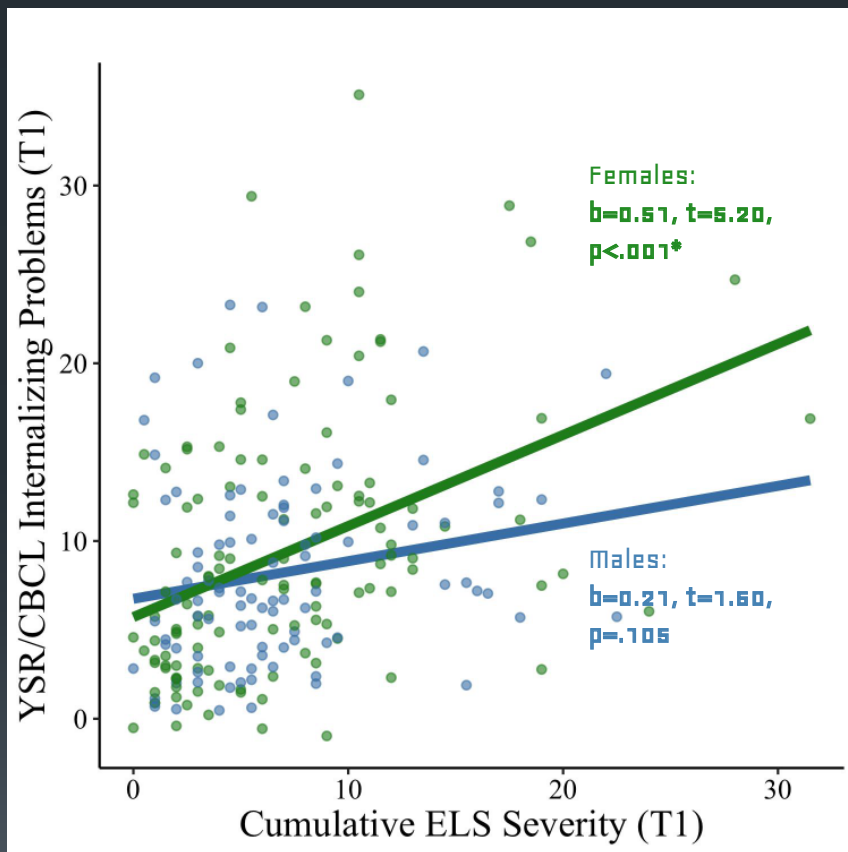
13-16 years

T4

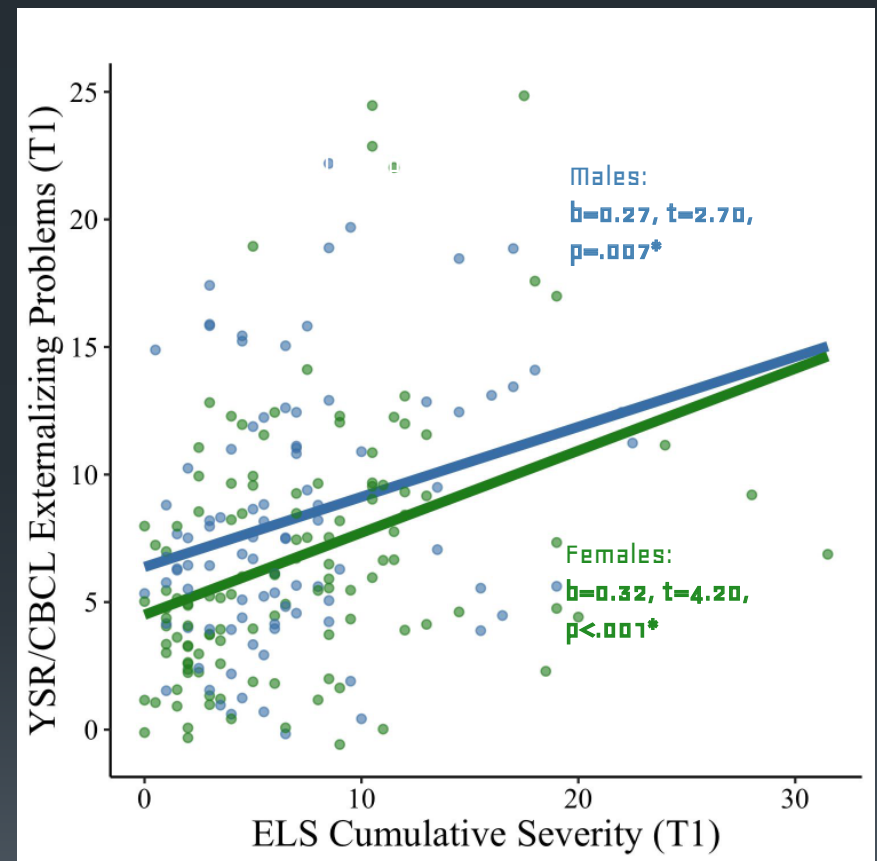
15-18 years



ELS and Internalizing / Externalizing Problems in Males and Females at T1



Internalizing Problems



Externalizing Problems

Mechanisms Underlying the Association Between ELS and Psychopathology

We examined possible mechanisms (*intermediate phenotypes*) underlying the association between ELS and the development of psychopathology in adolescents:

- Brain structure, function, and connectivity
- Cognitive functioning
- Pubertal status and sex hormones
- Cortisol secretion
- Inflammation
- Telomeres and other markers of biological aging
- Neighborhood disadvantage, including air and water quality
- Passive and active smartphone data collection
- Sleep

Early Life Stress and Hippocampal Volume

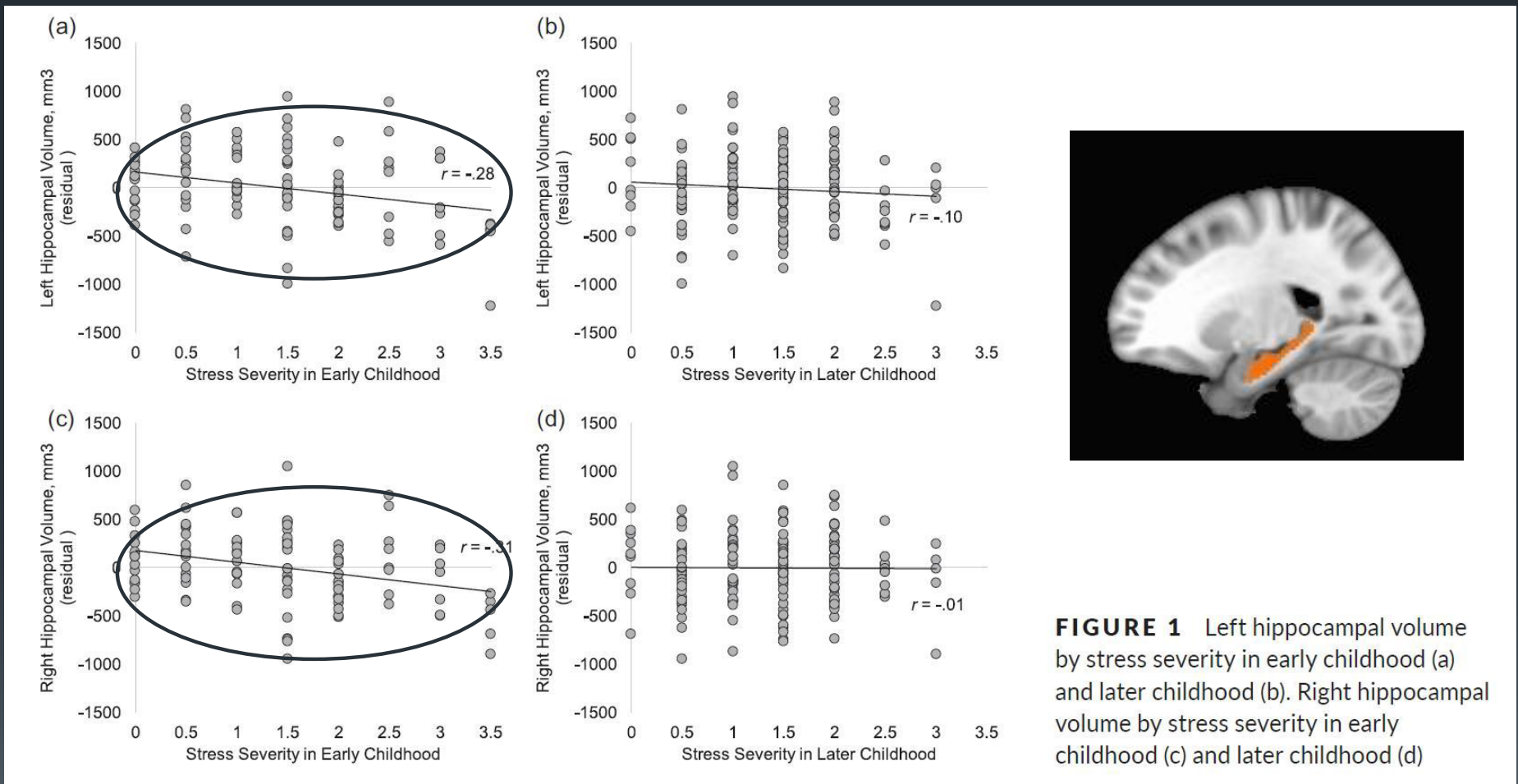
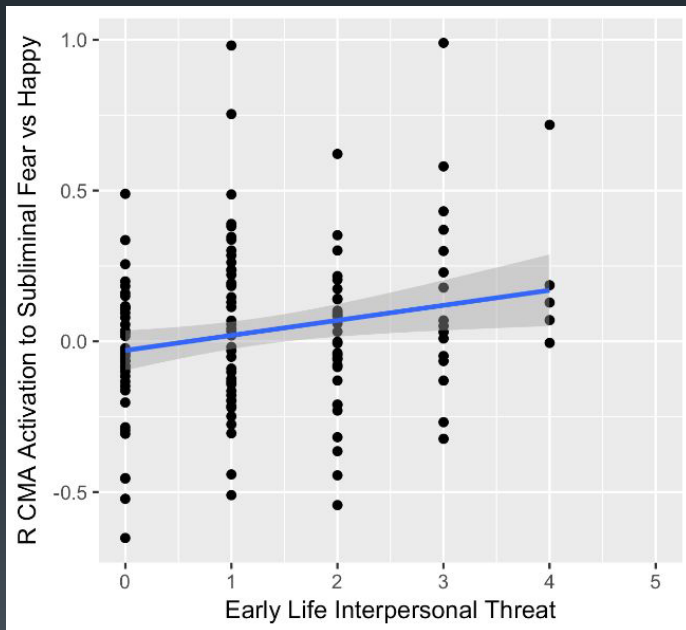


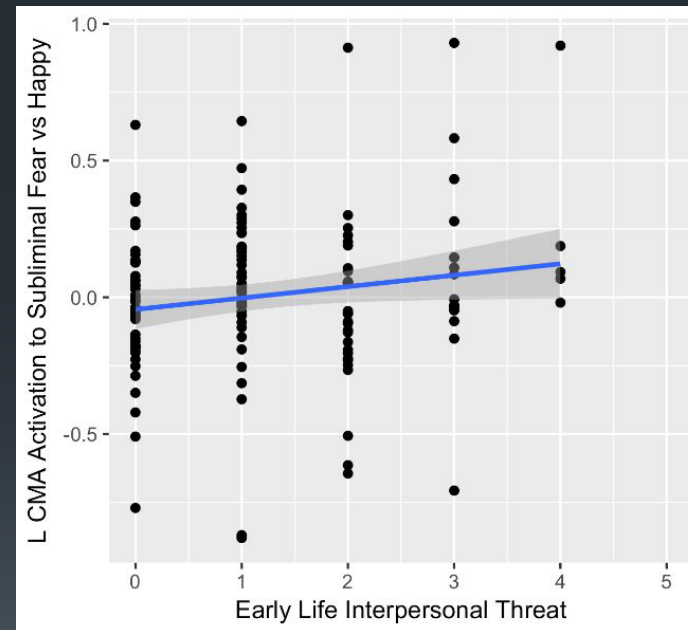
FIGURE 1 Left hippocampal volume by stress severity in early childhood (a) and later childhood (b). Right hippocampal volume by stress severity in early childhood (c) and later childhood (d)

Early Life Stress and Amygdala Activation

Exposure to Early Life Stress Explains Amygdala CMA Activation to Subliminal Fearful Faces

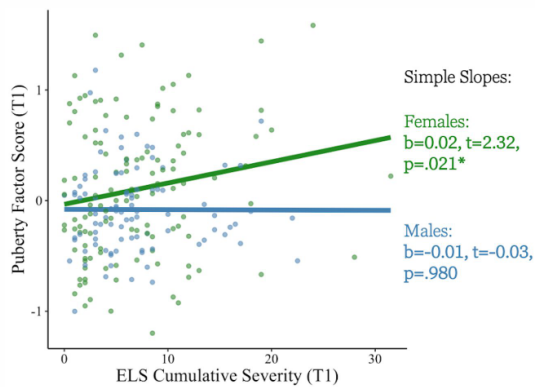


Interpersonal threat is associated with right CMA, $B=.23$, $p=.011$

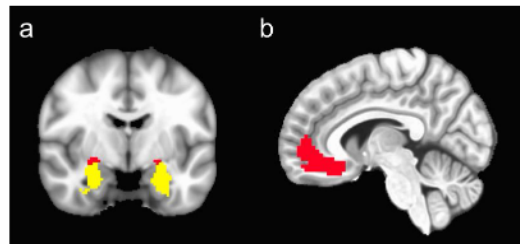


Interpersonal threat is associated with left CMA, $B=.18$, $p=.047$

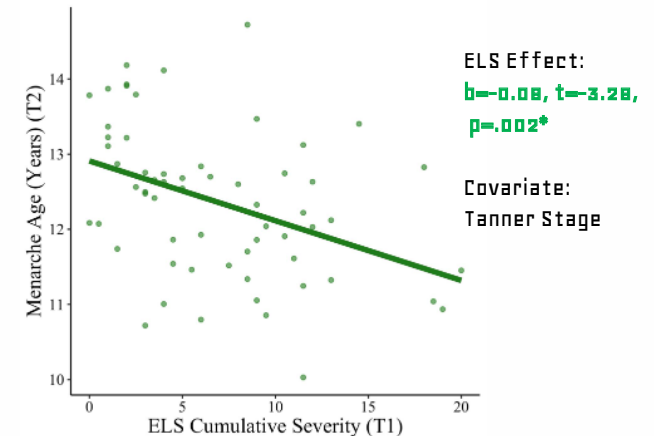
Early Life Stress and Accelerated Development



Advanced pubertal stage in females (Chahal, Kirshenbaum, Miller et al., 2021, Biological Psychiatry: CNI)

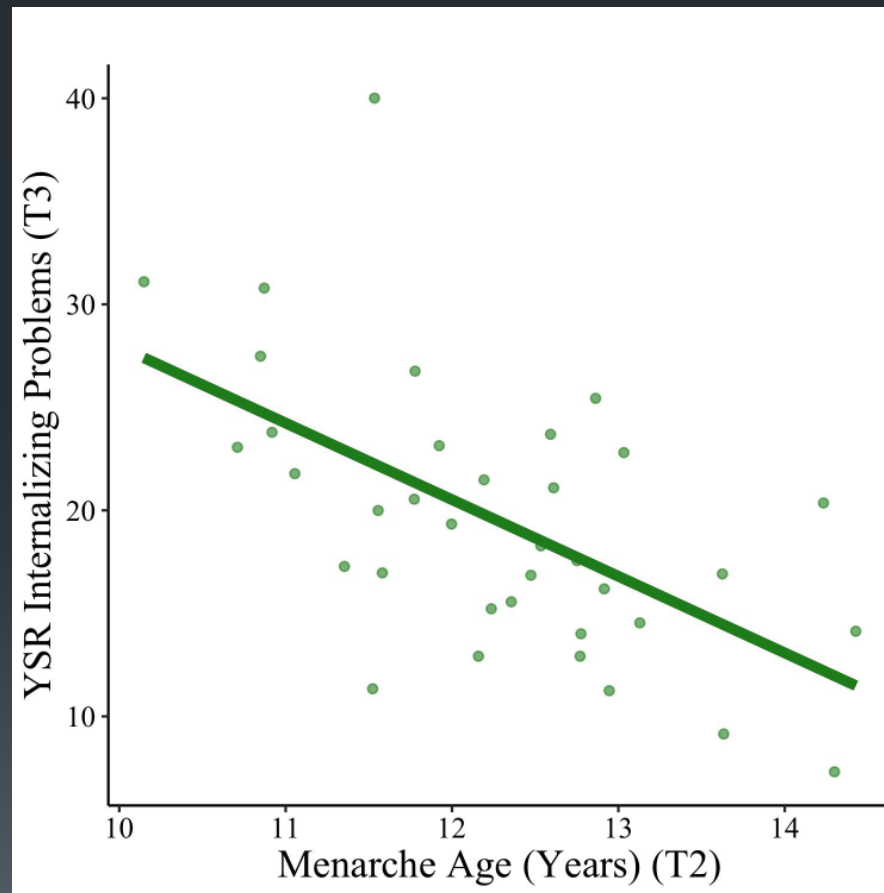


More mature neurophenotypes (lower amygdala-vmPFC connectivity) (Miller et al., 2020, Cerebral Cortex)



Earlier age of menarche (Chahal et al., in press)

Earlier Age of Menarche Predicts Higher Internalizing Problems Two Years Later



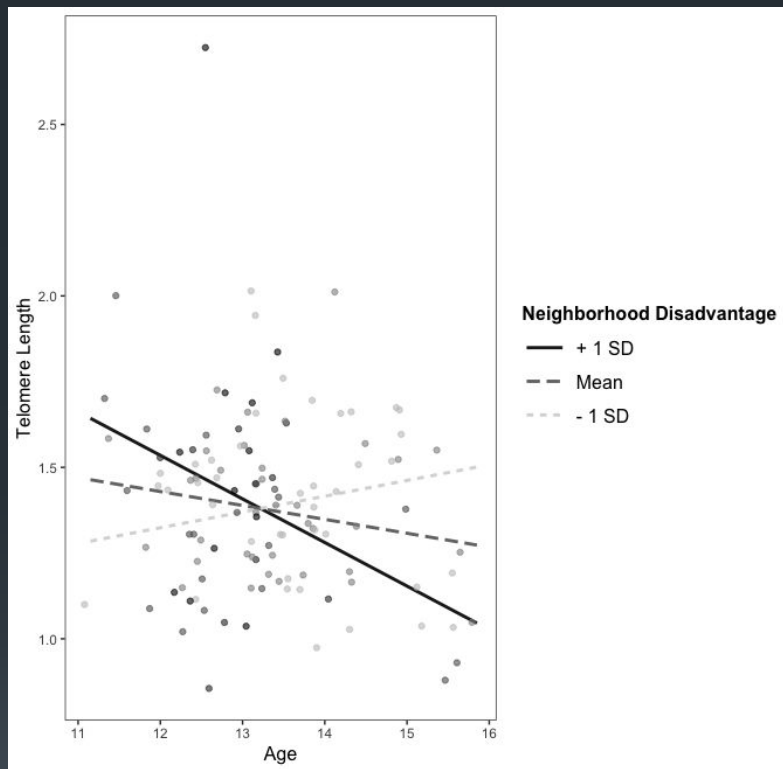
Menarche Age Effect:

$b = -3.36$, $t = -2.30$,
 $p = .022^*$

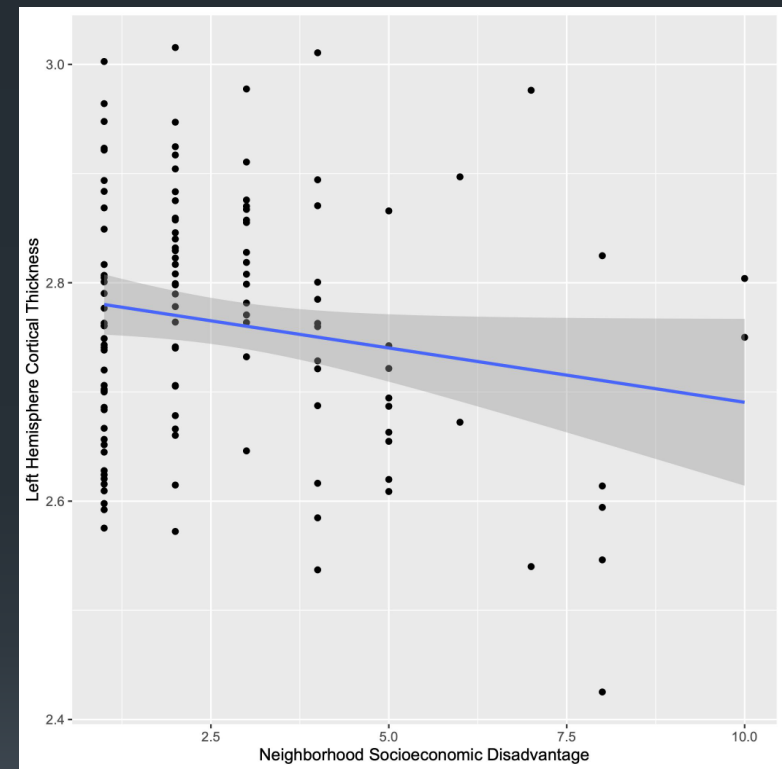
Covariates:

Age [T2, T3], YSR
Internalizing Problems
[T2], race, ELS

ELS is Associated with Neighborhood Disadvantage, Which Predicts Accelerated Biological Aging



Telomere Length



Cortical Thickness



Our Research and the COVID-19 Shut-Down

COVID-19 and Mental Health

The Washington Post
Democracy Dies in Darkness

Education Higher education Local Education The Answer Sheet Jay Mathews

EDUCATION

‘A cry for help’: CDC warns of a steep decline in teen mental health

More than 4 in 10 told the health agency they felt ‘persistently sad or hopeless’



By [Moriah Balingit](#)

March 31, 2022 at 1:00 p.m. EDT

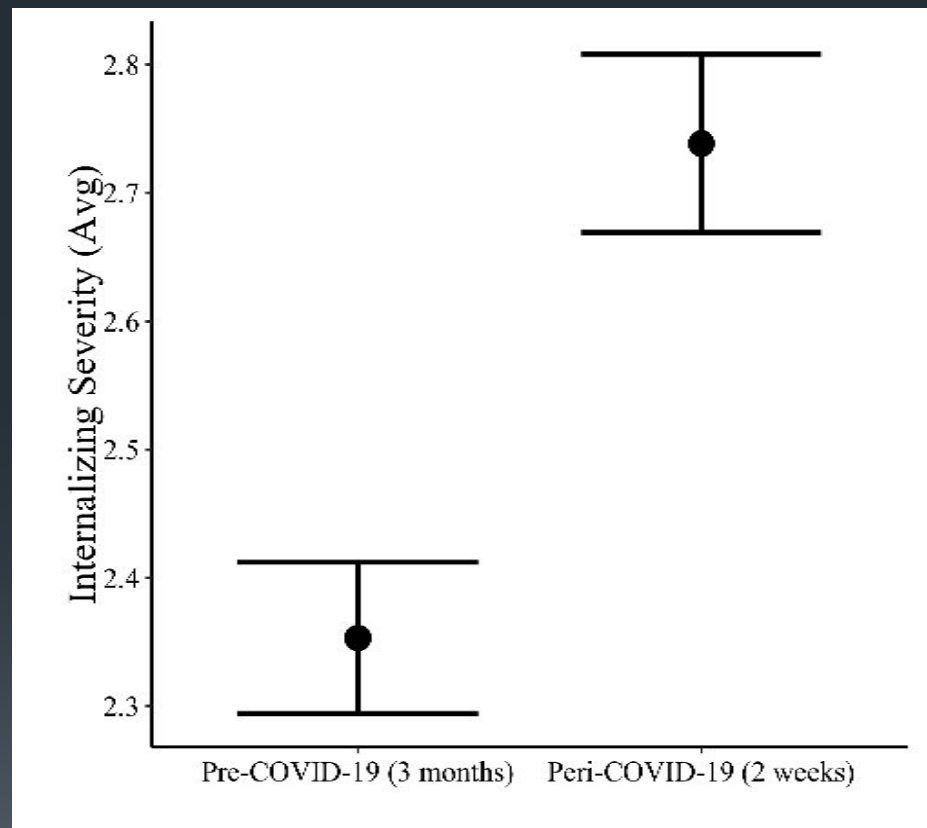


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Change in Internalizing Symptoms in our Sample During COVID-19



The Effects of the COVID-19 Pandemic *on Longitudinal Research*



The Effects of the COVID-19 Pandemic *on Longitudinal Research*

- The COVID-19 pandemic has had significant and widespread negative effects on adolescents' mental health
- What are the implications of the pandemic for interpreting findings of longitudinal studies that were interrupted or disrupted by the COVID-19 shut-down?

The Effects of the COVID-19 Pandemic *on Longitudinal Research*

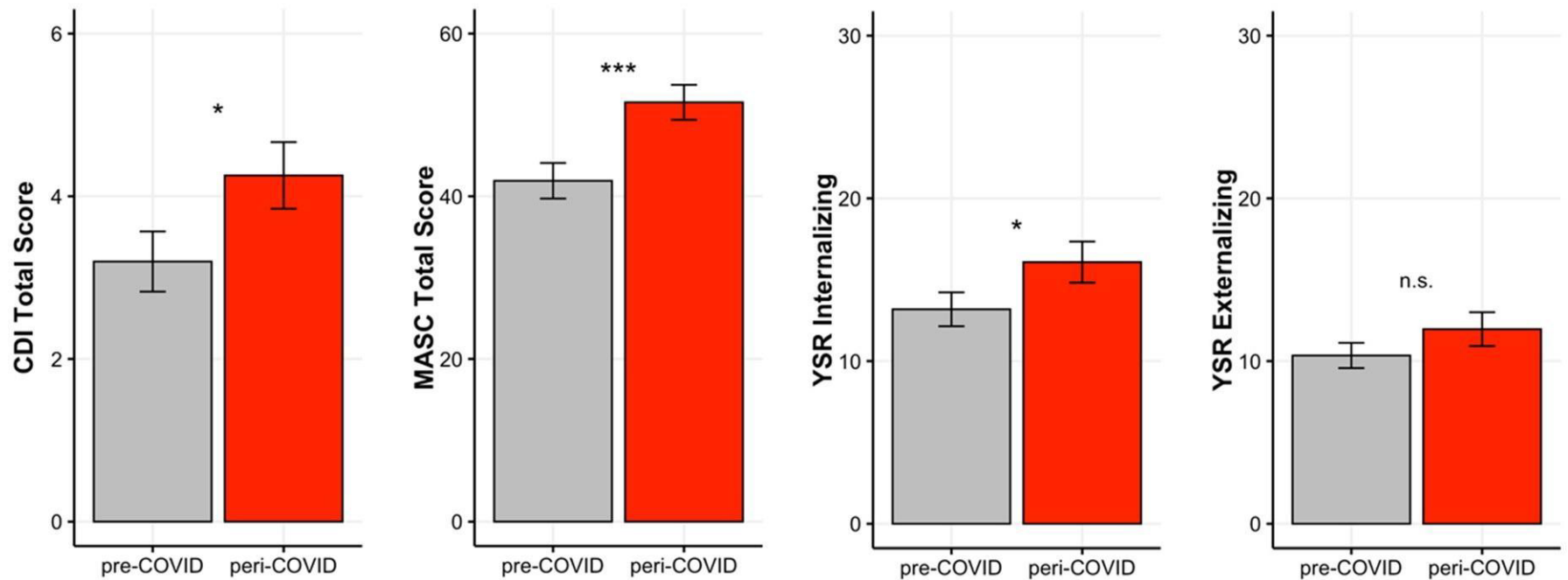
- It is not clear that adolescents today are equivalent to adolescents who were assessed before the pandemic.
 - *Best case*: adolescents are equivalent pre- and post-pandemic, and we simply use interval between assessments as a covariate in our analyses
 - *Worst case*: age-matched adolescents pre and post pandemic differ significantly in their functioning, with important implications for how we interpret longitudinal findings

The Effects of the COVID-19 Pandemic *on Longitudinal Research*

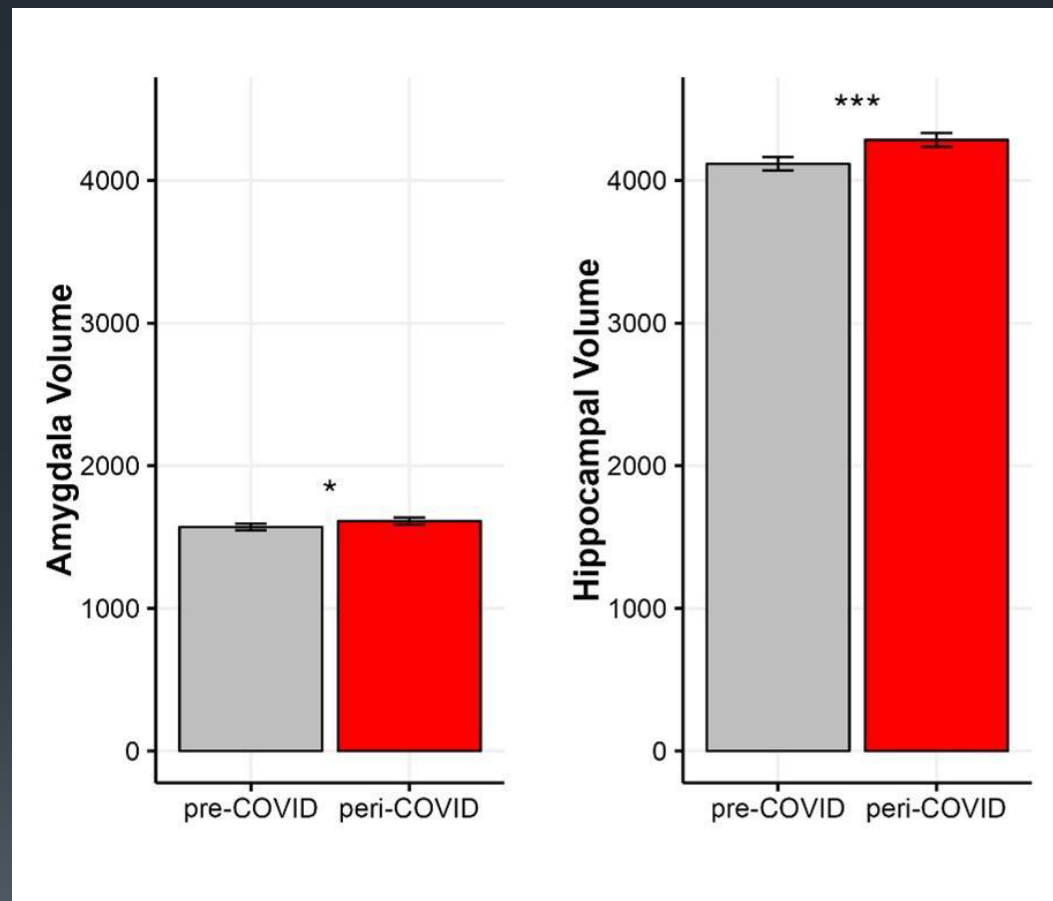


- We compared the functioning of age- and sex-matched adolescents from our ELS study, half of whom were assessed before the pandemic and half of whom were assessed one to two years after pandemic lock-downs were initiated
- The peri-COVID and pre-COVID groups did not differ in *baseline* levels of ELS or psychopathology

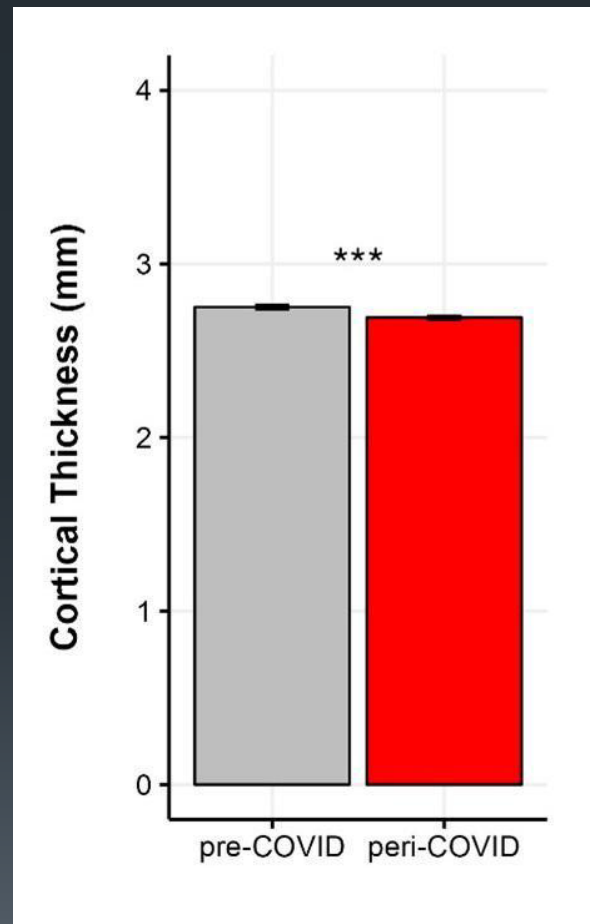
Differences Between Age-Matched Participants Pre- vs. Peri-COVID: *Self-Reported Symptomatology*



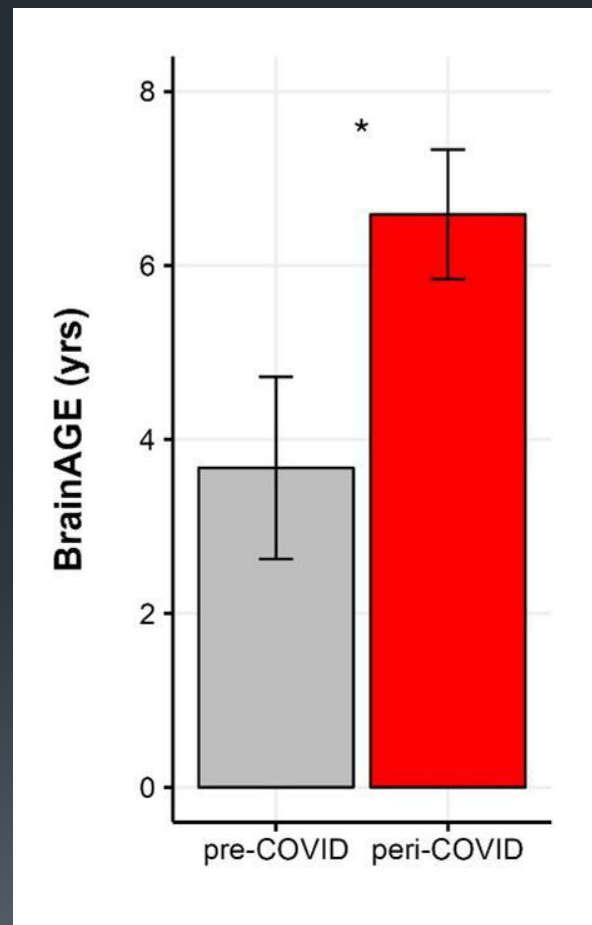
Differences Between Age-Matched Participants Pre- vs. Peri-COVID: *Amygdala and Hippocampal Volume*



Differences Between Age-Matched Participants Pre- vs. Peri-COVID: *Cortical Thickness*



Differences Between Age-Matched Participants Pre- vs. Peri-COVID: *Brain Age Gap Estimate (BrainAGE)*



Differences Between Adolescents Pre- vs. Peri-COVID



- Adolescents assessed during the pandemic differ from their age- and sex-matched peers who were assessed before the pandemic in internalizing symptoms and in metrics of brain structure that index accelerated biological aging.
- The psychobiological characteristics that are altered as a function of the COVID-19 pandemic are the same as those that have been found to be altered by exposure to early adversity, suggesting shared stress-related pathways to psychopathology.

Differences Between Adolescents Pre- vs. Peri-COVID

- These differences between adolescents pre- and peri-COVID have important implications not only for how we view and understand adolescents' mental health as a function of the COVID-19 pandemic, but also for how we analyze and interpret findings from longitudinal data that predate and follow the pandemic
- It will be important to continue to follow and assess adolescents to determine whether these pandemic-related difficulties and anomalies decrease over time or remain stable

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