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)\(^3\)

\(^1\) McLaughlin et al. (2012) *JAMA Psych*
\(^2\) Nanni et al. (2012) *AJP*
\(^3\) LeMoult 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.

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<th>T1</th>
<th>T2</th>
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<tbody>
<tr>
<td>Age range</td>
<td>9-12 years</td>
<td>11-14 years</td>
<td>13-16 years</td>
<td>15-18 years</td>
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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).

Humphreys et al. (2019) Dev Sci
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: CNNI)

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

Miller et al. (2021, 2022)
Our Research and the COVID-19 Shut-Down
COVID-19 and Mental Health

‘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

Listen to article 7 min
Change in Internalizing Symptoms in our Sample During COVID-19

Chahal et al. (2020) BP:CNNI
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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