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Commentary

Implications of the COVID-19 Pandemic for the Developing Adolescent Mind and Brain

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The COVID-19 pandemic caused a global shock not just to physical health as anticipated, but also to mental health. The pandemic's negative impact on mental health has been especially evident for adolescents, with rates of depressive and anxiety symptoms skyrocketing from prepandemic rates (1,2). Isolation from in-person social interactions and closures of established institutions, such as school and organized activities, while needed to protect health, interrupted core processes that are highly salient for adolescent development (3). Adolescents need to socialize with their peers, exert their autonomy, and explore their identity and place in the world. When these core needs are thwarted, mental health can suffer. Furthermore, the considerable neurodevelopment that occurs during adolescence opens sensitivity to experience and vulnerability to mental health problems (4). The significant toll the pandemic took, and continues to take, on adolescent mental health highlights the need to establish and track pandemic-related mental health consequences and to identify mechanisms of influence as a public health priority (5).

The current issue of *Biological Psychiatry: Global Open Science* includes a timely and novel contribution from Gotlib *et al.* (6) on how the pandemic affected adolescent mental health and brain development. The investigators examined differences in measures of mental health and brain structure between 2 groups of adolescents: one assessed before the pandemic (n = 81, pre-COVID group) and one that lived through the pandemic shutdown (n = 82, peri-COVID group). The researchers used rigorous methods to carefully match groups on key features to rule out confounds, and included reliable self-reported mental health measures and multiple brain metrics. Their findings offer unique insight into the consequences and mechanisms of how the pandemic got into the minds and brains of adolescents in the peri-COVID group.

One main study finding was that adolescents who lived through the pandemic shutdown had a more mature-appearing brain (advanced brain age), akin to what has been seen in youths who have experienced extreme adversity. Other brain differences included reduced cortical thickness and larger volume of amygdala and hippocampus in the peri-COVID compared with the pre-COVID group. A second key finding was that the pandemic worsened adolescents' mental health, particularly for internalizing problems such as depression and anxiety. Interestingly, the groups had similar levels of externalizing problems such as fighting and aggression. This pattern is consistent with other reports of pandemic-related increases in adolescent depression and anxiety (1,2). Gotlib *et al.*'s (6) study is an exemplar of the knowledge that can be gained by studying vulnerability to mental health problems through identifying developmental differences and neurobiological mechanisms that may differentially lead to resilience or disorder.

Using cutting-edge machine learning models, Gotlib *et al.* (6) drew on multiple cortical and subcortical measures from across the brain (volume, thickness, and surface area) to predict an adolescent's chronological age, or predicted brain age. They subtracted chronological age from predicted brain age to estimate the "brain age gap." The authors found an effect of the pandemic on adolescents' brain age gap whereby those assessed right after the shutdown lifted had an older brain age than those assessed before the pandemic. The group assessed after the shutdown also showed reduced cortical thickness and larger amygdala and hippocampus volumes. Two aspects of these findings are important for biological psychiatry. First, the group differences in these specific brain metrics provide some empirical support of the stress acceleration hypothesis (7), a neurobiological framework that posits that stress accelerates development in order to orient the system toward a more adult-like state of brain and behavior by implicating neural circuitry that modulates stress responses and emotions. Premature activation or accelerated aging of the brain's emotional circuitry may increase vulnerability to emotion and fear-based mental health problems. In addition to finding a more advanced brain age postpandemic, Gotlib *et al.*'s findings of reduced cortical thickness are consistent with the way typical cortical neurodevelopmental patterns unfold across childhood into adulthood (8), suggestive of aging, and of larger amygdala and hippocampus volumes, consistent with the effects of early adversity on these limbic regions (7). Second, our understanding of human neurodevelopmental benchmarks for the timing and rate of brain maturation is relatively nascent. Gotlib *et al.*'s application of the brain age gap model to their neuroimaging data adds to the growing literature (9,10) to help inform formulation of brain development benchmarks. Biological psychiatry lacks "brain growth" charts akin to those available for pediatric height and weight growth. Benchmarks of neurodevelopmental trajectories are needed to examine in relation to mental health symptoms and diagnoses in childhood and adolescence. As the range of environmental exposures becomes more frequent and varied with age (infancy vs. adolescence), disentangling biological timing and environmental influence can be difficult; nonetheless, data on patterns of brain age, such as that provided by Gotlib *et al.*, can help us better understand how biological and environmental contributions may hasten or slow brain maturation and affect mental health.

A second main finding is that the pandemic worsened adolescents' mental health, particularly for depression and anxiety, consistent with multiple reports. Adolescents assessed after the shutdown showed higher levels of internalizing problems than those assessed before the shutdown. It is interesting

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to note that this difference was specific to internalizing problems, as externalizing problems did not differ between the groups. Externalizing problems typically implicate others (often peers at this age) and frequently occur in school, e.g., aggression, fighting, stealing, and truancy. The potential for these kinds of behaviors was possibly reduced due to the stay-at-home orders. Adolescents were generally not with peers at school or in their neighborhoods, settings in which youth often engage in (and are seen doing) externalizing behaviors. Thus, it is interesting Gotlib *et al.* (6) did not find lower externalizing problems in the peri-COVID versus pre-COVID groups given the shutdown of school and peer settings. These patterns raise new questions about the role of social settings when diminished from the norm given the typical adolescent increase in risk taking and reward seeking—instead, depression and anxiety were elevated. Thus, Gotlib *et al.*'s findings reinforce the importance of considering adolescents' access to social contexts and opportunities when studying mental health problems.

The COVID-19 pandemic led to an influx of new research on how it affected adolescent mental health. While adding to the existing empirical evidence, Gotlib *et al.* (6) also offer considerations for researchers regarding analyses of longitudinal data given the cessation of ongoing data collection. These interruptions undoubtedly affected adolescent development and raise concerns about how research measures were affected and what researchers can do to account for these influences. The pandemic created an experiment of nature by introducing periods of time before and after the shutdowns, an unplanned factor cleverly leveraged by Gotlib *et al.* This led the authors to call attention to the fact that the pandemic interrupted planned, repeated assessments at specific intervals of time in longitudinal studies. Moving forward, researchers will need to account for these influences in their approaches to analyzing longitudinal datasets affected by the pandemic. Longitudinal designs allow us to track changes within and between people to inform the timing and progression or regression of development. Gotlib *et al.*'s findings leave open questions about whether the patterns they found are temporary or stable, addressable by continuing to study their sample over time. They offer suggestions such as including dummy variables to categorize pandemic interruptions or other variables as controls in their analyses, highlighting the importance of carefully characterizing samples and their experiences. It is also important to attend to the generalizability of adolescent mental health and brain development findings across cultures and sociodemographic groups. Careful description of studied groups is key as is sampling adolescents from a range of demographic groups and testing research questions across diverse samples. Stressors such as having COVID-19 oneself, illness or death of household members, or parental financial strain—while not collected or showed low base rates of in this study—will be important to examine in other datasets to determine how COVID-19 and related stressors directly affected adolescent mental health and brain development.

The pandemic undoubtedly created adversity across the globe and across all ages. Nonetheless, the uptick in depression and anxiety among youth suggests that the pandemic has had very specific impacts on, and may even have been especially adverse for, adolescents given their developmental needs and stages of brain maturation and social and emotional development. Researchers conducting longitudinal studies interrupted by the pandemic will face challenges when interpreting their results, as results may not reflect normative development. Yet, to fully understand mental health, it is critical to study developmental changes; thus, researchers studying the pandemic's effects are encouraged to consider what relations may be identified or obscured through cross-sectional data and group comparisons on mean levels of an outcome. Longitudinal data enable us to tie neural changes directly to behavioral changes, thereby expanding knowledge of normative mechanisms as well as individual variability. For researchers to rigorously and robustly address long-term consequences of the pandemic on adolescent wellbeing, research agencies will need to designate funding specifically for analyzing longitudinal datasets affected by the pandemic and research groups will need to collaborate and share datasets to keep the momentum going for addressing this mental health priority.

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Article Information

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