JAMA Network Open

Invited Commentary | Pediatrics

The Implications of Early Adversity Even Before Birth

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It has long been known that early experience can have a profound and long-lasting impact on the course of human development. Over the past few decades, however, it has increasingly been demonstrated that exposure to adversity during critical periods of brain development is specifically associated with adverse developmental outcomes, including compromised cognitive, social-emotional, and neural development.[1] More recently, it has become clear that various functional domains are differentially associated with different critical periods. For example, language, memory, and executive functions are all influenced differently depending on the timing of the adversity (eg, an impoverished language environment in the first 2 years of life will have a more detrimental effect on language development than for the development of executive functions).[2] Not surprisingly, the differential outcomes of adversity also influence brain development differently depending on timing (eg, the hippocampus may be more vulnerable in the early years than the prefrontal cortex).[2]

Animal models have proven to be particularly helpful in defining the onset and offset of critical periods as well as in elucidating the molecular events that regulate critical periods.[3] Unfortunately, it has proven difficult to identify the critical period onset and offset in humans with the same precision that animal models permit. Moreover, the current methods of visualizing human brain development lack the spatial resolution necessary to identify the regionally specific associations of adversity with brain development.

Over the past 2 decades, much of the work on early adversity has focused on the first years of life. Thus, we have learned that different types of adversity, such as physical abuse or neglect, have very deleterious outcomes.[2] Although it has long been known that prenatal experiences, such as exposure to alcohol, tobacco, or stress, can have a deleterious effect on postnatal development, how early these adverse events may affect development is unclear.

In a remarkable study by Wu et al,[4] we learned that not only is psychological distress common among a well-educated sample of healthy women (eg, >50% had a graduate degree) but also fetal exposure to maternal stress, anxiety, or depression has an association with prenatal brain development. Specifically, Wu et al[4] reported that 27% of the sample scored high on a perceived stress questionnaire, 26% had high scores for anxiety, and 11% had elevated symptoms of depression. Importantly, the authors then examined the association between these indices of psychological distress and fetal brain development as inferred from magnetic resonance imaging and magnetic resonance spectroscopy. They reported that increases in trait anxiety scores were associated with reductions in the volume of the left hemisphere. Elevations in both stress and anxiety scores were associated with increased gyrification in the frontal and temporal lobes. Increases in maternal depression scores were associated with reductions in creatine and choline levels.

The study by Wu et al[4] included several surprising findings. The relatively high base rate of psychological distress (27%) in an otherwise healthy, well-educated sample of pregnant women was disquieting; more worrisome was the association between psychological distress and fetal brain development. Reduced brain volume and increases in gyrification could have profound implications for behavioral development. Although white matter is potentially malleable, a reduction in gray matter before birth could foreshadow potentially permanent consequences for behavioral development.

Naturally, a single study leaves as many loose threads as knots. It is often arduous to systematically address the limitations of earlier work. In the case of Wu et al,[4] for example, the

authors offered no functional data; thus, how do these remarkable anatomical and neurochemical findings translate into behavior? And, if they do manifest in changes in behavior, can the postnatal environment compensate for the prenatal environment? That is, can the outcomes of prenatal stress, anxiety, or depression be compensated for by addressing these psychological issues in the mother after her baby is born? Also unknown from this study is how early these associations between maternal characteristics and fetal brain development begin; for example, might these associations have been present in the first trimester? In addition, the women who took part in this study were mostly healthy and well educated; what might we expect of a cohort with little access to social and financial supports, that meets the clinical criteria for an anxiety or a depressive disorder, or whose stress has reached so-called toxic levels?

Leaving aside the technical challenges that Wu et al[4] had to overcome to perform imaging of the fetal brain, the findings have enormous scientific, clinical, and public health implications. For example, we know that infants who experience a significant stroke in the perinatal period show nearly complete recovery in most developmental domains, including language (all the more remarkable if the stroke occurred in the left hemisphere).[5] It remains to be seen whether these prenatal effects are subsequently mitigated after birth, leaving little functional trace behind. In the context of clinical care, these findings could be interpreted to suggest that obstetricians and others who provide care for pregnant women should pay close attention to maternal psychological health and whether women have the resources to reduce the burden of stress during pregnancy. From a public health perspective, we know that anxiety, depression, and stress affect a huge percentage of the US population. Thus, should we be doing a better job of screening pregnant women for psychological distress and mental health issues? If so, how early do we start, who do we target, and what resources can be offered to these women?

Although considerable attention recently has been paid to so-called toxic stress,[6] nearly all of this attention has focused on postnatal development; we need to recalibrate our thinking to include the prenatal period as well. Precisely how far back in the prenatal period we should direct our attention remains unclear, as does whether the anatomical and neurochemical findings in this study will manifest in serious neurodevelopmental consequences. Assuming these findings can be replicated, we should all be concerned about how early the consequences of maternal psychological distress may manifest in prenatal brain development.

ARTICLE INFORMATION

Published: January 29, 2020. doi:10.1001/jamanetworkopen.2019.20030

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Conflict of Interest Disclosures: None reported.

Funding/Support: This article was supported by grant MH091363 from the National Institute of Mental Health and grant OPP1111625 from the Bill and Melinda Gates Foundation.

Role of the Funder/Sponsor: The funders had no role in the preparation, review, or approval of the manuscript and the decision to submit the manuscript for publication.

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