

Childhood adversity and the brain: Harnessing the power of neuroplasticity

Richard J. Davidson
Center for Healthy Minds
University of Wisconsin-Madison

The preparation of this manuscript was supported by NIMH grant MH043454-31. RJD is Founder and President of Healthy Minds Innovations, Inc., a non-profit organization affiliated with the Center for Healthy Minds. Please address correspondence to RJD: rjdaids@wisc.edu

Childhood adversity and the brain: Harnessing the power of neuroplasticity

Richard J. Davidson
Center for Healthy Minds
University of Wisconsin-Madison

The article by Gehred et al., (2021)(1) showcases unique new data and a novel window on the long-term impact of childhood adversity on structural changes in the brain. This report uses data from a by now well-known birth cohort in Dunedin, New Zealand creatively harnessed over many decades by Moffitt and Caspi. It is a testament to these scholars that they have continuously added to the measurement armamentarium of this project as new relevant measures and technologies have been developed. When this study was first launched, neuroimaging did not exist. The newly added neuroimaging measures along with the measurement of different aspects of development as the sample matured results in this birth cohort offering a gold mine of rich data that have so effectively been explored over the years by Moffitt and Caspi and their colleagues. This target article reports that both prospectively ascertained and retrospective measures of childhood adversity were associated with smaller total cortical surface area, average cortical thickness and smaller subcortical grey matter volume in a birth cohort of 861 participants. The imaging data were acquired when the participants were 45 years of age, with 94% of the original sample participating. They also reported that associations with prospectively-ascertained measures of adversity were consistently stronger than those with retrospectively-reported adversity. Finally, the findings revealed widely distributed effects throughout the brain with virtually no regional specificity.

In this commentary I will further discuss two striking findings from this study: 1. That prospective measures of adversity are more strongly associated with the structural variations in the brain than the retrospective measures; and 2. That the observed variations in the brain were widespread and not localized. Following this I will consider the implications of these findings for interventions that might reduce the deleterious impact of adverse events. Finally I end by calling for a parallel longitudinal investigation of positive protector factors that may reflect the neural embedding of early life enrichment. Throughout I will offer up some recommendations and questions for future research.

Prospective measures of early adversity are stronger predictors of structural variation in the brain at midlife than retrospective measures of early adversity

One of the key novel findings from this article is that the prospective measures of adversity were more consistently associated with smaller cortical surface area and volume, and smaller subcortical grey matter volume than retrospectively assessed measures. The prospective measures were derived from records gathered during the ages of 3-15 years and were obtained from notes from interviewers, pediatricians, nurses, and other examiners. The retrospective measures were obtained from structured interviews conducted when the participants were 38 years of age. Their data reveal that even for participants exposed to early adversity who as

young adults reported relatively little early adversity, widespread brain surface area and volume reductions were still apparent. This is a striking finding with both theoretical and practical import. The findings suggest that it is the adversity that occurs in the early years of life that is critically important with regard to brain structure and that a re-interpretation or reappraisal of these early life events in young adulthood has little bearing on the neural scarring produced by these early insults. It will be of interest in future analyses to explore the extent to which the structural changes in the brain are mediators of long-term effects of adversity on psychopathology.

It is curious that other research has reported that it is the retrospective subjective reports of child maltreatment that best predict the subsequent development of psychopathology. The presence of clear objective indicators of maltreatment in the absence of retrospective subjective reports is associated with minimal psychopathology (2). How to reconcile these divergent interpretations is not clear. The differences may in part stem from the different ways in which the retrospective subjective measures were derived in each study. In the Gehard et al. study[1] the retrospective measure was derived from a structured interview at a single age. In the Danese and Widom study(2) the retrospective measure was derived from an extensive battery of self-report and interview-based measures. In the future it will be informative to examine the extent to which the diffuse presence of smaller cortical surface area and volume mediates the relationship between prospective measures of early adversity and subsequent psychopathology. And it is also critical to evaluate the nature of the retrospective assessment measures and determine how different types of measures influence the observed associations.

The observed structural variations in the brain associated with childhood adversity are diffuse

The findings were quite striking in revealing associations between prospective measures of adversity with widespread areas of the cortex and across multiple subcortical locations. Other neuroimaging methods that emphasize connectivity including diffusion weighted imaging to examine white matter connectivity and resting state functional connectivity to measure functional connectivity among different brain circuits are methods that may reveal more specificity because they focus on connectivity rather than area or volume differences within regions. Such measures have revealed more localized effects of childhood adversity with several findings suggesting effects on both functional and structural connectivity with prefrontal cortex (3), (4). Whether the failure to detect other more diffuse effects in these studies is a power issue or whether connectivity measures may reveal more localized effects of adversity on the brain is an issue that remains to be resolved.

The question of developmental timing

One of the studies cited above from our group (4) reveals that measures of anxiety and depression in the mother in the third trimester of pregnancy predict prefrontal white matter connectivity in their infants at one month of age. Such findings raise the possibility that adversity experienced by the mothers during pregnancy might contribute to the findings

reported by Gehred et al(1). Other research suggests that prenatal adversity increases sensitivity to deleterious postnatal influences (5). Commencing longitudinal investigations before birth is warranted as this is a period during which important influences on neurodevelopment are established.

Implications for treatment?

While the authors are quite careful and clear in explaining that the association between childhood adversity and mid-life brain structure does not establish the casual role of such adversity in producing the decreased cortical surface area and thickness and decreased subcortical grey matter volume, it nevertheless raises the possibility that adversity “gets under the skin” and leads to these presumably deleterious alterations in brain structure. Does the absence of specific localized effects have implications for treatment? And does the diffuse pattern of structural variation lead to a trans-diagnostic vulnerability to a broad spectrum of psychopathology? Of course, these questions are ones that will motivate future research. Reviews of basic and translational research indicate that the same mechanisms of neuroplasticity that enable adversity to alter structural brain features can be harnessed to promote resilience through appropriate forms of experience and training(6). Recent evidence indicates that systematic mental training for skills that promote increased mindfulness, meta-awareness, prosocial behavior and perspective taking lead to widespread structural changes in different circuits of the brain(7) and may represent a form of trans-diagnostic intervention that can potentially be studied as an antidote to the adverse effects of early adversity.

A neural embedding of childhood enrichment?

While some evidence suggests that severe early adversity such as the extreme emotional deprivation of Romanian orphanages of the Ceausescu era are associated with diffuse alterations in brain structure that do not appear to normalize following environmental enrichment(8), it is possible that early exposure to loving, healthy social interactions in the form of positive secure attachment can result in a form of “affective reserve” that acts preventatively to decrease vulnerability to neuropsychiatric disorders later in life(9). We currently lack longitudinal evidence that potentially bears on this conjecture. It will be of great interest to see longitudinal datasets such as from the Dunedin project and other similar efforts to conduct analyses focused on early protective factors and explore to what degree such early advantage might similarly be neurally embedded as development unfolds. And while features of early adversity may reflect the intergenerational transmission of trauma, future research might usefully focus on the intergenerational transmission of well-being and through such analyses gain insight into the factors that might promote resilience and the neural and biological mechanisms that mediate such early beneficial influences.

Most importantly, this new work underscores the utility of longitudinal investigation and clearly highlights the critical importance of obtaining observational measures of early environmental influences as such measures reveal very different patterns of association with later measures of brain structure.

Financial Disclosures

The preparation of this manuscript was supported in part by NIMH grant MH043454-31. RJD is Founder and President of Healthy Minds Innovations, Inc., a non-profit organization affiliated with the Center for Healthy Minds from which he receives no direct or indirect financial compensation.

References

- [1] M. Z. Gehred *et al.*, “Long-term neural embedding of childhood adversity in a population-representative birth cohort followed for five decades,” *Biol. Psychiatry*, 2021.
- [2] A. Danese and C. S. Widom, “Objective and subjective experiences of child maltreatment and their relationships with psychopathology,” *Nat. Hum. Behav.*, vol. 4, no. 8, pp. 811–818, 2020.
- [3] C. L. Hendrix, D. D. Dilks, B. G. McKenna, A. L. Dunlop, E. J. Corwin, and P. A. Brennan, “Maternal Childhood Adversity Associates With Frontoamygdala Connectivity in Neonates,” *Biol. Psychiatry Cogn. Neurosci. Neuroimaging*, vol. 6, no. 4, pp. 470–478, 2021.
- [4] D. C. Dean *et al.*, “Association of Prenatal Maternal Depression and Anxiety Symptoms With Infant White Matter Microstructure,” *JAMA Pediatr.*, vol. 172, no. 10, p. 973, Oct. 2018.
- [5] K. J. O’Donnell and M. J. Meaney, “Fetal Origins of Mental Health: The Developmental Origins of Health and Disease Hypothesis,” *Am. J. Psychiatry*, vol. 174, no. 4, pp. 319–328, Apr. 2017.
- [6] R. J. Davidson and B. S. McEwen, “Social influences on neuroplasticity: stress and interventions to promote well-being,” *Nat. Neurosci.*, vol. 15, no. 5, pp. 689–695, May 2012.
- [7] S. L. Valk *et al.*, “Structural plasticity of the social brain: Differential change after socio-affective and cognitive mental training,” *Sci. Adv.*, vol. 3, no. 10, p. e1700489, Oct. 2017.
- [8] N. K. Mackes *et al.*, “Early childhood deprivation is associated with alterations in adult brain structure despite subsequent environmental enrichment,” *Proc. Natl. Acad. Sci. U. S. A.*, vol. 117, no. 1, pp. 641–649, 2020.
- [9] E. Walsh, Y. Blake, A. Donati, R. Stoop, and A. Von Gunten, “Early secure attachment as a protective factor against later cognitive decline and dementia,” *Front. Aging Neurosci.*, vol. 10, no. JUL, pp. 1–20, 2019.