HHS Public Access

Author manuscript

J Am Acad Child Adolesc Psychiatry. Author manuscript; available in PMC 2015 July 01.

Published in final edited form as:

J Am Acad Child Adolesc Psychiatry. 2015 July ; 54(7): 539–540. doi:10.1016/j.jaac.2015.04.009.

Unraveling the Meaning of Telomeres for Child Psychiatry

Dr. Stacy S. Drury, MD, PhD

Division of Child and Adolescent Psychiatry, Tulane University School of Medicine, New Orleans

More than 3 decades ago, Barker and Osmond[1] published a series of seminal articles demonstrating the association between fetal and childhood nutrition and life-long cardiovascular risk. Since then, the evidence linking early life stress, broadly defined, with disease and death across all health outcomes has continued to grow, culminating in the current focus on diminishing the lasting effects of "toxic stress" and deciphering the mechanisms underlying the developmental origins of health and disease.[2,3] Intriguingly, a brief search of the literature shows that the field of psychiatry had decades previously theorized about the impact of the early environment on disease, specifically psychopathology. Moreover, psychiatry recognized, even then, 2 critical caveats that remain absent, for the most part, from current perspectives in other areas of medicine. First, psychiatry recognized that the family and caregiving environment could function as a stress buffer, a source of stress, or even a magnifier of the impact of other adversity.[4] Second, one of the earliest leaders of American psychiatry, E. James Anthony,[5] noted that, despite adversity, not all children are affected equally. As psychiatry and other fields of medicine begin to converge in their recognition of the bidirectional link between physical and mental health and the inescapable relevance of early life experiences, the need to more effectively capture and measure stress and define the underlying molecular mechanisms linking stress, particularly early life stress, to health becomes paramount. A first glimpse into this molecular mechanism might lie in the microscopic tips at the end of every chromosome.

In 2009 Elizabeth Blackburn, Carol Greider, and Jack Szostak received the Nobel Prize in Medicine for their roles in discovering the DNA sequence that defined telomeres and telomerase, the RNA and protein complex responsible for maintaining telomere length. For decades it had been recognized that DNA polymerase, the enzyme responsible for copying DNA during cell division, could synthesize DNA only in 1 direction and that, without some additional structure, 1 strand of DNA would be shortened every time a cell divided. Telomeres, the cap at the end of every chromosome, minimize the shortening of DNA and are conserved in all vertebrates, arising from a common ancestor more than 400 million years ago.[6] Initially considered a biological clock, or time bomb, that, when too short, triggered cellular senescence and apoptosis (e.g., programmed cell death), telomeres are, in fact, far more dynamic, serving as global sensors of the changing cellular environment and epigenetic transmitters correlated with methylation, which also has significant association

Correspondence to Stacy S. Drury, MD, PhD, Tulane University School of Medicine, Department of Psychiatry, Division of Child and Adolescent Psychiatry, 1430 Tulane Ave, #8055, New Orleans, LA 70112; sdrury@tulane.edu.

Disclosure: Dr. Drury has received funding not related to this editorial from the Altria Foundation, the Bill and Melinda Gates Foundation, the National Institutes of Health, the Substance Abuse and Mental Health Services Administration, Tulane University, and the Louisiana Board of Regents.

with stress.[7] Oxidative stress, DNA damage, cortisol exposure, inflammation, and environmental toxins such as lead also affect telomere length. Not only does telomere length signal the terminal differentiation of cells, including oligodendrocytes, but also telomere shortening results in the unwinding of the ends of the chromosome and the release of noncoding RNA species expected to have broad effects on gene expression.[8] The complex processes regulating telomere length and the multifaceted functional significance of telomeres and telomerase are active areas of research.

The literature linking telomeres to health outcomes (e.g., obesity, cardiovascular disease, and cancer) and stress exposure, including stress within the family context, continues to grow.[9] In this issue of the Journal, Nelson et al.[10] take an innovative perspective that the metabolic processes linked to autism, including inflammation and increased oxidative stress, and the increased familial stress associated with autism affect telomere length. In addition to replicating the 1 previous report of shorter telomere length in individuals with autism,[11] this study finds that the parents and siblings of children with autism have shorter telomere lengths compared with family members who do not have an affected child. Limitations to this study, acknowledged by the researchers, include the lack of a direct measurement of family stress and the racial heterogeneity of the cohort. Those limitations notwithstanding, this study suggests that in families with a child with autism, underlying biological differences in the mechanisms regulating telomere dynamics and/or the family stress level associated with caring for an impaired child can have health effects beyond psychopathology and extend to nonaffected siblings. This is a finding consistent with several other studies that have associated shorter telomere length with elevated caregiving stress, family instability, and parental responsiveness.[12–14]

What are the implications of the increasing evidence linking stress, in and outside the family context, to psychopathology, negative health, and telomeres for child psychiatry? First, it reminds us that mental health and physical health are intricately interwoven, and that even for our youngest patients, health monitoring and interventions ought to be part of our clinical treatment plan. Second, if exposure to early adversity and the family context are primary factors interacting to predict lifelong health, research needs to focus on defining the underlying mechanisms. Equally important, treatment and interventions seeking to decrease the lasting impact of stress across health outcomes and across the life course ought to target these factors. Telomeres might allow us to more precisely track the cumulative impact of stress, a construct challenging to effectively measure, while also identifying individual differences in resilience and vulnerability. It is unlikely that all the solutions to the negative effects of early life stress will be found embedded in telomeres, the tiny shoelace caps at the end of each of our chromosomes. However, unraveling the relation between these complex structures and developmental psychopathology, health, and families might lead to powerful new interventions and treatments while ideally simultaneously driving positive policy change for at-risk children. As efforts intensify to better understand, and prevent, the biological embedding of early life stress,[15] child psychiatry is uniquely poised to lead because our field sits at the intersection of neuroscience, child development, molecular genetics, and the family. Developing a proactive health and wellness-focused message that originates from the field of child psychiatry, when coupled with powerful neurobiological

and molecular genetic evidence that tracks down to the very ends of a chromosome, could initiate transformative public health efforts.

Acknowledgments

Funding for the editorial comes from the National Institute of Mental Health (R01MH101533) (Drury, principal investigator).

References

1. Barker D, Osmond C. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. Lancet. 1986; 1:1077–1081. [PubMed: 2871345]
2. Shonkoff JP, Garner AS, Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. Pediatrics. 2012; 129:e232–e246. [PubMed: 22201156]
3. Wadhwa P, Buss C, Entringer S, Swanson J. Developmental origins of health and disease: brief history of the approach and current focus on epigenetic mechanisms. Semin Reprod Med. 2009; 27:358–368. [PubMed: 19711246]
4. Bowlby J. Maternal care and mental health. Bull World Health Organ. 1951; 3:355–533. [PubMed: 14821768]
5. Anthony, EJ. The Syndrome of the Psychologically Invulnerable Child. Oxford, UK: John Wiley and Sons; 1974.
6. Meyne J, Ratliff R, Moyzis R. Conservation of the human telomere sequence (TTAGGG) among vertebrates. Proc Natl Acad Sci U S A. 1989; 86:7049–7053. [PubMed: 2780561]
7. Buxton J, Suderman M, Pappas J, et al. Human leukocyte telomere length is associated with DNA methylation levels in multiple subtelomeric and imprinted loci. Sci Rep. 2014; 4:4954. [PubMed: 24828261]
8. Ye J, Renault V, Jamet K, Gilson E. Transcriptional outcome of telomere signalling. Nat Rev Genet. 2014; 15:491–503. [PubMed: 24913665]
9. Blaze J, Asok A, Roth T. The long-term impact of adverse caregiving environments on epigenetic modifications and telomeres. Front Behav Neurosci. 2015; 9:79. [PubMed: 25904853]
10. Nelson CA, Varcin KJ, Coman NK, DeVivo I, Tager-Flusberg H. Shortened telomeres in families with a propensity to autism. J Am Acad Child Adolesc Psychiatry. 2015; 54:588–594. [PubMed: 26088664]
11. Li Z, Tang J, Li H, et al. Shorter telomere length in peripheral blood leukocytes is associated with childhood autism. Sci Rep. 2014; 4:7073. [PubMed: 25399515]
12. Epel ES, Blackburn EH, Lin J, et al. Accelerated telomere shortening in response to life stress. Proc Natl Acad Sci U S A. 2004; 101:17312–17315. [PubMed: 15574496]
13. Asok A, Bernard K, Roth T, Rosen J, Dozier M. Parental responsiveness moderates the association between early-life stress and reduced telomere length. Dev Psychopathol. 2013; 25:577–585. [PubMed: 23527512]
14. Drury S, Mabile E, Brett S, et al. The association of telomere length with family violence and disruption. Pediatrics. 2014; 134:e128–e137. [PubMed: 24936002]
15. Nelson CA. Biological embedding of early life adversity. JAMA Pediatr. 2013; 167:1098–1100. [PubMed: 24165859]