Early Hits and Long-Term Consequences: Tracking the Lasting Impact of Prenatal Smoke Exposure on Telomere Length in Children

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We examined the association between telomere length and prenatal tobacco exposure (PTE) in 104 children aged 4 to 14 years. Salivary telomere length (STL) was determined from salivary DNA using quantitative polymerase chain reaction. Of the children, 18% had maternal reported PTE. Mean STL was significantly lower among children with PTE (6.4 vs 7.5, $P < .05$). Findings extend the literature demonstrating the negative long-term effects of PTE to include a cellular marker of aging linked to multiple negative health outcomes. (*Am J Public Health.* 2013;103:S133–S135. doi:10.2105/AJPH.2012.301208)

Although substantial evidence has indicated that smoking during pregnancy remains a leading cause of fetal morbidity and mortality, approximately 20% of women continue to smoke during pregnancy.[1,2] Oxidative stress has been proposed as one mechanism linking prenatal tobacco exposure (PTE) to the negative health outcomes observed in exposed children. To provide additional support for this mechanism, we examined the association between PTE and telomere length (TL), an alternative biological indicator that has also been associated with both oxidative stress and similar negative health consequences.

Telomeres are nucleotide repeats on the distal ends of eukaryotic chromosomes that play a critical role in the maintenance of the chromosomal structures. TL is an established biomarker of cellular aging.[3,4] Similar to PTE and cigarette smoking, accelerated TL shortening has been linked to multiple negative health outcomes across the life span.[5,6] Several studies have found a dose–response relationship between cumulative lifetime exposure to cigarette smoking and TL in adults[7–9]; however, to our knowledge, no studies have looked at the relationship between PTE and TL in children. In this report, we expand on our previous work examining the impact of a range of early adversity on TL in children to include PTE.[10] Specifically, we test the hypothesis that exposure to PTE will be associated with decreased salivary telomere length (STL) during childhood.

METHODS

We recruited participants through inner-city public schools in New Orleans, Louisiana, from January through May 2010 as part of a larger study examining neighborhood influences on childhood health disparities. A total of 104 African American children aged 4 to 14 years were enrolled, and caregivers provided child data through questionnaires.

We extracted DNA from Oragene saliva kits using standard procedures and determined the average relative TL, as represented by the telomere repeat copy number to single gene copy number (T/S) ratio, by means of quantitative real-time polymerase chain reaction in triplicate as previously described.[10] Samples with inconsistent replicates (triplicate) and outliers were removed from analysis. We also classified STL values as a dichotomous variable on which low STL values were defined as below the standardized mean score (< 0) versus at the average mean score or higher (≥ 0) and as the presence of maternal smoking during pregnancy (yes–no), exposure to secondhand smoke in the household during pregnancy (yes–no), or both.

We performed univariate, bivariate, and multivariate analyses using SAS version 9.2 (SAS Institute, Cary, NC), including PROC GENMOD for generalized estimating equations with an unstructured correlation structure that took into account any clustering of children within neighborhood. The final analytic sample of 92 children (not including 9 children who were missing neighborhood data and 3 outliers) was from 49 census tracts, with a range of 1 to 7 children per tract.

RESULTS

Respondent characteristics are presented in Table 1. Relative STL was 7.3 (SD = 2.4; range = 2.5–18.0), with 61.4% classified as having low relative STL. Of the children, 18.8% (n = 19) had caregivers who indicated the child was prenatally exposed to tobacco smoke in the home, and a smaller proportion also reported maternal smoking (6.8%; n = 7). Mean STL was significantly lower among children who were exposed to smoke during pregnancy than among unexposed children. A greater proportion of children exposed to PTE were classified as having short TL than those not exposed (79.0% and 57.3%, respectively; $P < .05$) or were nearly 3 times as likely to have short STL than those not exposed (crude odds ratio = 2.47; 95% confidence interval = 0.81, 7.51; $P = .11$).

Table 2 presents the results of the crude and adjusted models estimating the effect of PTE. Because of missing data on covariates, the final analytic sample was 92. Children with PTE had TL 1 unit lower, on average, than children not exposed to PTE (adjusted B = –0.901; SE = 0.3634; $P < .05$).

DISCUSSION

In this study, we demonstrated a large effect of retrospective report of PTE on STL in children. These findings and the growing telomere literature suggest that STL may reflect cumulative exposures from a range of different sources. Our results are consistent with those of studies demonstrating accelerated telomere shortening in tobacco-exposed adults and extend these findings to include PTE, providing cellular evidence for the transgenerational transmission of the negative impact of tobacco exposure.[11–13]

Despite the limited power, our results support an environmental transmission model of risk associated with early exposure to smoking and demonstrate, for the first time, that smoke exposure during pregnancy is associated with shortened STL. It is increasingly clear that

TABLE 1—Sample Characteristics Overall and by Prenatal Tobacco Exposure: New Orleans, LA, January–May 2010

Variable	Total, No. (%) or Mean ±SD	Prenatal Tobacco Exposure, No. (%) or Mean ±SD	No Prenatal Tobacco Exposure, No. (%) or Mean ±SD
		9 (18.8)	82 (81.2)
Age, y			
4–6 (mean STL ±SD = 7.1 ±1.9)	50 (49.5)	9 (47.4)	41 (50.0)
7–9 (mean STL ±SD = 8.0 ±2.5)	22 (21.8)	3 (15.8)	19 (23.2)
10–14 (mean STL ±SD = 6.9 ±2.9)	29 (28.7)	7 (36.8)	22 (26.8)
Gender			
Male	47 (46.5)	8 (42.1)	39 (47.6)
Female	54 (53.5)	11 (57.9)	43 (52.4)
STL[a] (range = 2.5–18.0)	7.3 ±2.2	6.4 ±1.5	7.5 ±2.3*
Short STL (< 0 on *z* score)	62 (61.4)	15 (79.0)	47 (57.3)
Mother's marital status			
Not married	77 (76.2)	15 (79.0)	62 (75.6)
Married	24 (23.8)	4 (21.1)	20 (24.4)
SEP score[b] (range = 11–49)	18.9 ±6.3	18.6 ±5.5	18.9 ±6.5*
No. of children in the household			
1–2	72 (74.2)	15 (79.0)	57 (73.1)
≥ 3	25 (25.8)	4 (21.1)	21 (26.9)
Presence of any dental caries			
Yes	45 (44.6)	9 (47.4)	36 (43.9)
No	56 (55.5)	10 (52.6)	46 (56.1)
Physical activity[c]			
High	76 (75.3)	12 (63.2)	64 (78.1)
Low	25 (24.8)	7 (36.8)	18 (22.0)
Fruits and vegetable consumption[d]			
High	39 (38.6)	6 (31.6)	33 (40.2)
Low	62 (61.4)	13 (68.4)	49 (59.8)
Obese or overweight[e]			
Yes	20 (19.8)	3 (15.8)	17 (20.7)
No	81 (80.2)	16 (84.2)	65 (79.3)
Familial risk[f]			
Yes	78 (77.2)	15 (79.0)	63 (76.8)
No	23 (22.8)	4 (21.1)	19 (23.2)

Note. SEP = socioeconomic position; STL = salivary telomere length. Values based on nonmissing data. The sample size was n = 101.

[a]STL was defined by using the repeat copy number to single gene copy number (T/S) ratio.

[b]SEP is a measure of socioeconomic position taking into account maternal and paternal education, employment, and household income.

[c]High physical activity was defined as 1–5 hours spent engaging in moderate- or vigorous-intensity activities daily.

[d]Fruit and vegetable consumption was defined as high with ≥ 2 servings of both fruits and vegetables.

[e]Obesity or overweight status was defined as being above the 85th percentile in age for gender body mass index.

[f]Familial health risk includes family history of heart disease or heart attack, high blood pressure, diabetes, and anxiety disorder.

*$P < .05$ based on the likelihood ratio χ^2 or Fisher exact or *t* test or Mann–Whitney U test when appropriate.

many different early life stress exposures influence TL and health, as well as behavioral outcomes. Stress exposure, both environmental and psychosocial, during prenatal life can result in biological changes that alter developmental trajectories and may alter lifelong health trajectories. Identifying the earliest developmental time points for prevention and intervention is challenging but critical if we expect to improve health outcomes. ■

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Contributors

K. P. Theall was responsible for conceptualization and design of the research, interpretation, and reporting. S. McKasson and E. Mabile were responsible for the data analysis. L. F. Dunaway contributed substantive writing and editorial comments and participated in finalizing the article. S. S. Drury was responsible for analysis of telomere data, assisting in design, interpretation, and reporting of research findings.

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Human Participant Protection

This study was approved by the Tulane and Louisiana State University institutional review boards.

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TABLE 2—Association Between Secondhand Smoke Exposure During Pregnancy and Salivary Telomere Length in Children: New Orleans, LA, January–May 2010

Variables	Crude Models,[a] B (SE)	Adjusted Model,[b] B (SE)	Full Model,[c] B (SE)
Prenatal tobacco exposure (yes)	−0.9006* (0.3634)	−0.8780* (0.3702)	−0.9597* (0.3541)
Female	−0.0655 (0.4123)	−0.0318 (0.0870)	0.0389 (0.3588)
Age, y	−0.0803 (0.0787)	−0.0744 (0.4190)	−0.0678 (0.0956)
Cavities	−0.3058 (0.3907)	. . .	−0.4197 (0.3960)
SEP score	−0.0782* (0.0213)	. . .	−0.0735* (0.0299)
Fruit and vegetable consumption	0.4049 (0.4182)	. . .	0.2813 (0.3774)
Family history	−0.9774 (0.4569)	. . .	−0.6062 (0.4655)
Married	−0.3103 (0.5410)	. . .	−0.0918 (0.5827)
High physical activity	0.2896 (0.5523)	. . .	−0.1547 (0.5734)
Obese or overweight	−0.7773 (0.4097)	. . .	−0.7925 (0.5010)

Note. SEP = socioeconomic position. SEP is a measure of socioeconomic position taking into account maternal and paternal education, employment, and household income. The sample size was n = 92.
[a]Modeling telomere length as a continuous variable.
[b]An adjusted model including gender and age as covariates.
[c]A full model including female, age, cavities, SEP score, fruit and vegetable consumption, family history, marital status, physical activity, and obese or overweight status as covariates.
*$P < .05$.

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