Father Loss and Child Telomere Length

Colter Mitchell, PhD,[a] Sara McLanahan, PhD,[b] Lisa Schneper, PhD,[b] Irv Garfinkel, PhD,[c] Jeanne Brooks-Gunn, PhD,[c] Daniel Notterman, MD, FAAP[b]

abstract

BACKGROUND AND OBJECTIVES: Father loss during childhood has negative health and behavioral consequences, but the biological consequences are unknown. Our goal was to examine how father loss (because of separation and/or divorce, death, or incarceration) is associated with cellular function as estimated by telomere length.

METHODS: Data come from the 9-year follow-up of the Fragile Families and Child Wellbeing Study, a birth cohort study of children in 20 large American cities (N = 2420). Principal measures are as follows: salivary telomere length (sTL), mother reports of father loss, and polymorphisms in genes related to serotonergic and dopaminergic signaling.

RESULTS: At 9 years of age, children with father loss have significantly shorter telomeres (14% reduction). Paternal death has the largest association (16%), followed by incarceration (10%), and separation and/or divorce (6%). Changes in income partially mediate these associations (95% mediation for separation and/or divorce, 30% for incarceration, and 25% for death). Effects are 40% greater for boys and 90% greater for children with the most reactive alleles of the serotonin transporter genes when compared with those with the least reactive alleles. No differences were found by age at father loss or a child's race/ethnicity.

CONCLUSIONS: Father loss has a significant association with children's sTL, with the death of a father showing the largest effect. Income loss explains most of the association between child sTL and separation and/or divorce but much less of the association with incarceration or death. This underscores the important role of fathers in the care and development of children and supplements evidence of the strong negative effects of parental incarceration.

[a]*University of Michigan, Ann Arbor, Michigan;* [b]*Princeton University, Princeton, New Jersey; and* [c]*Columbia University, New York, New York*

Dr Mitchell drafted the initial manuscript; Drs McLanahan, Schneper, Garfinkel, Brooks-Gunn, and Notterman conceptualized and designed the study and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2016-3245

Accepted for publication Apr 25, 2017

Address correspondence to Daniel Notterman, MD, FAAP, Department of Molecular Biology, Princeton University, Princeton, NJ 08544. E-mail: dan1@princeton.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health through awards P2CHD047879, R01HD36916, R01HD39135, R01HD40421, 5R01HD036916, and 5R01HD076592. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

WHAT'S KNOWN ON THIS SUBJECT: Telomeres are the protective end caps of chromosomes. They shorten with age and are like a biological clock. Chronic stress is associated with accelerated telomere shortening, adverse health outcomes, and possibly more rapid biological aging.

WHAT THIS STUDY ADDS: Separation from a father by death, incarceration, or parental separation and/or divorce is associated with shorter telomeres in his children. Shortening is partly mediated by income loss, which is greater in children whose fathers die (in boys) and among children with alleles that enhance stress sensitivity.

To cite: Mitchell C, McLanahan S, Schneper L, et al. Father Loss and Child Telomere Length. *Pediatrics.* 2017;140(2): e20163245

The loss of a father is widely known to impair a child's physical and psychological functioning.[1–11] Although the link between father loss and poor health is well documented, much less is known about the biological factors that underlie the association. A recent line of research suggests that telomere length (TL)[7,12–22] may be a useful tool for helping us understand the biological processes that underlie the link between father loss and child health.[14,19,23,24]

Telomeres are repetitive DNA sequences (TTAGGG repeats) that are located at the ends of chromosomes. In most mature somatic cells (excluding stem cells, germ cells, and many types of cancer cells), TL decreases progressively with each cell division. When telomeres are sufficiently short, the cell enters a state of replicative senescence and stops dividing. This process means that for most people, TL decreases with age.[25] Thus, the telomere has been referred to as a "mitotic clock,"[26–28] and TL has been construed as a measure of biological age. Consistent with these considerations, TL has been shown to be associated with a wide range of diseases and health morbidities in adults[12,22,29–39] and children[22,40,41] and recently has become a popular biomarker for stress and accelerated biological aging.[25,41]

Research also documents a negative association between TL in adulthood and a wide range of adverse environmental inputs and morbidities, including smoking,[39,42] mental illness,[35,43,44] stress,[17,20,29,35,45,46] obesity,[23,47,48] intense caregiving,[49] poor sleep quality,[50] and poverty.[14,18,19,23,51,52] For children, findings have revealed associations between shorter TL and maltreatment, poverty, and maternal depression.[7,15,21,22,52–54] Mitchell et al[7] recently documented a link between family instability in early childhood and shorter TL, but they did not distinguish among types of loss. In sum, although authors of past studies have not established a causal effect (or mechanistic role) of father loss on TL attrition, there is ample evidence that TL is a reliable biomarker of stress that may manifest long before health consequences are discernable, especially in children. Thus, using TL as a marker for potentially harmful stress can provide us with a more time-sensitive and graded predictor of a child's long-term health and wellbeing than current disease status or mortality.

This article uses recently assayed (in DNA extracted from saliva) TL data from the Fragile Families and Child Wellbeing Study (FFCWS) to examine the association between father loss and children's TL. We examine whether the type of loss (death, separation and/or divorce, or incarceration) and the timing of loss (early childhood and middle childhood) matter. We also examine whether associations are mediated by income changes and moderated by sex, race/ethnicity, and gene variants in the serotonergic and dopaminergic pathways).

METHODS

Sample

FFCWS is based on a stratified, multistage probability sample of children who were born in large US cities between 1998 and 2000, with an oversample of children born to unmarried parents.[55] Because of the large oversample of nonmarital births and the urban nature of the sample, the data contain a large number of low-income families and a wide range of family types. Baseline interviews with mothers and fathers were conducted within 48 hours of their children's birth, and subsequent interviews were conducted when the children were 1, 3, 5, and 9 years old. Salivary DNA samples were taken at the age of 9 by using the Oragene DNA sample collection kit (DNA Genotek Inc, Ottawa, ON).

We used the following 2 analytic samples for this study: (1) all children for whom we have salivary telomere length (sTL) data and who have had some contact with their biological fathers since birth (n = 2437) and (2) a subsample of children whose parents were living together (married or cohabiting) at the time of their birth (n = 1270). The first sample is used to study associations between sTL and loss in the form of the fathers' death and incarceration, and the second subsample is used to study the association between sTL and parents' separation and/or divorce (Table 1). Sample 1 is used to examine the effect of any father loss.

Telomere Measurement

TL was measured by using a quantitative real-time polymerase chain reaction (PCR) assay that incorporates an oligomer standard to permit the measurement of absolute TL (in kilobase [kb] per chromosome).[7,27,56] To determine absolute TL, an 84-mer oligomer incorporating the sequence TTAGGG was used to construct a standard curve. A separate standard curve for a single-copy gene incorporates a 79-mer oligomer that represents the reference gene *36B4*. This enables the calculation of total TL in a diploid genome, whereas the 36B4 product gives the number of diploid genomes. TL per chromosome is given by dividing TL per genome by 92 (the number of telomeres per diploid genome). Samples were measured in triplicate, and the results were averaged. Distribution of samples in the 96-well plates was randomized, and each plate contained repeats from previous runs to detect and limit potential batch effects. To mitigate batch effects, reference DNA from a cell line with a relatively short telomere

(3C167b)[57] and a fibroblast cell line after stable integration of the hTERT gene (cell line NHFpreT)[58] were included in each plate (both cell lines were a gift from Dr Yuanjun Zhao of Pennsylvania State University). In our laboratory, 3C167b has a mean TL of 3.1 kb, whereas NHFpreT has a mean TL of 16.8 kb. Reference DNA was harvested at a single time, aliquoted, and frozen. TL was normalized by this reference to ensure plate-to-plate consistency. A replicate sample (DNA from volunteers) was included in triplicate in all plates, and the results of this measurement were used to compute an interrun coefficient of variation, which was <11% across all runs. Outliers were dealt with by trimming 1% off both tails of the sample and by using a natural log transformation.[7,59] The log transformation also corrected for the positive skew of the data. However, using the raw sTL measurement does not substantively change the results.

In this study, we examined the link between sTL and father loss. We have previously reported that saliva and peripheral blood mononuclear cell (PBMC) DNA were significantly correlated in the same individual ($r = 0.72$, $P < .002$), but that TL measured in PBMC was significantly shorter in adult volunteers (6.5 kb ± 1.8 SD, saliva versus 4.2 kb ± 1.2 SD, PBMC $P < .001$).[7] Daniali et al[60] also found a significant correlation between leukocyte TL and TL in several other tissues (they did not study sTL). Notably, differences between TL in various tissues was stable over time.[60] In addition, Theall et al[21] reported that in children 4 to 14 years old, there was a significant link between neighborhood disorder and sTL. Thus, there is good reason to conclude that sTL is a feasible source of DNA for TL measurement, although the exact TL values from different tissues may not be congruent.[61]

TABLE 1 Descriptive Statistics of Dependent and Independent Variables for the Analytic Sample ($N = 2420$)

	Mean	SD	Minimum	Maximum
Dependent Variables				
Child's TL	8.08	2.7	3.2	19.7
Child's TL (ln, trimmed)	2.03	0.4	1.25	2.9
Independent variables				
Father loss, with ages of child at loss				
No father loss	0.48	—	0	1
Loss at age 0–1	0.19	—	0	1
Loss at age 1–3	0.13	—	0	1
Loss at age 3–5	0.10	—	0	1
Loss at age 5–9	0.10	—	0	1
Incarceration at age 0–5	0.09	—	0	1
Incarceration at age 5–9	0.11	—	0	1
Death	0.03	—	0	1
Mediator variables				
Change in income (after loss − before loss), %	5.2	120.3	−100	727
Change in social support	0.1	0.2	−3	3
Moderators				
Race				
African American	0.49	—	0	1
White	0.21	—	0	1
Hispanic	0.27	—	0	1
Other	0.03	—	0	1
Child is female	0.48	—	0	1
Control variables (baseline)				
Ln (household income)	9.89	1.10	0	11.8
Social support	2.63	0.5	0	3
Mother's age	25.02	5.94	14	47
Mother's education	12.01	—	—	—
Child is low birth weight (<2.5 kg)	0.09	—	0	1
Child is firstborn	0.38	—	0	1
Mother lives with child's father	0.61	—	0	1
Mother discussed abortion	0.37	—	0	1
Mother or father ever depressed	0.49	—	0	1
Mother or father ever had an alcohol problem	0.48	—	0	1
Mother or father ever incarcerated	0.45	—	0	1
Mother lived with both parents at 15	0.43	—	0	1
Mother's report of relationship quality	11.26	4.4	4	16
Mother's report of overall health	2.89	0.94	1	4

ln, natural logarithm.

Genetic Measures

We examined several genetic variants that have been shown to moderate the association between a child's social environment and sTL. Gene variants that may affect function of the dopaminergic system include the following: the Taq1a polymorphism of the dopamine receptor gene (DRD2, 11q23, rs1800497); the Val154Met polymorphism of the catechol-O-methyltransferase gene (COMT, 22q11.21, rs4680); the 48bp VNTR in the third exon of the dopamine receptor 4 gene (DRD4, 11p15.5); and 2 variants of the serotonin transporter gene (5-HTT, SLC6A, 17q11.2), 5-HTTLPR and STin2. The genotypes listed in Table 2 were obtained by PCR followed by gel or capillary electrophoresis or by real-time PCR, as previously described.[7] Similar to our previous publications,[7,62] for the genetic measures, we summed the alleles that have been coded as "sensitizing" or "reactive" in the literature[7,63–73] (0, 1, or 2 for each individual). This produced a dopamine pathway genetic score and a serotonin transporter (5-HTT) genetic score.

For the sake of this comparison, we divided the samples into terciles of genetic score, with the highest tercile being the one in which we expect to see the largest effect of father loss.

Father Loss

At each wave of data collection, each mother was asked whether her child's biological father was living with the child and, if not, the reason for his absence. These questions were used to measure losses because of separation, divorce, and death. Parents were also asked a series of questions about whether the father had been incarcerated since the previous interview wave. We coded fathers as having been incarcerated if either parent reported such an event. For a small subset of cases, reports of a father's death and incarceration came from responses to other questions or information provided by interviewers.

Table 1 shows distributions for the FFCWS variables that were used in the analyses. Approximately half of the children who were living with their biological fathers at the time of their birth experienced a divorce or separation by age 9. Generally speaking, losses were most common during the first year of a child's life (19%). Losses because of incarceration were evenly distributed between early and middle childhood. We could not separate death by age because of the small sample size.

Changes in Income

Percent income change was measured by taking the difference in family income during the period before and after father loss and dividing it by family income during the period before the loss. Income was adjusted for inflation and household size and was averaged over the number of years since it was last measured (ie, average change in income). Over the entire sample, there was little change in income across waves; however, all types of father loss (on average) resulted in declines in income: 18% for any father loss, 12% for separation and/or divorce, 19% for incarceration, and 35% for death.

TABLE 2 Distribution of Genotypes for the Serotonin Transporter Gene (5-HTT) and Dopaminergic Pathway ($N = 2420$)

Gene or Locus	Variant		
5-HTTLPR	LL	LS	SS
	42%	42%	16%
STin2	10/10	10/12	12/12
	10%	40%	50%
DRD2	CC	CT	TT
	45%	42%	13%
COMT	Val/Val	Val/Met	Met/Met
	38%	48%	14%
DRD4	4R/4R	4R/7R	7R/7R
	55%	37%	8%

Less than 2% of the sample had rare genotypes not represented in Table 2. 5-HTTLPR, serotonin-transporter-linked polymorphic region; COMT, catechol-O-methyltransferase; DRD2, dopamine receptor D2; DRD4, dopamine receptor D4; STin2, a variable number of tandem repeats in intron 2 of the seratonin transporter.

Controls

FFCWS data include a rich set of variables that allowed us to control for many family and individual characteristics that are likely to affect both father loss and child sTL (Table 1). Each of these variables is measured at the baseline interview or retrospectively at the 1-year interview. Although our approach does not eliminate the possibility that an unmeasured (or at least an unaccounted for) characteristic is responsible for the association between father loss and child sTL, the rich set of controls gives us more confidence in our estimates. Included in the FFCWS data are the following: self-reported race/ethnicity; mother's age and education at baseline; household income at baseline; child's sex, birth weight, and birth order; whether parents discussed an abortion; parents' relationship at birth; parental history of depression at baseline; parental history of an alcohol problem at baseline; parental incarceration history; domestic violence during the pregnancy; mother's self-reported health; and mother's family structure at age 15.

TABLE 3 Percent Difference Child TL at Age 9 Associated With Types of Father Loss ($N = 2420$)

Type of Father Loss	M1	M2[a]	M3	M4
Any	−14*			
	(.006)			
Separation and/or divorce		−6*		
		(.03)		
Incarceration			−10*	
			(.01)	
Death				−16**
				(.008)

All analyses were controlled for race/ethnicity; mother's age and education at baseline; household income at baseline; child's sex, birth weight, and birth order; report of whether parents discussed an abortion; parental report of how their relationship was going before the child's birth; parental history of depression at baseline; parental history of an alcohol problem at baseline; parental incarceration history; if there was any domestic violence during the pregnancy; mother's self-report of health; and if the mother lived with her parents at age 15.

[a] A separate analysis comparing those children who experienced a divorce or separation with those who were born in a 2-parent household but stayed together found a slightly higher reduction of 7%.

* $P < .05$.

** $P < .01$, 2-tailed (P values in parentheses).

Analytic Technique

We used ordinary least squares regression in which the log transformation of sTL is regressed onto our explanatory variables (ie, father loss, controls, and mediating variables) in a series of models. We first modeled an overall estimate of father loss, types of father loss, and age-specific father loss and adjusted for controls (Table 3). Next, we added income change to the model to test for mediation effects (Table 4). The most widely cited mediator of father loss is income change.[74] We calculated mediation (0%–100%) by comparing the change in the effect of father loss between the models with and without the income variable. Finally, we examined moderation by regressing sTL on controls and any father loss stratified by sex, race (African American, white, Hispanic), and serotonergic and dopaminergic

TABLE 4 Mediation Analysis of Income on the Association Between Child TL at Age 9 and Father Loss, Exit, Incarceration, and Death (N = 2420)

	Any Loss		Separation and/or Divorce		Incarceration		Death	
Father loss (% difference in TL)	−14** (.008)	−7* (.02)	−6* (.05)	−0 (.75)	−10* (.01)	−7* (.03)	−16** (.005)	−12** (.007)
Change in income (% difference in TL)	—	3* (.02)	—	3* (.02)	—	3* (.02)	—	3* (.02)
Mediation (%)	—	53	—	95	—	30	—	25

All analyses control for race/ethnicity; mother's age and education at baseline; household income at baseline; child's sex, birth weight, and birth order; report of whether parents discussed an abortion; parental report of how their relationship was going before the child's birth; parental history of depression at baseline; parental history of an alcohol problem at baseline; parental incarceration history; if there was any domestic violence during the pregnancy; mother's self-report of health; and if the mother lived with her parents at age 15.

* $P < .05$.

** $P < .01$, 2-tailed (P values in parentheses).

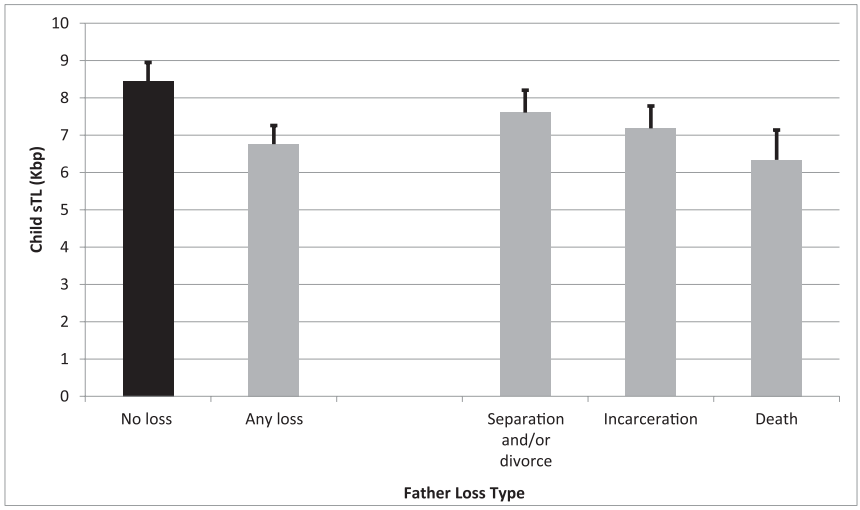

FIGURE 1
Mean age 9 sTL for children by father loss type (N = 2420, error bars = 95% confidence interval). All analyses were controlled for race/ethnicity; mother's age and education at baseline; household income at baseline; child's sex, birth weight, and birth order; report of whether parents discussed an abortion; parental report of how their relationship was going before the child's birth; parental history of depression at baseline; parental history of an alcohol problem at baseline; parental incarceration history; if there was any domestic violence during the pregnancy; mother's self-report of health; and if the mother lived with her parents at age 15.

pathway genes. We used a χ^2 test to determine the equivalency of coefficients across subgroups.

RESULTS

Table 3 provides estimates for the association between overall father loss and natural log–transformed child sTL. Supplemental Table 6 provides separate estimates for each type of loss at different ages in childhood. According to model 1 in Table 3, any father loss between birth and age 9 is associated with a −0.15 reduction in the natural log sTL or approximately a (1-exp(−0.15)), 14% reduction in sTL. The coefficients are higher for losses at younger ages, but the difference is not statistically significant.

The associations between different types of father loss and natural log sTL are reported in models 2 to 4. Model 2 shows that parents' separation and/or divorce is associated with a TL reduction of ~6%. Again, although the size of the coefficients is larger for early breakups, the difference is not significant. Estimates based on comparisons with children who were born to 2-parent households (instead of children who did not experience a divorce or separation) are similar to the findings shown in Table 3 (see Supplemental Table 6). Incarceration has an equally strong association with sTL (~10% shorter), and the effect is consistent across age groups. Finally, death is associated with a 16% reduction in sTL. Figure 1 displays the TL by different loss types, all of which provide strong support for the argument that father loss is associated with shorter sTL among children.

Mediation Analyses

There are multiple reasons why father loss might be a major stressor for a child. Table 4 presents income mediation for each type of father loss and reports estimates from 2 models. The first model is in the left column for each loss type and repeats the estimate reported in Table 3. The second model shows the estimate controlling for income change (from the wave of data collection before the loss to the wave after the loss). Row 2 shows the association between income change and child sTL. Row 3 (column 2) shows income mediation as a percent change in the original father loss effect. Decline in income accounts for 95% of the child telomere decrease after separation or divorce, but it only accounts for 53%, 30%, and 19% of the decreases after any loss, incarceration, and death, respectively.

Moderation Analysis

Our final set of analyses focuses on potential moderators of the effect of father loss. Here, we included standard moderators (ie, a child's sex and race/ethnicity) as well as a novel moderator (the genotype of the child with respect to specific variants in the serotonergic and dopaminergic pathways). Although boys and girls should have similar levels of exposure to father loss, there is

TABLE 5 Moderation Analysis of the Association of Any Father Loss and Child TL at Age 9 by Sex, Race/Ethnicity, and Serotonergic and Dopaminergic Pathway Genes of Child ($N = 2420$)

	Sex		Race			Serotonergic Pathway (Terciles)			Dopaminergic Pathway (Terciles)		
	Boy	Girl	African American	White	Hispanic	First	Second	Third	First	Second	Third
Any loss (% change in TL)	−16* (.03)	−12[a] (.06)	−13* (.04)	−16** (.008)	−14* (.02)	−10 (.15)	−14* (.04)	−17**,[a] (.006)	−15* (.01)	−14* (.02)	−15* (.01)
Any loss 0–5 (% change in TL)	−17* (.04)	−13* (.03)	−14* (.01)	−18** (.005)	−15* (.01)	−8 (.21)	−16 (.17)	−22**,[a] (.009)	−13* (.03)	−16* (.02)	−18* (.01)
Any loss 5–9 (% change in TL)	−12 (.12)	−14* (.05)	−17** (.01)	−12 (.11)	−14* (.03)	−10 (.24)	−12 (.20)	−16 (.16)	−16* (.03)	−10* (.05)	−14* (.04)

Each model is run within 1 group (ie, boys or girls who were either African American, white, or Hispanic). All analyses were controlled for race/ethnicity; mother's age and education at baseline; household income at baseline; child's sex, birth weight, and birth order; report of whether parents discussed an abortion; parental report of how their relationship was going before the child's birth; parental history of depression at baseline; parental history of an alcohol problem at baseline; parental incarceration history; if there was any domestic violence during the pregnancy; mother's self-report of health; and if the mother lived with her parents at age 15. For the genetic measures, we took the alleles that have been coded as "sensitizing" or "reactive" (0, 1, or 2 for each) and summed them. We divided the samples into terciles of genetic sensitization, with the highest tercile being the one in which we expect to be the most sensitizing.

[a] Indicates that the effects are significantly different between groups (eg, boys versus girls) by using a χ^2 test of equality, $P < .05$.

* $P < .05$.

** $P < .01$, 2-tailed (P values in parentheses).

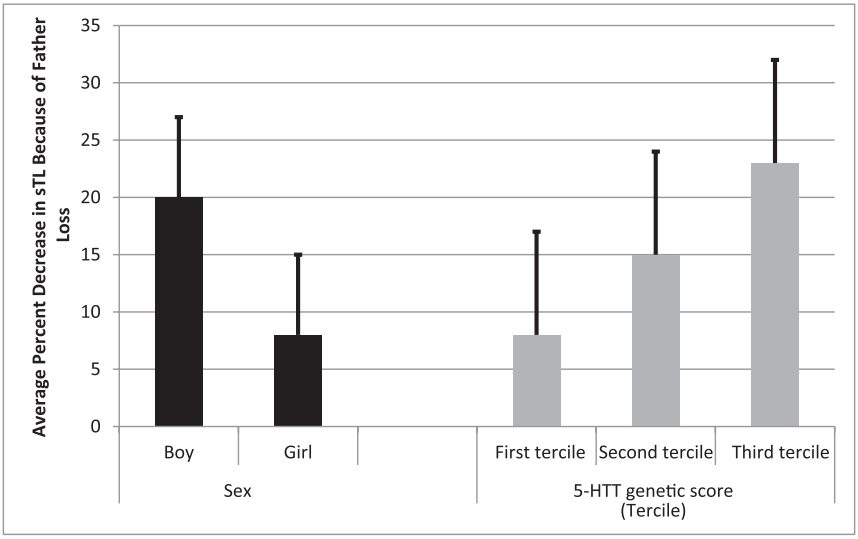

FIGURE 2
Effect of father loss in percent shorter age 9 sTL by sex and serotonin transporter (5-HTT) genetic score ($N = 2420$, error bars = 95% confidence interval). All analyses were controlled for race/ethnicity; mother's age and education at baseline; household income at baseline; child's sex, birth weight, and birth order; report of whether parents discussed an abortion; parental report of how their relationship was going before the child's birth; parental history of depression at baseline; parental history of an alcohol problem at baseline; parental incarceration history; if there was any domestic violence during the pregnancy; mother's self-report of health; and if the mother lived with her parents at age 15. For the serotonin transporter (5-HTT) genetic score, we summed the alleles that have been coded as "sensitizing" or "reactive" based on the literature (0, 1, or 2 for each individual). We divided the samples into terciles of genetic sensitization, with the highest tercile being the one in which we expect to be the most sensitizing.

some evidence that boys are more negatively affected than girls.[2,3,75] There is also some evidence that the association between family instability and child health and wellbeing differs by race/ethnicity,[76,77] although findings are inconsistent with respect to which group suffers more.[78]

Table 5 shows the effect of general father loss on sTL by different moderators over 2 developmental periods. With respect to sex, there is some evidence that boys respond more negatively than girls to father loss. The difference appears to be primarily because of a strong effect on boys who lose their fathers before age 5. Interestingly, we found no significant moderation by race/ethnicity. Finally, there is strong support that the variants associated with the serotonin transporter (but not the dopaminergic) pathway moderate the association between father loss and sTL. This finding fits with previous work, which suggests that the serotonergic pathway has a more direct effect on TL than the dopaminergic pathway,[7] mostly likely through the stress-physiology pathway. Figure 2 shows the moderation of father loss by sex and serotonin transporter (5-HTT) score.

DISCUSSION

This study uses data from a large birth cohort study to examine the association between father loss and children's sTL and to determine if the association is mediated by income loss and/or moderated by the type of loss, a child's sex, race/ethnicity, age at exposure, and genetic characteristics. Consistent with previous studies, we found that father loss is associated with shorter sTL in children. The association is robust across all types of loss and by a child's sex, race/ethnicity, and age at exposure. We also found that

the association is more pronounced among boys than girls and among children with the most reactive alleles of the serotonin transporter system. Two findings stand out for being inconsistent with previous research. First, previous research has found that the death of a father is less harmful for children than parents' separation or divorce,[2,10,79] whereas we found that a father's death is more strongly associated with child sTL. This finding may be due to something about our sample, which is urban and disadvantaged, or it may indicate that for some outcomes (eg, health), the negative consequences of a father's death are underestimated in studies that rely exclusively on survey questions to measure health and disease, especially in children. Second, previous research suggests that income loss accounts for half of the association between a father's death and negative outcomes for a child, whereas in our study, it accounts for only 25% of the association between a father's death and child sTL. Besides income loss, previous research highlighted 2 other possible mechanisms that underlie the link between father loss and negative outcomes for children: parenting quality and stability and neighborhood quality and stability. With respect to parenting, it is known that parenting quality can buffer the effect of adversity on TL.[80] It is possible that the greater effect of a father's death is due to a difference in a mother's parenting behavior that is unique to the father's death. It may also be due to a change in the father's behavior. Whereas other types of father loss do not necessarily mean an end to the father-child relationship, death is a permanent loss. Future research should examine whether the quality and quantity of a mother's parenting or father's involvement after the initial loss can account for the large effect of a father's death. Also, although father loss was measured prospectively since birth, TL was only measured at age 9. Additional research is needed to examine to what extent changes in a father's presence is associated with changes in sTL. The current article cannot determine the temporal ordering of sTL shortening and the time the father stopped living with the child.

With respect to neighborhoods, the death of a father may be a marker of some condition that is associated with child sTL as well as the father's death.[7,13,15,21,22,52,53,81] Whereas in most studies, a father's death is viewed as a more or less random event, in our sample of low-income, urban families, death may be a marker of neighborhood violence or the presence of other environmental liabilities. Future research should pay close attention to the cause of fathers' deaths to see if the negative association between child sTL and death is affected by different causes.

CONCLUSIONS

Although telomeres appear to be responsive to stressful environments during childhood, more basic biological research needs to be done before we can draw firm conclusions about the causal relationships between stress and TL. Such research could examine epigenetic modification of telomerase expression or activity as well as changes to cellular signaling pathways that could affect both telomere attrition and extension. Overall, however, this research provides a clear biological context for the association between all forms of father loss and previously described adult health effects later in life.

ABBREVIATIONS

FFCWS: Fragile Families and Child Wellbeing Study
PCR: polymerase chain reaction
sTL: salivary telomere length
TL: telomere length

REFERENCES

1. Allison PD, Furstenberg FF. How marital dissolution affects children: variations by age and sex. *Dev Psychol*. 1989;25(4):540–549
2. Biller HB. *Fathers and Families: Paternal Factors in Child Development*. Santa Barbara, CA: ABC-CLIO; 1993
3. Cavanagh SE, Crissey SR, Raley RK. Family structure history and adolescent romance. *J Marriage Fam*. 2008;70(3):698–714
4. Geller A, Garfinkel I, Cooper CE, Mincy RB. Parental incarceration and child well-being: implications for urban families. *Soc Sci Q*. 2009;90(5):1186–1202
5. Hofferth SL. Residential father family type and child well-being: investment versus selection. *Demography*. 2006;43(1):53–77
6. Lang K, Zagorsky JL. Does growing up with a parent absent really hurt? *J Hum Resour*. 2001;36(2):253–273
7. Mitchell C, Hobcraft J, McLanahan SS, et al. Social disadvantage, genetic sensitivity, and children's telomere length. *Proc Natl Acad Sci USA*. 2014;111(16):5944–5949
8. Mitchell C, McLanahan S, Brooks-Gunn J, Garfinkel I, Hobcraft J, Notterman D. Genetic differential sensitivity to social environments: implications for research. *Am J Public Health*. 2013;103(suppl 1):S102–S110
9. Roettger ME, Swisher RR, Kuhl DC, Chavez J. Paternal incarceration and trajectories of marijuana and other illegal drug use from adolescence into young adulthood: evidence from longitudinal panels of males and females in the United States. *Addiction*. 2011;106(1):121–132
10. Sigle-Rushton W, McLanahan S. Father absence and child wellbeing: a critical review. In: Moynihan DP, Rainwater L, Smeeding T, eds. *The Future of the Family*. New York, NY: Russell Sage Foundation; 2004:116–155
11. Tweed JL, Schoenbach VJ, George LK, Blazer DG. The effects of childhood parental death and divorce on six-month history of anxiety disorders. *Br J Psychiatry*. 1989;154(6):823–828

12. Aviv A, Chen W, Gardner JP, et al. Leukocyte telomere dynamics: longitudinal findings among young adults in the Bogalusa Heart Study. *Am J Epidemiol*. 2009;169(3):323–329

13. Beach SR, Lei MK, Brody GH, Yu T, Philibert RA. Nonsupportive parenting affects telomere length in young adulthood among African Americans: mediation through substance use. *J Fam Psychol*. 2014;28(6):967–972

14. Carroll JE, Diez-Roux AV, Adler NE, Seeman TE. Socioeconomic factors and leukocyte telomere length in a multi-ethnic sample: findings from the multi-ethnic study of atherosclerosis (MESA). *Brain Behav Immun*. 2013;28:108–114

15. Drury SS, Mabile E, Brett ZH, et al. The association of telomere length with family violence and disruption. *Pediatrics*. 2014;134(1). Available at: www.pediatrics.org/cgi/content/full/134/1/e128

16. Drury SS, Theall K, Gleason MM, et al. Telomere length and early severe social deprivation: linking early adversity and cellular aging. *Mol Psychiatry*. 2012;17(7):719–727

17. Entringer S, Eppel ES, Lin J, et al. Maternal psychosocial stress during pregnancy is associated with newborn leukocyte telomere length. *Am J Obstet Gynecol*. 2013;208(2):134.e1–134.e7

18. Needham BL, Adler N, Gregorich S, et al. Socioeconomic status, health behavior, and leukocyte telomere length in the National Health and Nutrition Examination Survey, 1999-2002. *Soc Sci Med*. 2013;85:1–8

19. Robertson T, Batty GD, Der G, Fenton C, Shiels PG, Benzeval M. Is socioeconomic status associated with biological aging as measured by telomere length? *Epidemiol Rev*. 2013;35:98–111

20. Shalev I, Entringer S, Wadhwa PD, et al. Stress and telomere biology: a lifespan perspective. *Psychoneuroendocrinology*. 2013;38(9):1835–1842

21. Theall KP, Brett ZH, Shirtcliff EA, Dunn EC, Drury SS. Neighborhood disorder and telomeres: connecting children's exposure to community level stress and cellular response. *Soc Sci Med*. 2013;85:50–58

22. Zeichner SL, Palumbo P, Feng Y, et al. Rapid telomere shortening in children. *Blood*. 1999;93(9):2824–2830

23. Cherkas LF, Aviv A, Valdes AM, et al. The effects of social status on biological aging as measured by white-blood-cell telomere length. *Aging Cell*. 2006;5(5):361–365

24. Rewak M, Buka S, Prescott J, et al. Race-related health disparities and biological aging: does rate of telomere shortening differ across blacks and whites? *Biol Psychol*. 2014;99:92–99

25. Marioni RE, Harris SE, Shah S, et al. The epigenetic clock and telomere length are independently associated with chronological age and mortality. *Int J Epidemiol*. 2016;45(2):424–432

26. Lin J, Epel E, Cheon J, et al. Analyses and comparisons of telomerase activity and telomere length in human T and B cells: insights for epidemiology of telomere maintenance. *J Immunol Methods*. 2010;352(1–2):71–80

27. Cawthon RM. Telomere measurement by quantitative PCR. *Nucleic Acids Res*. 2002;30(10):e47

28. Cawthon RM, Smith KR, O'Brien E, Sivatchenko A, Kerber RA. Association between telomere length in blood and mortality in people aged 60 years or older. *Lancet*. 2003;361(9355):393–395

29. Aubert G, Lansdorp PM. Telomeres and aging. *Physiol Rev*. 2008;88(2):557–579

30. Epel ES, Merkin SS, Cawthon R, et al. The rate of leukocyte telomere shortening predicts mortality from cardiovascular disease in elderly men. *Aging (Albany NY)*. 2008;1(1):81–88

31. Njajou OT, Hsueh WC, Blackburn EH, et al; Health ABC Study. Association between telomere length, specific causes of death, and years of healthy life in health, aging, and body composition, a population-based cohort study. *J Gerontol A Biol Sci Med Sci*. 2009;64(8):860–864

32. Artandi SE, DePinho RA. Telomeres and telomerase in cancer. *Carcinogenesis*. 2010;31(1):9–18

33. Atturu G, Brouilette S, Samani NJ, London NJ, Sayers RD, Bown MJ. Short leukocyte telomere length is associated with abdominal aortic aneurysm (AAA). *Eur J Vasc Endovasc Surg*. 2010;39(5):559–564

34. Farzaneh-Far R, Lin J, Epel E, Lapham K, Blackburn E, Whooley MA. Telomere length trajectory and its determinants in persons with coronary artery disease: longitudinal findings from the heart and soul study. *PLoS One*. 2010;5(1):e8612

35. Huzen J, van der Harst P, de Boer RA, et al. Telomere length and psychological well-being in patients with chronic heart failure. *Age Ageing*. 2010;39(2):223–227

36. Oeseburg H, de Boer RA, van Gilst WH, van der Harst P. Telomere biology in healthy aging and disease. *Pflugers Arch*. 2010;459(2):259–268

37. Risques RA, Arbeev KG, Yashin AI, et al. Leukocyte telomere length is associated with disability in older U.S. population. *J Am Geriatr Soc*. 2010;58(7):1289–1298

38. Willeit P, Willeit J, Brandstätter A, et al. Cellular aging reflected by leukocyte telomere length predicts advanced atherosclerosis and cardiovascular disease risk. *Arterioscler Thromb Vasc Biol*. 2010;30(8):1649–1656

39. Fitzpatrick AL, Kronmal RA, Kimura M, et al. Leukocyte telomere length and mortality in the Cardiovascular Health Study. *J Gerontol A Biol Sci Med Sci*. 2011;66(4):421–429

40. Guttmacher AE, Raju TN. The child is father of the man, and mother of the woman. *Pediatrics*. 2014;134(5). Available at: www.pediatrics.org/cgi/content/full/134/5/e1411

41. Shalev I, Caspi A, Ambler A, et al. Perinatal complications and aging indicators by midlife. *Pediatrics*. 2014;134(5). Available at: www.pediatrics.org/cgi/content/full/134/5/e1315

42. Bendix L, Thinggaard M, Fenger M, et al. Longitudinal changes in leukocyte telomere length and mortality in humans. *J Gerontol A Biol Sci Med Sci*. 2014;69(2):231–239

43. Martin-Ruiz C, Dickinson HO, Keys B, Rowan E, Kenny RA, Von Zglinicki T. Telomere length predicts poststroke mortality, dementia, and cognitive decline. *Ann Neurol*. 2006;60(2):174–180

44. Rius-Ottenheim N, Houben JM, Kromhout D, et al. Telomere length and

mental well-being in elderly men from the Netherlands and Greece. *Behav Genet*. 2012;42(2):278–286

45. Geronimus AT, Hicken M, Keene D, Bound J. "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *Am J Public Health*. 2006;96(5):826–833
46. Ladwig K-H, Brockhaus AC, Baumert J, et al. Posttraumatic stress disorder and not depression is associated with shorter leukocyte telomere length: findings from 3,000 participants in the population-based KORA F4 study. *PLoS One*. 2013;8(7):e64762
47. Buss J, Havel PJ, Epel E, Lin J, Blackburn E, Daubenmier J. Associations of ghrelin with eating behaviors, stress, metabolic factors, and telomere length among overweight and obese women: preliminary evidence of attenuated ghrelin effects in obesity? *Appetite*. 2014;76:84–94
48. García-Calzón S, Gea A, Razquin C, et al. Longitudinal association of telomere length and obesity indices in an intervention study with a Mediterranean diet: the PREDIMED-NAVARRA trial. *Int J Obes*. 2014;38(2):177–182
49. Brennan KA, Shaver PR. Attachment styles and personality disorders: their connections to each other and to parental divorce, parental death, and perceptions of parental caregiving. *J Pers*. 1998;66(5):835–878
50. Cribbet MR, Carlisle M, Cawthon RM, et al. Cellular aging and restorative processes: subjective sleep quality and duration moderate the association between age and telomere length in a sample of middle-aged and older adults. *Sleep*. 2014;37(1):65–70
51. Cohen S, Janicki-Deverts D, Chen E, Matthews KA. Childhood socioeconomic status and adult health. *Ann N Y Acad Sci*. 2010;1186:37–55
52. Needham BL, Fernandez JR, Lin J, Epel ES, Blackburn EH. Socioeconomic status and cell aging in children. *Soc Sci Med*. 2012;74(12):1948–1951
53. Stathopoulou MG, Petrelis AM, Buxton JL, Froguel P, Blakemore AI, Visvikis-Siest S. Genetic determinants of leucocyte telomere length in children: a neglected and challenging field. *Paediatr Perinat Epidemiol*. 2015;29(2):146–150
54. Price LH, Kao H-T, Burgers DE, Carpenter LL, Tyrka AR. Telomeres and early-life stress: an overview. *Biol Psychiatry*. 2013;73(1):15–23
55. Reichman NE, Teitler JO, Garfinkel I, McLanahan SS. Fragile families: sample and design. *Child Youth Serv Rev*. 2001;23(4–5):303–326
56. O'Callaghan NJ, Fenech M. A quantitative PCR method for measuring absolute telomere length. *Biol Proced Online*. 2011;13:3
57. Wang S, Zhu J. Evidence for a relief of repression mechanism for activation of the human telomerase reverse transcriptase promoter. *J Biol Chem*. 2003;278(21):18842–18850
58. Cheng D, Zhao Y, Wang S, et al. Repression of telomerase gene promoter requires human-specific genomic context and is mediated by multiple HDAC1-containing corepressor complexes. *FASEB J*. 2017;31(3):1165–1178
59. Schutte NS, Malouff JM. The relationship between perceived stress and telomere length: a meta-analysis. *Stress Health*. 2016;32(4):313–319
60. Daniali L, Benetos A, Susser E, et al. Telomeres shorten at equivalent rates in somatic tissues of adults. *Nat Commun*. 2013;4:1597
61. Wren ME, Shirtcliff EA, Drury SS. Not all biofluids are created equal: chewing over salivary diagnostics and the epigenome. *Clin Ther*. 2015;37(3):529–539
62. Mitchell C, Notterman D, Brooks-Gunn J, et al. Role of mother's genes and environment in postpartum depression. *Proc Natl Acad Sci USA*. 2011;108(20):8189–8193
63. Bakermans-Kranenburg MJ, Van IJzendoorn MH, Pijlman FT, Mesman J, Juffer F. Experimental evidence for differential susceptibility: dopamine D4 receptor polymorphism (DRD4 VNTR) moderates intervention effects on toddlers' externalizing behavior in a randomized controlled trial. *Dev Psychol*. 2008;44(1):293–300
64. Buckholtz JW, Treadway MT, Cowan RL, et al. Dopaminergic network differences in human impulsivity. *Science*. 2010;329(5991):532
65. Jorm AF, Prior M, Sanson A, Smart D, Zhang Y, Easteal S. Association of a polymorphism of the dopamine transporter gene with externalizing behavior problems and associated temperament traits: a longitudinal study from infancy to the mid-teens. *Am J Med Genet*. 2001;105(4):346–350
66. Schmidt LA, Fox NA, Hamer DH. Evidence for a gene-gene interaction in predicting children's behavior problems: association of serotonin transporter short and dopamine receptor D4 long genotypes with internalizing and externalizing behaviors in typically developing 7-year-olds. *Dev Psychopathol*. 2007;19(4):1105–1116
67. Young SE, Smolen A, Corley RP, et al. Dopamine transporter polymorphism associated with externalizing behavior problems in children. *Am J Med Genet*. 2002;114(2):144–149
68. Nikolova YS, Ferrell RE, Manuck SB, Hariri AR. Multilocus genetic profile for dopamine signaling predicts ventral striatum reactivity. *Neuropsychopharmacology*. 2011;36(9):1940–1947
69. Karg K, Burmeister M, Shedden K, Sen S. The serotonin transporter promoter variant (5-HTTLPR), stress, and depression meta-analysis revisited: evidence of genetic moderation. *Arch Gen Psychiatry*. 2011;68(5):444–454
70. Navarro-Mateu F, Escámez T, Koenen KC, Alonso J, Sánchez-Meca J. Meta-analyses of the 5-HTTLPR polymorphisms and post-traumatic stress disorder. *PLoS One*. 2013;8(6):e66227
71. Xie P, Kranzler HR, Poling J, et al. Interactive effect of stressful life events and the serotonin transporter 5-HTTLPR genotype on posttraumatic stress disorder diagnosis in 2 independent populations. *Arch Gen Psychiatry*. 2009;66(11):1201–1209
72. Auerbach J, Geller V, Lezer S, et al. Dopamine D4 receptor (D4DR) and serotonin transporter promoter (5-HTTLPR) polymorphisms in the determination of temperament in 2-month-old infants. *Mol Psychiatry*. 1999;4(4):369–373

73. Caspi A, Hariri AR, Holmes A, Uher R, Moffitt TE. Genetic sensitivity to the environment: the case of the serotonin transporter gene and its implications for studying complex diseases and traits. *Am J Psychiatry*. 2010;167(5):509–527

74. McLanahan SS, Sandefur G. *Growing Up With a Single Parent: What Hurts, What Helps*. Cambridge, MA: Harvard University Press; 1994

75. Hetherington EM, Cox M, Cox R. Long-term effects of divorce and remarriage on the adjustment of children. *J Am Acad Child Psychiatry*. 1985;24(5):518–530

76. Fomby P, Mollborn S, Sennott CA. Race/ethnic differences in effects of family instability on adolescents' risk behavior. *J Marriage Fam*. 2010;72(2):234–253

77. McLoyd VC, Cauce AM, Takeuchi D, Wilson L. Marital processes and parental socialization in families of color: a decade review of research. *J Marriage Fam*. 2000;62(4):1070–1093

78. Lee D, McLanahan S. Family structure transitions and child development: Instability, selection, and population heterogeneity. *Am Sociol Rev*. 2015;80(4):738–763

79. Yogman M, Garfield CF; Committee on Psychosocial Aspects of Child and Family Health. Fathers' roles in the care and development of their children: the role of pediatricians. *Pediatrics*. 2016;138(1):e20161128

80. Asok A, Bernard K, Roth TL, Rosen JB, Dozier M. Parental responsiveness moderates the association between early-life stress and reduced telomere length. *Dev Psychopathol*. 2013;25(3):577–585

81. Brody GH, Yu T, Beach SR, Philibert RA. Prevention effects ameliorate the prospective association between nonsupportive parenting and diminished telomere length. *Prev Sci*. 2015;16(2):171–180