Early life stress is associated with earlier emergence of permanent molars

Cassidy L. McDermott*, Katherine Hiltonb, Anne T. Parka, Ursula A. Tooleya, Austin L. Boroshok*, Muralidhar Mupparapub, JoAnna M. Scott*, Erin E. Bumannc, and Allyson P. Mackeya*

*aDepartment of Psychology, University of Pennsylvania, Philadelphia, PA 19104; bSchool of Dental Medicine, University of Pennsylvania, Philadelphia, PA 19104; and School of Dentistry, University of Missouri–Kansas City, Kansas City, MO 64108

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Exposure to adversity can accelerate biological aging. However, existing biomarkers of early aging are either costly and difficult to collect, like epigenetic signatures, or cannot be detected until late childhood, like pubertal onset. We evaluated the hypothesis that early adversity is associated with earlier molar eruption, an easily assessed measure that has been used to track the length of childhood across primates. In a preregistered analysis (Fig. 1), we investigated whether adversity impacts the timing of first permanent molars, as rated in T2-weighted magnetic resonance images (MRI). We replicate relationships between income and molar eruption in a population-representative dataset (National Health and Nutrition Examination Survey; n = 1,973). These findings suggest that the impact of stress on the pace of biological development is evident in early childhood, and detectable in the timing of molar eruption.

Results

We conducted a preregistered analysis (https://osf.io/fsnnd/) to investigate how experiences of early adversity relate to the timing of emergence of the first permanent molars. We focused on two measures: family income, as low income is associated with high risk for chronic stress, and ACEs, as they have been consistently linked with poor health outcomes (1). We measured molar eruption by rating T2-weighted MRI scans, which are sensitive to tissues in the dental follicle (Fig. 1). Our analyses included 117 4- to 7-y-old children (64 female/53 male; 48 Black/36 white/5 Asian/14 Hispanic/14 multiracial or other).

Effects of age, gender, and race/ethnicity on molar eruption were consistent with previous reports (11). Molar eruption was positively associated with age (β = 0.842, 95% CI [0.743, 0.942], P < 0.001; Fig. 2A). Girls had earlier molar eruption than boys (β = 0.349, 95% CI [0.159, 0.539], P < 0.001 controlling for age; Fig. 2B). Compared with Black children, white (β = −0.307, 95% CI [−0.524, −0.090], P = 0.006), Asian (β = −0.548, 95% CI [−1.011, −0.086], P = 0.021), and multiracial (β = −0.340, 95% CI [−0.639, −0.041] P = 0.026) children had later molar eruption. Body mass index (BMI) was not associated with molar eruption (β = 0.050, 95% CI [−0.063, 0.163], P = 0.381). As preregistered, age and gender were included as covariates in all subsequent models of molar eruption, and models were run with and without race/ethnicity and BMI.

Lower family income was significantly associated with earlier molar eruption (β = −0.167, 95% CI [−0.261, −0.073], P = 0.001; Fig. 2C). This association remained significant after controlling for BMI (β = −0.199, 95% CI [−0.301, −0.098], P < 0.001), race/ethnic group (β = −0.144, 95% CI [−0.261, −0.028], P = 0.015), or both BMI and race/ethnic group (β = −0.184, 95% CI [−0.306, −0.061], P = 0.004). Greater exposure to ACEs was also significantly associated with earlier molar eruption (β = 0.119, 95% CI [0.027, 0.212], P = 0.012; Fig. 2D). This association remained significant when controlling for BMI (β = 0.126, 95% CI [−0.024, 0.228], P = 0.016) but was at trend level when including race/ethnic group (β = 0.086, 95% CI [−0.005, 0.178], P = 0.065). When family income and ACEs were included in the same model, only family income was significantly associated with molar eruption (income: β = −0.150, 95% CI [−0.246, −0.053], P = 0.003; ACEs: β = 0.065, 95% CI [−0.030, 0.161], P = 0.178).

We conducted a parallel set of analyses using data from the National Health and Nutrition Examination Survey (NHANES; 2011–2016). Analyses were restricted to subjects between ages
4.8 and 7.8 y with available oral health data, resulting in a sample of 1,973 participants. Age was related to number of first molars ($\beta = 0.736$, 95% CI $[0.712, 0.76]$, $P < 0.001$), and girls had more first molars than boys ($\beta = 0.113$, 95% CI $[0.05, 0.196]$, $P = 0.01$, controlling for age). Black ($\beta = 0.137$, 95% CI $[0.043, 0.23]$, $P = 0.006$), Hispanic ($\beta = 0.144$, 95% CI $[0.072, 0.217]$, $P < 0.001$), and multiracial ($\beta = 0.156$, 95% CI $[0.036, 0.277]$, $P = 0.015$) children had more first molars than white children. Lower family income was significantly associated with having more first molars erupted ($\beta = -0.060$, 95% CI $[-0.101, -0.019]$, $P = 0.006$, controlling for age and gender). Family income was significantly associated with number of first molars after controlling for BMI ($\beta = -0.047$, 95% CI $[-0.087, -0.006]$, $P = 0.029$), but not racial/ethnic category ($\beta = -0.042$, 95% CI $[-0.087, 0.003]$, $P = 0.076$).

Finally, we tested whether relationships between income and molar eruption extended to second molars, which erupt, on average, at age 12 y. Among 2,993 children aged 9.1 to 14.3 y, family income was significantly associated with number of erupted second molars ($\beta = -0.046$, 95% CI $[-0.074, -0.018]$, $P = 0.002$, controlling for age and gender). Family income was no longer significantly associated with number of second molars after controlling for BMI ($\beta = -0.026$, 95% CI $[-0.055, 0.002]$, $P = 0.079$) or racial/ethnic category ($\beta = -0.025$, 95% CI $[-0.057, 0.006]$, $P = 0.126$). Consistent with prior work (12), molar eruption was associated with

![Fig. 1.](image1.png) Molar eruption rating criteria in MRI. The dashed lines represent the planes of occlusion (i.e., the planes at which the top and bottom teeth meet).

![Fig. 2.](image2.png) Associations between molar eruption and (A) age, (B) gender, (C) income, and (D) ACEs.
Finally, our work was done only in the United States, and may not generalize to other contexts (19).

Despite these limitations, our work provides insight into the timing of molar eruption among children from lower-income families. Molar eruption can be characterized both in existing MRI datasets and in radiographs obtained through routine dental care. Longitudinal research is necessary to evaluate downstream correlates of early molar eruption, including early puberty, early brain development, and mental and physical health. If molar eruption timing can identify children at risk for accelerated aging early in childhood, it may serve as a useful screening tool to direct early intervention resources to the children who need them most.

Methods

Detailed materials and methods are provided in the SI Appendix.

MRI Sample. This study was approved by the Institutional Review Board at the University of Pennsylvania. All parents provided written informed consent. Molar eruption was rated from raw T2-weighted MRI scans (Fig. 1). Molar eruption associations with age, gender, race/ethnicity, BMI percentile, family income, and ACEs were examined using linear models in R.

Replication in NHANES. We combined three cycles of NHANES (2011–2012, 2013–2014, and 2015–2016). The number of erupted molars was summed from the Coronal Caries: Tooth Count variables. Molar eruption associations with age, gender, race/ethnicity, BMI percentile, and family income were examined using linear models with appropriate sample weights applied using the “survey” package in R (20).

Data Availability. Deidentified data and code for the MRI sample are deposited on OSF (https://osf.io/4tvvn/) (21). NHANES data are publicly available through the National Center for Health Statistics (https://www.cdc.gov/nchs/nhanes/ContinuousNhanes/default.aspx?BeginYear=2011, https://www.cdc.gov/nchs/nhanes/ContinuousNhanes/default.aspx?BeginYear=2013, and https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/default.aspx?BeginYear=2015) (22).

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