

Original Contribution

Targeted Estimation of the Relationship Between Childhood Adversity and Fluid Intelligence in a US Population Sample of Adolescents

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Many studies have shown inverse associations between childhood adversity and intelligence, although most are based on small clinical samples and fail to account for the effects of multiple co-occurring adversities. Using data from the 2001–2004 National Comorbidity Survey Adolescent Supplement, a cross-sectional US population study of adolescents aged 13–18 years (n = 10,073), we examined the associations between 11 childhood adversities and intelligence, using targeted maximum likelihood estimation. Targeted maximum likelihood estimation incorporates machine learning to identify the relationships between exposures and outcomes without overfitting, including interactions and nonlinearity. The nonverbal score from the Kaufman Brief Intelligence Test was used as a standardized measure of fluid reasoning. Childhood adversities were grouped into deprivation and threat types based on recent conceptual models. Adjusted marginal mean differences compared the mean intelligence score if all adolescents experienced each adversity to the mean in the absence of the adversity. The largest associations were observed for deprivation-type experiences, including poverty and low parental education, which were related to reduced intelligence. Although lower in magnitude, threat events related to intelligence included physical abuse and witnessing domestic violence. Violence prevention and poverty-reduction measures would likely improve childhood cognitive outcomes.

childhood adversity; fluid reasoning; targeted maximum likelihood estimation

Abbreviations: K-BIT, Kaufman Brief Intelligence Test; SES, socioeconomic status; TMLE, targeted maximum likelihood estimation.

Adversity experienced during childhood and adolescence can have substantial consequences for developmental processes throughout the life course (1). Childhood adversity refers to a broad array of negative events experienced during the early years of life and into adolescence (2). The consequences of childhood adversity may affect social (3, 4), affective (5, 6), and cognitive development (7–9). Here, we examined the links between childhood adversity and intelligence in a general population sample.

Intelligence is currently defined by a generalized intelligence factor (g) that is composed of subdimensions, such as visuospatial reasoning, language, and working memory (10, 11). A widely accepted model of cognitive functioning distinguishes between fluid and crystallized intelligence as 2 primary components (12). Fluid intelligence reflects reasoning and the ability to solve novel problems; crystallized intelligence reflects knowledge and skills from learned experiences (13) and is considered a valid measure of generalized intelligence (14, 15).

Studies examining the association between childhood adversity and intelligence have identified negative correlations resulting from physical and sexual abuse (16–19) and exposure to violence (20, 21). These types of experiences are characterized as threats of harm to one's physical integrity (22). The effects of threat experiences may influence development of many different brain regions through well-characterized stress pathways (23, 24), associated with reductions in hippocampal volume and associated parahippocampal regions (25–28), which may in turn influence learning and memory (29).

There is also evidence that growing up with chronic exposure to neglect (30–33) and poverty (34, 35) may affect cognitive functioning. These deprivation-type experiences are characterized by an absence of expected environmental inputs (e.g., complex language, consistent interactions with caregivers) and an absence of cognitive stimulation (22, 36). Children raised in environments that may lack cognitive stimulation, including poverty, neglect, and institutional rearing, have consistently shown reduced cognitive ability, which may be mediated by accelerated and extreme synaptic pruning in cortical regions involved in complex cognitive functions in response to an absence of expected environmental inputs (30, 36–39).

Childhood adversity is a multidimensional experience, which can make it challenging to model analytically. Most studies make unverified assumptions about the relationship between multiple childhood adversities and related outcomes. For example, studies often examine the effects of individual (40) or a linear accumulation of adversities (41) or use a latent variable framework (42). Applications of these approaches have relied on the assumptions that the effect of each adversity can be estimated independently of other adversities (i.e., no interaction between adversities), and that the effect of cumulative exposures is linear. There are 2 additional limitations from studies of adversity and cognition. Few studies use a standardized measure of intelligence, making comparisons across studies difficult. Furthermore, most studies use data from small samples with potentially limited generalizability. Although these studies allow for an investigation of specific adversities, using a national sample allows for study of a broader set of exposures in a population-representative context, increasing the likelihood that results will be broadly relevant (43).

We hypothesized that both threat- and deprivation-type adversities would be significantly associated with intelligence but that associations would be largest for adversities reflecting deprivation. To address the above limitations and test this hypothesis, we investigated the relationship between childhood adversity and a standardized measure of intelligence in a populationrepresentative sample of US adolescents. We addressed the limitations in modeling multiple adversities by examining these relationships using targeted maximum likelihood estimation (TMLE). TMLE is a semiparametric estimation method that can be used to minimize bias in the relationship between each adversity and the outcome, including interactions and nonlinearity (44).

METHODS

Data

Data were from the National Comorbidity Survey Adolescent Supplement (NCS-A), a cross-sectional survey of a US population-representative sample of 10,148 adolescents, aged 13-18 years, from 2001-2004 (45). The study was designed to measure the prevalence, demographic correlates, and risk factors for a broad range of psychiatric disorders in adolescence (46). Participants from a school-based sample completed computerassisted interviews. Survey weights were developed, based on the 2000 Census frequencies, to yield population-representative estimates (47). Study participants were compensated \$50 for participation. Parents/guardians gave written informed consent, and adolescent participants gave written informed assent, in accordance to the procedures approved by human subjects committees of Harvard Medical School and the University of Michigan. The Institutional Review Board of Columbia University approved the present analysis. Further study details can be found elsewhere

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(48). The final sample included those with nonmissing outcome and survey weight variables (n = 10,073, 99.3%).

Outcome

The study outcome was the nonverbal score from the Kaufman Brief Intelligence Test (K-BIT), which was developed as a standardized measure of fluid intelligence (49, 50). The K-BIT test administration includes a series of 48 abstract questions of progressively greater difficulty. Participants answer each question in 9 sets of 5 items and 1 set of 3 items; test administration is continued until a participant answers all items in a set incorrectly. The K-BIT has been shown to have good reliability and validity in child, adolescent, and adult populations. For 91.1% of the sample, raw K-BIT scores were created by summing the number of items that a participant answered correctly. The remaining participants received a nonstandard test administration. For example, some respondents were asked only the most difficult item in each set. In these cases, the K-BIT score was imputed based on the number of correct items and the level at which they met discontinuation criteria (8.6%). The remaining cases received invalid test administration and were excluded (0.3%).

The K-BIT scale was renormed to account for the size and representativeness of the sample, as well as to update the current normative intelligence levels to account for known cohort effects of intelligence (51, 52). Finally, the scale was standardized to a mean of 100 and standard deviation of 15, within 6-month age groups. The scores ranged from 42 to 137. Consistent with prior work (15), we defined the cutoff for a low K-BIT score as greater than 1 standard deviation below the mean (i.e., 85), representing a clinically relevant threshold for low fluid reasoning (49, 53, 54). The final scale demonstrated excellent reliability ($\omega = 0.96$) (55), and a single-factor solution provided the best-fitting confirmatory factor analytic model (15). To ensure that the estimation procedure respected the observed bounds on the outcome, the outcome was transformed from continuous to a [0,1] bounded distribution; then results were back-transformed to yield estimated K-BIT means.

Exposure

Eleven childhood adversities were considered, using sociodemographic variables and a trauma checklist administered in the Composite International Diagnostic Interview (56) in line with previous research (41). Items were grouped into separate threat and deprivation domains, according to an established conceptual framework (22). Dichotomous (ever vs. never) threat experiences included physical abuse, domestic violence, sexual abuse, violent victimization, witnessing violence, and emotional abuse. Deprivation experiences included financial insecurity, food insecurity, neglect, poverty (<1.5, 1.5–2.9, 3.0–5.9, or \geq 6.0 times the poverty level), and low parental education (some high school, high school diploma, some college, or college degree). Web Table 1 (available at https://academic.oup.com/aje) details how the exposure variables were created.

Covariates

Models adjusted for potential confounding by including a set of covariates that were associated with both the exposure and outcome. Variables included: age (range, 13–18 years), race/ ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, other), birth order (range, 1–13), nativity (US- or foreign-born), number of biological siblings (range, 0 to 10 or more), any lifetime parent psychiatric disorder, and any lifetime parent substance-use disorder.

Analysis

TMLE is a semiparametric method that incorporates machine learning to maximize the accuracy for estimating a targeted exposure parameter (44). This study used TMLE to estimate the study parameters to be interpreted within a potential outcomes framework. We estimated 2 parameters: 1) the differences in the covariate-adjusted mean K-BIT score of adolescents who experienced each adversity separately compared with the mean of those who did not experience that adversity, and 2) the risk of low versus average K-BIT score if all adolescents had experienced a given adversity compared with the risk in the absence of that adversity. As a sensitivity analysis, we also fitted a set of models including parental education as a covariate rather than an exposure. Parental education has been shown to predict more proximate childhood adversities (57).

Implementation of TMLE included the following steps. First, we fitted a regression model to calculate the expected K-BIT score (Y), conditional on adversity status (A) and covariate values (W), E(Y | A, W). The regression used a cross-entropy loss to ensure that the parameter respected the bounds of Y. Next, we estimated the propensity score for each adversity, adjusted for model covariates: P(A = 1|W). This score was used to update the initial outcome model in order to minimize the bias and maximize the precision of the targeted estimator of the parameter of interest. The resulting estimator is asymptotically normal with a known influence curve, thereby allowing construction of 95% Wald-type confidence intervals. The machine-learning procedure was implemented using the SuperLearner algorithm. SuperLearner selects the weighted combination of estimators that best captures the functional relationships between the set of adversities, covariates, and the outcome (58). In determining the best-fitting regression estimates, several candidate estimators were considered, including a generalized linear model with and without firstorder interactions and stepwise regression models with and without first-order interactions. More flexible estimators were also considered, including a generalized additive model (59) and a single-hidden-layer neural network (60). Two algorithms were run to consider a vector of single adversities and a cumulative sum of adversities.

The best combination was determined via 10-fold cross-validation, whereby, for each adversity Y, an estimator of the outcome regression was fitted on a 90% random sample of the observed data. To prevent overfitting, cross-validated meansquared error was minimized through subsequent iterations of 10% random samples of the data. The SuperLearner estimate comprised a weighted proportion of all the candidate estimates. The TMLE, which represents a fluctuation of this initial SuperLearner estimate, provides doubly robust estimates that will be unbiased if either the outcome regression or the propensity score model is correctly specified. TMLE was implemented using the tmle (61) and SuperLearner (62) packages in R (R Foundation for Statistical Computing, Vienna, Austria).

Several causal assumptions must be considered in order to interpret the parameters of interest in a potential outcomes framework. They have been elaborated elsewhere (for example, in Imbens and Rubin (63)). In brief, exposure must precede the outcome (temporality), all confounding must be controlled (exchangeability), one person's potential outcomes must not depend on another's treatment (no interference), no unrepresented versions of treatment (consistency), and individuals must have a positive probability of receiving every level of exposure and confounders (positivity).

With respect to temporality, all adversities occurred prior to the K-BIT administration, although there was no measure of intelligence prior to adversity exposures. While the estimates were adjusted for confounding due to observed covariates, we cannot empirically verify that the exchangeability assumption has been met using observational data. Interference between individuals is unlikely in a nationally representative sample. Consistency might be violated if there is heterogeneity in the potential outcomes of respondents who report experiencing the same adversity. If this were to occur, the estimates could be interpreted as a random draw of the variation present under each adversity (64). The positivity assumption was assessed by examining the influence of individual observations on the estimator, as a highly influential observation indicates near positivity violations in that individual's covariate strata (65). There were minimal influential outliers in our mean difference estimates (see Web Table 2), satisfying the positivity assumption. A description of the influence curve quantiles can be found in Web Appendix 1. Although many are untestable, careful consideration of these assumptions allows us consider the specific strengths and limitations of the data with respect to a causal inference framework (66).

RESULTS

Figure 1 presents the mean differences comparing the K-BIT scores if all adolescents had experienced a given adversity with the mean in the absence of that adversity. There were significant differences in K-BIT mean scores among those who reported ever experiencing several types of threat experiences, including physical abuse and domestic violence. Experiencing any threat was associated with a mean score of 1.82 (95% confidence interval: 0.82, 2.83) units lower than no threat experience. Among deprivation experiences, there were significant mean differences in K-BIT associated with a household income at the poverty line, having parents with less than a high school diploma, and having financial insecurity. Experiencing any deprivation was associated with a mean score of 2.32 (95% confidence interval: 1.21, 3.43) units less than those with no experience of deprivation. Full results are presented in Table 1. There was no evidence of a doseresponse relationship with greater cumulative adversities.

Figure 2 presents the risk of a low versus average K-BIT score if all adolescents had experienced a given adversity compared with the risk in the absence of that adversity. The risk difference of low K-BIT from experiencing any threat was 6 cases per 100 (95% confidence interval: 0.03, 0.10). The specific threat experiences of physical abuse, domestic violence, and emotional abuse were significantly associated

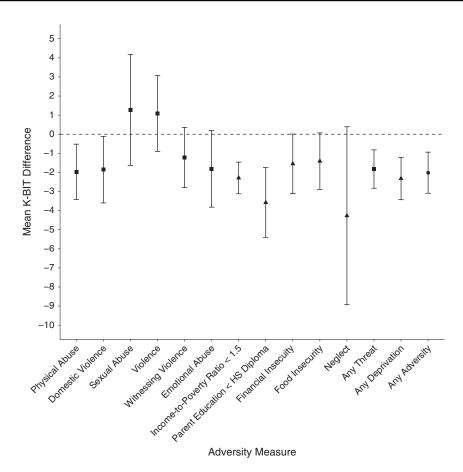


Figure 1. Targeted maximum likelihood estimated differences in mean scores on the Kaufman Brief Intelligence Test (K-BIT) in the presence versus absence of childhood adversities among a representative sample of 10,073 adolescents in the United States, 2001–2004. Square, threat-type adversities; triangle, deprivation-type adversities; circle, any adversity. HS, high school.

with a low K-BIT score. The difference in risk of low K-BIT from experiencing any deprivation experience was 7 cases per 100 (95% confidence interval: 0.03, 0.11). Specifically, having parents with less than a high school diploma and experiencing neglect both significantly increased the risk of a low K-BIT. There was no evidence that the risk differences increased with greater cumulative adversities. Full results are presented in Table 2.

Results from the sensitivity analysis, including parental education as a covariate rather than an adversity can be found in Web Table 3. Overall, K-BIT mean differences were attenuated but remained significant for those experiencing any threat, living near the poverty line, and experiencing any deprivation or any adversity.

DISCUSSION

Using TMLE, we identified several significant relationships between diverse forms of childhood adversity and lower levels of fluid intelligence. These were identified by estimating differences in mean K-BIT scores in the presence and absence of the adversities, as well as the risk of low vs. average K-BIT score. Although both threat and deprivation types of adversities were related to K-BIT, mean and risk differences were greater for

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deprivation experiences, specifically education- and incomerelated exposures that comprise low socioeconomic status (SES). This study is strengthened by the use of a nationally representative sample, which allows us to generalize our findings to the US population. These results are consistent with a large literature documenting strong associations between SES and cognitive ability in children, including fluid reasoning (8, 9, 67, 68). Rather than make a priori assumptions regarding the form of the analytic models, a second strength of this study is the use of TMLE and machine-learning methods to capture the form of the relationships between childhood adversities, intelligence, and covariates. The need to incorporate this information is seen in the model parameter weights, which used estimates from multiple candidate algorithms, including methods to model highdimensional nonlinear data with interactions between individual exposures (see Web Appendix 1 and Web Table 4) (69). This novel approach represents an improvement when studying multidimensional exposures, such as childhood adversities.

An additional strength of the study is the grouping of threat and deprivation adversities. Categorizing individual adversities in this way may illuminate distinct pathways through which experiences affect childhood intelligence. The effect of low SES on a child's cognitive development is hypothesized to be mediated through -

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Adversity Type	Mean K-BIT Score ^a	95% CI	K-BIT Mean Difference	95% CI
Threat adversities				
Physical abuse	98.8	97.3, 100.2	-1.97	-3.42, -0.52
No physical abuse	100.8	99.3, 102.2		
Domestic violence	99.1	97.3, 100.8	-1.86	-3.60, -0.11
No domestic violence	100.9	99.2, 102.7		
Sexual abuse	101.3	98.4, 104.2	1.27	-1.63, 4.18
No sexual abuse	100.1	97.2, 103.0		
Violence	101.3	99.3, 103.3	1.09	-0.90, 3.07
No violence	100.2	98.2, 102.2		
Witnessing violence	99.9	98.3, 101.4	-1.22	-2.80, 0.36
No witnessing violence	101.1	99.5, 102.7		
Emotional abuse	99.5	97.5, 101.5	-1.81	-3.82, 0.20
No emotional abuse	101.3	99.3, 103.3		
No. of cumulative threat-experience adversities				
1	99.4	98.2, 100.6		
2	100.1	98.4, 101.9		
≥3	100.3	97.8, 102.8		
≥1	100.5	99.5, 101.6	-1.82	-2.83, -0.82
0	102.4	101.4, 103.4		
Deprivation adversities				
Income-to-poverty ratio < 1.5	98.6	97.7, 99.4	-2.29	-3.12, -1.46
Income-to-poverty ratio ≥ 1.5	100.9	100.0, 101.7		
Parental education < HS diploma	97.3	95.5, 99.2	-3.58	-5.40, -1.75
Parental education \geq HS diploma	100.9	99.1, 102.8		
Financial insecurity	99.6	98.1, 101.2	-1.55	-3.11, 0.01
No financial insecurity	101.2	99.6, 102.7		
Food insecurity	99.6	98.2, 101.1	-1.41	-2.89, 0.07
No food insecurity	101.0	99.6, 102.5		
Neglect	98.0	93.4, 102.7	-4.27	-8.93, 0.39
No neglect	102.3	97.6, 106.9		
No. of cumulative deprivation experiences				
1	99.9	98.8, 101.0		
2	98.4	95.6, 101.1		
≥3	98.8	96.0, 101.7		
≥1	99.2	98.1, 100.3	-2.32	-3.43, -1.21
0	101.5	100.4, 102.6		
No. of cumulative total adversities				
1	99.9	98.7, 101.0		
2	97.6	92.5, 102.7		
≥3	98.6	96.8, 100.4		
≥1	99.8	98.7, 100.9	-2.02	-3.09, -0.94
0	101.8	100.7, 102.9		

Table 1. Targeted Maximum Likelihood Estimated Mean Scores on the Kaufman Brief Intelligence Test in the Presence Versus Absence of Individual and Cumulative Childhood Adversities Among a Representative Sample of Adolescents (n = 10,073), United States, 2001–2004

Abbreviations: CI, confidence interval; HS, high school; K-BIT, Kaufman Brief Intelligence Test.

^a Adjusted for age, number of siblings, birth order, sex, race, parent birthplace, any parent psychiatric disorder, and any parent substance-use disorder.

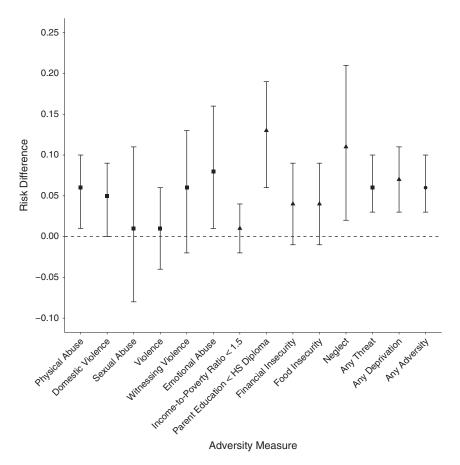


Figure 2. Targeted maximum likelihood estimated differences in the risk of low versus average scores on the Kaufman Brief Intelligence Test (K-BIT) in the presence versus absence of childhood adversities among a representative sample of 10,073 adolescents in the United States, 2001–2004. Square, threat-type adversities; triangle, deprivation-type adversities; circle, any adversity. HS, high school.

either decreased cognitive stimulation and environmental complexity or increased stress (70). Environmental complexity includes exposure to social, perceptual, and linguistic stimulation, as well as opportunities for varied activities (71). This type of stimulation has consistently been shown to be reduced in children raised in low-SES environments and/or exposed to neglect (36, 68, 72). The absence of these expected inputs has been shown to influence neural development throughout the cortex, including the development of frontoparietal systems involved in executive functioning and frontotemporal networks underlying language (35, 37, 38, 73), which in turn may adversely affect systems for working memory, cognitive control, and language processing (74). Additionally, children raised in low-SES families face greater exposure to chronic stress (75). Chronic stress has been shown to damage hippocampal neurons and lead to reductions in hippocampal volume in animal models as well as in observational studies of children exposed to adversity (26-28). The hippocampus is centrally involved in learning and memory (76, 77), and altered structure and function of this region may ultimately contribute to reduced cognitive ability. Extensive evidence from decades of work in behavioral and molecular genetics has demonstrated substantial genetic effects on cognitive ability and intelligence (78-80). While we could not directly examine genetic pathways, we did investigate the impact of adjusting our models for parental education as a proxy for these pathways. Our results are consistent with studies that identified parental education as a predictor of more proximate threat-type adversities (57, 81).

Existing evidence is also quite consistent in demonstrating that while genetics plays a large role in shaping variability in cognitive ability, the environment also plays a meaningful role. For example, interventions that alter the environment have been shown to have strong influences on children's cognitive ability. Substantial increases in intelligence were observed among children randomized to be removed from a deprived institutional setting and raised in a high-quality family environment as compared with children randomized to remain in institutional care (30). These findings are consistent with experimental evidence from the United States demonstrating that placement into high-quality child care early in life for children from socioeconomically disadvantaged family backgrounds produces lasting improvements in cognitive ability and academic achievement (82, 83). The experimental design of these studies provides strong evidence for environmentally mediated effects of cognitive enrichment and stimulation on intelligence in children, particularly early in development. It is this environmental component that our research addresses. In particular, it suggests that environmental experiences

Adversity Type	K-BIT Score <85 With Exposure ^{a,b}	K-BIT Score <85 Without Exposure ^{a,c}	RD	95% CI
Threat adversities				
Physical abuse	0.29	0.23	0.06	0.01, 0.10
Domestic violence	0.25	0.20	0.05	0.00, 0.09
Sexual abuse	0.25	0.23	0.01	-0.08, 0.11
Violence	0.22	0.21	0.01	-0.04, 0.06
Witnessing violence	0.28	0.23	0.06	-0.02, 0.13
Emotional abuse	0.31	0.23	0.08	0.01, 0.16
No. of cumulative threat-experience adversities				
1	0.28	0.22	0.06	0.02, 0.10
2	0.28	0.23	0.05	-0.01, 0.11
≥3	0.29	0.25	0.04	-0.03, 0.11
≥1	0.24	0.18	0.06	0.03, 0.10
Deprivation adversities				
Income-to-poverty ratio < 1.5	0.23	0.22	0.01	-0.02, 0.04
Parental education < HS diploma	0.35	0.22	0.13	0.06, 0.19
Financial insecurity	0.28	0.24	0.04	-0.01, 0.09
Food insecurity	0.27	0.23	0.04	-0.01, 0.09
Neglect	0.34	0.22	0.11	0.02, 0.21
No. of cumulative deprivation- experience adversities				
1	0.26	0.23	0.03	-0.01, 0.07
2	0.33	0.22	0.11	0.02, 0.20
≥3	0.35	0.25	0.10	0.03, 0.18
≥1	0.28	0.21	0.07	0.03, 0.11
No. of cumulative total adversities				
1	0.26	0.24	0.02	-0.02, 0.07
2	0.35	0.17	0.18	-0.02, 0.38
≥3	0.29	0.22	0.07	0.03, 0.12
≥1	0.26	0.20	0.06	0.03, 0.10

Table 2. Targeted Maximum Likelihood Estimated Risk Differences for the Risk of Low (<85) Versus Average (\geq 100) Score on the Kaufman Brief Intelligence Test, Under Individual and Cumulative Adversities Compared With the Risk Absent That Exposure in a Representative Sample of Adolescents (n = 10,073), United States, 2001–2004

Abbreviations: CI, confidence interval; HS, high school; K-BIT, Kaufman Brief Intelligence Test; RD, risk difference. ^a Adjusted for age, number of siblings, birth order, sex, race, parent birthplace, any parent psychiatric disorder, and any parent substance-use disorder.

^b The risk of a K-BIT of <85, given exposure to each adversity.

^c The risk of a K-BIT of <85, given no exposure to each adversity.

of deprivation influence cognitive ability, likely due to reductions in the degree of cognitive stimulation that children receive early in life, including lower levels of exposure to complex language, learning opportunities within the home and in early schooling, and consistent interactions with caregivers and adults (68, 71, 84–88). Indeed, prior work from genetically informed samples indicates that family SES primarily influences environmentally mediated effects on cognitive ability (89).

Though smaller in magnitude, several threat experiences were also significantly related to lower intelligence. These exposures may affect intelligence through physiological responses to the stress and fear that results from direct and indirect threat experiences (90–92). Responses may cause sleep disturbances, increased anxiety, difficulty in maintaining awareness and concentration, and other symptoms of posttraumatic stress disorder (93–95), all of which may lead to impaired cognitive performance (96, 97). These effects have been shown even among those with more indirect threat experiences, such as witnessing violence (21).

The results of this study should be interpreted in the light of several limitations. Study data are cross-sectional, which limits the ability to assign temporality and may affect the recall of adversity experiences. However, because the data are from an adolescent sample, the period of recall was relatively short, which we expect to mitigate any significant effects of recall bias. Also, we were unable to examine differences in the timing, duration, and intensity of the adversities. Further research might consider these temporal effects, including cognitive deficits that occurred prior to childhood adversity, in more detail (98). While parameter estimates were adjusted for a number of known confounders, there may be unmeasured confounding and exchangeability violations. For example, poverty and low SES are often perpetuated by additional experiences that may themselves affect adolescent intelligence, such as physical health and exposure to environmental toxins (99). These exposures were not measured in the National Comorbidity Survey Adolescent Supplement. While we do not believe that such exposures would fully explain the relationship between fluid reasoning and such a broad array of adversities, they should be considered in future replication studies. Finally, adolescents who experienced adversities may show decreased effort during K-BIT administration (100), especially given that the testing was performed by lay interviewers. While these testing effects should be considered in addition to any differences in true cognitive ability, the K-BIT has been validated in children with intellectual disability and other challenges, (101-103), and the test reliability was comparable for the present sample and the standardization sample.

Due to the complex nature of childhood adversity, methodological approaches, such as TMLE, to study its effects are needed. Although interpretations using a causal inference framework rely on previously described assumptions, the results of this study suggest that the prevention of childhood adversity would improve the cognitive functioning of a general population of adolescents. The normal distribution of intelligence in a population shifts upward over time, at a rate of approximately 3 points every 10 years (104), a phenomenon known as the Flynn effect (51, 105). The results of this study highlight how individuals who have experienced adversity are being left behind in typical cognitive development compared with their counterparts who did not experience adversity.

Interventions attempting to support and improve cognition in individuals who report childhood adversity can be a useful complement to interventions for emotional and behavioral disturbances (106, 107). Fortunately, there is evidence that interventions to improve the developmental environment lead to cognitive recovery in children (108, 109). This study adds further support for these relationships, and estimates the relationships between specific deprivation and threat adversities and childhood intelligence.

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REFERENCES

- 1. Shonkoff JP, Garner AS, Committee on Psychosocial Aspects of Child and Family Health, et al. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*. 2012;129(1): e232–e246.
- McLaughlin KA. Future directions in childhood adversity and youth psychopathology. *J Clin Child Adolesc Psychol*. 2016; 45(3):361–382.
- 3. Almas AN, Degnan KA, Radulescu A, et al. Effects of early intervention and the moderating effects of brain activity on institutionalized children's social skills at age 8. *Proc Natl Acad Sci USA*. 2012;109(suppl 2):17228–17231.
- Dodge KA, Pettit GS, Bates JE, et al. Social informationprocessing patterns partially mediate the effect of early physical abuse on later conduct problems. *J Abnorm Psychol*. 1995;104(4):632–643.
- 5. Cicchetti D, Toth SL. A developmental psychopathology perspective on child abuse and neglect. *J Am Acad Child Adolesc Psychiatry*. 1995;34(5):541–565.
- Turner HA, Butler MJ. Direct and indirect effects of childhood adversity on depressive symptoms in young adults. *J Youth Adolesc*. 2003;32(2):89–103.
- Carrey NJ, Butter HJ, Persinger MA, et al. Physiological and cognitive correlates of child abuse. J Am Acad Child Adolesc Psychiatry. 1995;34(8):1067–1075.
- Liaw F, Brooks-Gunn J. Cumulative familial risks and lowbirthweight children's cognitive and behavioral development. *J Clin Child Psychol*. 1994;23(4):360–372.
- Noble KG, McCandliss BD, Farah MJ. Socioeconomic gradients predict individual differences in neurocognitive abilities. *Dev Sci*. 2007;10(4):464–480.
- Neisser U, Boodoo G, Bouchard TJ Jr, et al. Intelligence: knowns and unknowns. *Am Psychol.* 1996;51(2):77–101.
- 11. Sternberg RJ. *Handbook of Intelligence*. New York, NY: Cambridge University Press; 2000.
- Schneider W, McGrew K. The Cattell-Horn-Carroll model of intelligence. In: Flanagan DP, Harrison PL, eds. *Contemporary Intellectual Assessment: Theories, Tests, and Issues.* New York, NY: Guilford Press; 2012:99–144.
- 13. Cattell RB. Intelligence: Its Structure, Growth and Action. New York, NY: Elsevier; 1987.
- Benson NF, Kranzler JH, Floyd RG. Examining the integrity of measurement of cognitive abilities in the prediction of achievement: comparisons and contrasts across variables from higher-order and bifactor models. *J Sch Psychol.* 2016; 58:1–19.
- Keyes KM, Platt J, Kaufman AS, et al. Association of fluid intelligence and psychiatric disorders in a populationrepresentative sample of US adolescents. *JAMA Psychiatry*. 2017;74(2):179–188.

- 16. Leiter J, Johnsen MC. Child maltreatment and school performance. *Am J Educ*. 1994;102(2):154–189.
- Sameroff AJ, Seifer R, Barocas R, et al. Intelligence quotient scores of 4-year-old children: social-environmental risk factors. *Pediatrics*. 1987;79(3):343–350.
- Trickett PK. Maladaptive development of school-aged, physically abused children: relationships with the childrearing context. *J Fam Psychol*. 1993;7(1):134–147.
- Trickett PK, McBride-Chang C, Putnam FW. The classroom performance and behavior of sexually abused females. *Dev Psychopathol.* 1994;6(1):183–194.
- 20. Koenen KC, Moffitt TE, Caspi A, et al. Domestic violence is associated with environmental suppression of IQ in young children. *Dev Psychopathol*. 2003;15(2):297–311.
- Sharkey P. The acute effect of local homicides on children's cognitive performance. *Proc Natl Acad Sci USA*. 2010; 107(26):11733–11738.
- McLaughlin KA, Sheridan MA, Lambert HK. Childhood adversity and neural development: deprivation and threat as distinct dimensions of early experience. *Neurosci Biobehav Rev.* 2014;47:578–591.
- 23. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med.* 1998;338(3):171–179.
- 24. McEwen BS. Brain on stress: how the social environment gets under the skin. *Proc Natl Acad Sci USA*. 2012;109(suppl 2):17180–17185.
- Dannlowski U, Stuhrmann A, Beutelmann V, et al. Limbic scars: long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. *Biol Psychiatry*. 2012;71(4):286–293.
- Hanson JL, Nacewicz BM, Sutterer MJ, et al. Behavioral problems after early life stress: contributions of the hippocampus and amygdala. *Biol Psychiatry*. 2015;77(4): 314–323.
- McLaughlin KA, Sheridan MA, Gold AL, et al. Maltreatment exposure, brain structure, and fear conditioning in children and adolescents. *Neuropsychopharmacology*. 2016;41(8): 1956–1964.
- Teicher MH, Anderson CM, Polcari A. Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum. *Proc Natl Acad Sci USA*. 2012;109(9):E563–E572.
- 29. Lupien SJ, McEwen BS, Gunnar MR, et al. Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat Rev Neurosci.* 2009;10(6):434–445.
- Nelson CA 3rd, Zeanah CH, Fox NA, et al. Cognitive recovery in socially deprived young children: the Bucharest Early Intervention Project. *Science*. 2007;318(5858): 1937–1940.
- Tibu F, Sheridan MA, McLaughlin K, et al. Disruptions of working memory and inhibition mediate the association between exposure to institutionalization and symptoms of attention deficit hyperactivity disorder. *Psychol Med.* 2016; 46(3):529–541.
- 32. Tottenham N, Hare TA, Millner A, et al. Elevated amygdala response to faces following early deprivation. *Dev Sci.* 2011; 14(2):190–204.
- Windsor J, Benigno JP, Wing CA, et al. Effect of foster care on young children's language learning. *Child Dev.* 2011; 82(4):1040–1046.
- Hackman DA, Farah MJ. Socioeconomic status and the developing brain. *Trends Cogn Sci.* 2009;13(2):65–73.
- Noble KG, Houston SM, Brito NH, et al. Family income, parental education and brain structure in children and adolescents. *Nat Neurosci*. 2015;18(5):773–778.

- McLaughlin KA, Sheridan MA, Nelson CA. Neglect as a violation of species-expectant experience: neurodevelopmental consequences. *Biol Psychiatry*. 2017; 82(7):462–471.
- Mackey AP, Finn AS, Leonard JA, et al. Neuroanatomical correlates of the income-achievement gap. *Psychol Sci.* 2015; 26(6):925–933.
- McLaughlin KA, Sheridan MA, Winter W, et al. Widespread reductions in cortical thickness following severe early-life deprivation: a neurodevelopmental pathway to attentiondeficit/hyperactivity disorder. *Biol Psychiatry*. 2014;76(8): 629–638.
- Perez CM, Widom CS. Childhood victimization and longterm intellectual and academic outcomes. *Child Abuse Negl*. 1994;18(8):617–633.
- Green JG, McLaughlin KA, Berglund PA, et al. Childhood adversities and adult psychiatric disorders in the National Comorbidity Survey replication I: associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry*. 2010;67(2): 113–123.
- McLaughlin KA, Greif Green J, Gruber MJ, et al. Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. *Arch Gen Psychiatry*. 2012; 69(11):1151–1160.
- Kessler RC, McLaughlin KA, Green JG, et al. Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *Br J Psychiatry*. 2010;197(5): 378–385.
- 43. Open Science Collaboration. Estimating the reproducibility of psychological science. *Science*. 2015;349(6251):aac4716.
- 44. van der Laan M, Rose S. *Targeted Learning: Causal Inference for Observational and Experimental Data*. Berlin, Germany: Springer Science & Business Media; 2011.
- Merikangas K, Avenevoli S, Costello J, et al. National Comorbidity Survey replication adolescent supplement (NCS-A): I. Background and measures. J Am Acad Child Adolesc Psychiatry. 2009;48(4):367–369.
- Kessler RC, Avenevoli S, Costello EJ, et al. National Comorbidity Survey replication adolescent supplement (NCS-A): II. Overview and design. J Am Acad Child Adolesc Psychiatry. 2009;48(4):380–385.
- 47. Kessler RC, Avenevoli S, Costello EJ, et al. Design and field procedures in the US National Comorbidity Survey Replication Adolescent Supplement (NCS-A). *Int J Methods Psychiatr Res.* 2009;18(2):69–83.
- Kessler RC, Avenevoli S, Green J, et al. National Comorbidity Survey replication adolescent supplement (NCS-A): III. Concordance of DSM-IV/CIDI diagnoses with clinical reassessments. J Am Acad Child Adolesc Psychiatry. 2009;48(4):386–399.
- Kaufman AS, Kaufman NL. K-BIT: Kaufman Brief Intelligence Test Manual. Circle Pines, MN: American Guidance Service; 1990.
- 50. Kaufman AS, Wang J-J. Gender, race, and education differences on the K-BIT at ages 4 to 90 years. *J Psychoeduc Assess*. 1992;10(3):219–229.
- 51. Flynn JR. The mean IQ of Americans: massive gains 1932 to 1978. *Psychol Bull*. 1984;95(1):29–51.
- 52. Weiss LG. Considerations on the Flynn effect. *J Psychoeduc Assess*. 2010;28(5):482–493.
- 53. Kaufman AS, Lichtenberger EO. *Assessing Adolescent* and Adult Intelligence. Hoboken, NJ: John Wiley & Sons; 2005.
- 54. Lichtenberger EO, Kaufman AS. *Essentials of WAIS-IV* Assessment. Hoboken, NJ: John Wiley & Sons; 2009.

- Dunn TJ, Baguley T, Brunsden V. From alpha to omega: a practical solution to the pervasive problem of internal consistency estimation. *Br J Psychol.* 2014;105(3):399–412.
- 56. Kessler RC, Ustün TB. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res.* 2004;13(2):93–121.
- 57. Sidebotham P, Golding J, ALSPAC Study Team. Child maltreatment in the "Children of the Nineties": a longitudinal study of parental risk factors. *Child Abuse Negl.* 2001;25(9): 1177–1200.
- 58. van der Laan MJ, Polley EC, Hubbard AE. Super learner. *Stat Appl Genet Mol Biol*. 2007;6(1):Article 25.
- 59. Hastie TJ, Tibshirani RJ. *Generalized Additive Models*. Boca Raton, FL: CRC press; 1990.
- Hovakimyan N, Nardi F, Calise A, et al. Adaptive output feedback control of uncertain nonlinear systems using singlehidden-layer neural networks. *IEEE Trans Neural Netw.* 2002;13(6):1420–1431.
- Gruber S, van der Laan MJ. tmle: an R package for targeted maximum likelihood estimation. *J Stat Softw.* 2013;51(13): 1–35.
- 62. Polley E, van der Laan M. *SuperLearner: Super Learner Prediction, Package Version 2.0-4.* Vienna, Austria: R Foundation for Statistical Computing; 2011.
- Imbens GW, Rubin DB. Causal Inference in Statistics, Social, and Biomedical Sciences. New York, NY: Cambridge University Press; 2015.
- 64. van der Laan MJ, Haight TJ, Tager IB. van der Laan et al. respond to "hypothetical interventions to define causal effects." *Am J Epidemiol.* 2005;162(7):621–622.
- Petersen ML, Porter KE, Gruber S, et al. Diagnosing and responding to violations in the positivity assumption. *Stat Methods Med Res.* 2012;21(1):31–54.
- Petersen ML, van der Laan MJ. Causal models and learning from data: integrating causal modeling and statistical estimation. *Epidemiology*. 2014;25(3):418–426.
- 67. Baydar N, Brooks-Gunn J, Furstenberg FF. Early warning signs of functional illiteracy: predictors in childhood and adolescence. *Child Dev.* 1993;64(3):815–829.
- Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annu Rev Psychol*. 2002;53:371–399.
- Westreich D, Lessler J, Funk MJ. Propensity score estimation: machine learning and classification methods as alternatives to logistic regression. *J Clin Epidemiol*. 2010; 63(8):826–833.
- Farah MJ, Shera DM, Savage JH, et al. Childhood poverty: specific associations with neurocognitive development. *Brain Res.* 2006;1110(1):166–174.
- Bradley RH, Corwyn RF, McAdoo HP, et al. The home environments of children in the United States part I: Variations by age, ethnicity, and poverty status. *Child Dev*. 2001;72(6):1844–1867.
- Adams BN. *The Family: A Sociological Interpretation*. 4th ed. New York, NY: Harcourt; 1998.
- Noble KG, Houston SM, Kan E, et al. Neural correlates of socioeconomic status in the developing human brain. *Dev Sci.* 2012;15(4):516–527.
- McLaughlin KA, Sheridan MA. Beyond cumulative risk: a dimensional approach to childhood adversity. *Curr Dir Psychol Sci.* 2016;25(4):239–245.
- Dohrenwend BS, Dohrenwend BP. Stressful Life Events: Their Nature and Effects. New York, NY: John Wiley & Sons; 1974.

- McClelland JL, McNaughton BL, O'Reilly RC. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol Rev.* 1995;102(3):419–457.
- Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol Rev.* 1992; 99(2):195–231.
- Deary IJ, Spinath FM, Bates TC. Genetics of intelligence. Eur J Hum Genet. 2006;14(6):690–700.
- Plomin R, Deary IJ. Genetics and intelligence differences: five special findings. *Mol Psychiatry*. 2015; 20(1):98–108.
- 80. Plomin R, Spinath FM. Intelligence: genetics, genes, and genomics. *J Pers Soc Psychol*. 2004;86(1):112–129.
- Brown J, Cohen P, Johnson JG, et al. A longitudinal analysis of risk factors for child maltreatment: findings of a 17-year prospective study of officially recorded and self-reported child abuse and neglect. *Child Abuse Negl.* 1998;22(11): 1065–1078.
- 82. Ramey CT, Campbell FA, Burchinal M, et al. Persistent effects of early childhood education on high-risk children and their mothers. *Appl Dev Sci*. 2000;4(1):2–14.
- Campbell FA, Ramey CT, Pungello E, et al. Early childhood education: young adult outcomes from the Abecedarian Project. *Appl Dev Sci*. 2002;6(1):42–57.
- Crosnoe R, Leventhal T, Wirth RJ, et al. Family socioeconomic status and consistent environmental stimulation in early childhood. *Child Dev.* 2010;81(3): 972–987.
- Garrett P, Ng'andu N, Ferron J. Poverty experiences of young children and the quality of their home environments. *Child Dev.* 1994;65(2 Spec No):331–345.
- Hart B, Risley TR. Meaningful Differences in the Everyday Experience of Young American Children. Baltimore, MD: Paul H Brookes Publishing; 1995.
- Linver MR, Brooks-Gunn J, Kohen DE. Family processes as pathways from income to young children's development. *Dev Psychol.* 2002;38(5):719–734.
- Sheridan MA, Sarsour K, Jutte D, et al. The impact of social disparity on prefrontal function in childhood. *PLoS One*. 2012;7(4):e35744.
- 89. Hanscombe KB, Trzaskowski M, Haworth CM, et al. Socioeconomic status (SES) and children's intelligence (IQ): in a UK-representative sample SES moderates the environmental, not genetic, effect on IQ. *PLoS One*. 2012; 7(2):e30320.
- Glaser JP, van Os J, Portegijs PJ, et al. Childhood trauma and emotional reactivity to daily life stress in adult frequent attenders of general practitioners. *J Psychosom Res.* 2006; 61(2):229–236.
- 91. Pollak SD, Cicchetti D, Klorman R, et al. Cognitive brain event-related potentials and emotion processing in maltreated children. *Child Dev.* 1997;68(5):773–787.
- Jamieson JP, Nock MK, Mendes WB. Mind over matter: reappraising arousal improves cardiovascular and cognitive responses to stress. *J Exp Psychol Gen.* 2012;141(3): 417–422.
- Martinez P, Richters JE. The NIMH community violence project: II. Children's distress symptoms associated with violence exposure. *Psychiatry*. 1993;56(1):22–35.
- 94. Horowitz K, Weine S, Jekel J. PTSD symptoms in urban adolescent girls: compounded community trauma. *J Am Acad Child Adolesc Psychiatry*. 1995;34(10):1353–1361.

- 95. Pynoos RS, Frederick C, Nader K, et al. Life threat and posttraumatic stress in school-age children. *Arch Gen Psychiatry*. 1987;44(12):1057–1063.
- Saltzman KM, Weems CF, Carrion VG. IQ and posttraumatic stress symptoms in children exposed to interpersonal violence. *Child Psychiatry Hum Dev*. 2006;36(3):261–272.
- De Bellis MD, Keshavan MS, Clark DB, et al. A.E. Bennett Research Award. Developmental traumatology. Part II: Brain development. *Biol Psychiatry*. 1999;45(10):1271–1284.
- Danese A, Moffitt TE, Arseneault L, et al. The origins of cognitive deficits in victimized children: implications for neuroscientists and clinicians. *Am J Psychiatry*. 2017;174(4): 349–361.
- 99. Evans GW, Kantrowitz E. Socioeconomic status and health: the potential role of environmental risk exposure. *Annu Rev Public Health*. 2002;23:303–331.
- Scult MA, Paulli AR, Mazure ES, et al. The association between cognitive function and subsequent depression: a systematic review and meta-analysis. *Psychol Med.* 2017;47(1):1–17.
- Canivez GL. Validity and diagnostic efficiency of the Kaufman Brief Intelligence Test in reevaluating students with learning disability. *J Psychoeduc Assess*. 1996;14(1):4–19.
- 102. Mervis CB, Kistler DJ, John AE, et al. Longitudinal assessment of intellectual abilities of children with Williams syndrome: multilevel modeling of performance on the

Kaufman Brief Intelligence Test—Second Edition. *Am J Intellect Dev Disabil.* 2012;117(2):134–155.

- 103. Webber LS, McGillivray JA. An Australian validation of the Kaufman Brief Intelligence Test (K-BIT) with adolescents with an intellectual disability. *Aust Psychol.* 1998;33(3): 234–237.
- Flynn JR. Wechsler Intelligence Tests: do we really have a criterion of mental retardation?. *Am J Ment Defic*. 1985;90(3): 236–244.
- 105. McGrew K. Norm obsolescence: the Flynn effect. In: Polloway E, ed. *The Death Penalty and Intellectual Disability*. Washington, DC: American Association on Intellectual and Developmental Disabilities; 2015;155–169.
- 106. Millan MJ, Agid Y, Brüne M, et al. Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nat Rev Drug Discov*. 2012;11(2): 141–168.
- 107. Harvey AG, Lee J, Williams J, et al. Improving outcome of psychosocial treatments by enhancing memory and learning. *Perspect Psychol Sci.* 2014;9(2):161–179.
- Jackson MI. Early childhood WIC participation, cognitive development and academic achievement. *Soc Sci Med.* 2015; 126:145–153.
- 109. Duncan GJ, Brooks-Gunn J. Family poverty, welfare reform, and child development. *Child Dev.* 2000;71(1):188–196.