The Origins of Cognitive Deficits in Victimized Children: Implications for Neuroscientists and Clinicians

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Objective: Individuals reporting a history of childhood violence victimization have impaired brain function. However, the clinical significance, reproducibility, and causality of these findings are disputed. The authors used data from two large cohort studies to address these research questions directly.

Method: The authors tested the association between prospectively collected measures of childhood violence victimization and cognitive functions in childhood, adolescence, and adulthood among 2,232 members of the U.K. E-Risk Study and 1,037 members of the New Zealand Dunedin Study who were followed up from birth until ages 18 and 38 years, respectively. Multiple measures of victimization and cognition were used, and comparisons were made of cognitive scores for twins discordant for victimization.

Results: Individuals exposed to childhood victimization had pervasive impairments in clinically relevant cognitive functions, including general intelligence, executive function, processing speed, memory, perceptual reasoning, and verbal comprehension in adolescence and adulthood. However, the observed cognitive deficits in victimized individuals were largely explained by cognitive deficits that predated childhood victimization and by confounding genetic and environmental risks.

Conclusions: Findings from two population-representative birth cohorts totaling more than 3,000 individuals and born 20 years and 20,000 km apart suggest that the association between childhood violence victimization and later cognition is largely noncausal, in contrast to conventional interpretations. These findings support the adoption of a more circumspect approach to causal inference in the neuroscience of stress. Clinically, cognitive deficits should be conceptualized as individual risk factors for victimization as well as potential complicating features during treatment.

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Individuals reporting a history of childhood violence victimization have impaired brain function (1–4). It is biologically plausible that exposure to extreme stressors, such as violence victimization, might harm brain function (5), particularly during periods of enhanced developmental plasticity (1). However, the interpretation and implications of these findings continue to fuel debate in neuroscience (6–8), clinical psychiatry (9, 10), and social policy (11, 12) because of unanswered questions about clinical significance, reproducibility, and causal inference.

With regard to *clinical significance*, it is unclear whether research findings reflect clinically relevant impairment of brain function in victimized children. This is unclear because neuroimaging methods that have been used to describe structural and functional brain differences in victimized individuals have, at present, only limited ability to predict everyday functioning and clinical outcomes (13). Neuropsychological assessments have greater reliability and predictive value (14, 15) and have shown that individuals with a history of childhood victimization have deficits in general intelligence and more specialized cognitive functions (16, 17). However, the origins of such cognitive deficits are unclear.

With regard to *reproducibility*, it is unclear whether research findings reflect the effects of child victimization in the general population. This is unclear because sampling for research studies is often done in convenience groups (e.g., students answering research study advertisements) or extreme groups (e.g., postinstitutionalized young people), and on a small scale. While these sampling strategies can be easily implemented, they may lead to nonreproducible results (18). Studies undertaken in selected samples may lead to nongeneralizable results that are conditional on sample-specific characteristics (low external validity) (19). Studies undertaken in small samples may produce spurious positive results (type II error) (20).

With regard to *causality*, it is unclear whether correlational findings from observational studies reflect causal effects

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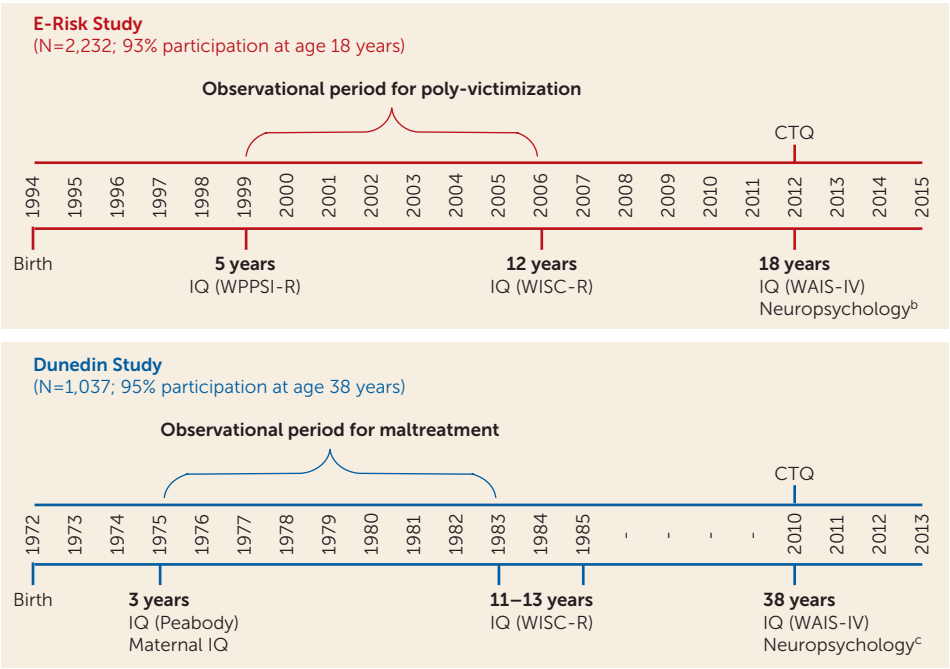
FIGURE 1. Timeline for Assessments of Childhood Victimization and Cognitive Functioning in the E-Risk Study and the Dunedin Study[a]



[a] CTQ=Childhood Trauma Questionnaire; Peabody=Peabody Picture Vocabulary Test; WAIS-IV=Wechsler Adult Intelligence Scale, 4th edition; WISC-R=Wechsler Intelligence Scale for Children–Revised; WPPSI-R=Wechsler Preschool and Primary Scale of Intelligence–Revised.
[b] Executive function (Cambridge Neuropsychological Test Automated Battery [CANTAB]) and processing speed (CANTAB).
[c] Executive function (CANTAB, WAIS-IV, Wechsler Memory Scale–III [WMS-III], Trail Making Test, part B), processing speed (CANTAB, WAIS-IV), memory (CANTAB, WMS-III, Rey Auditory Verbal Learning Test), perceptual reasoning (WAIS-IV), and verbal comprehension (WAIS-IV).

of child victimization on later brain function. This is unclear because victimized children often have preexisting impairment in brain function and live in disadvantaged socioeconomic conditions (21). Both factors provide alternative explanations for observed differences in brain function between victimized and nonvictimized individuals (22, 23). Ruling out the effects of these confounding factors is necessary in order to infer causal effects of child victimization (24, 25). However, this has been difficult to achieve because research designs are typically cross-sectional, rely on retrospective recall of childhood victimization, and are limited to measurement of brain function at a single point in time in adolescence or adult life.

We addressed these questions directly in this study. To understand the clinical significance of deficits in brain function associated with childhood victimization, we tested whether victimized children showed later global deficits in IQ or specific deficits in a wide range of cognitive functions associated with clinical and functional outcomes (14, 15, 26, 27). To ensure reproducibility of these observations, we tested whether the results were consistent across a range of prospectively collected and validated measures of childhood victimization (28, 29) (including both broad poly-victimization [30] and specific types of victimization), across repeated cognitive assessments in childhood, adolescence, and adulthood (26), and across two large population-representative cohorts in the United Kingdom and New Zealand. Finally, to generate information about causality, we took advantage of three methodological features—repeated cognitive assessments of study members and their parents since before victimization, prospectively collected information about family circumstances, and a twin-difference design—to test the alternative hypothesis that the associations between childhood victimization and later cognitive deficits have their origins in preexisting and stable cognitive vulnerabilities and in confounding familial influences.

METHOD

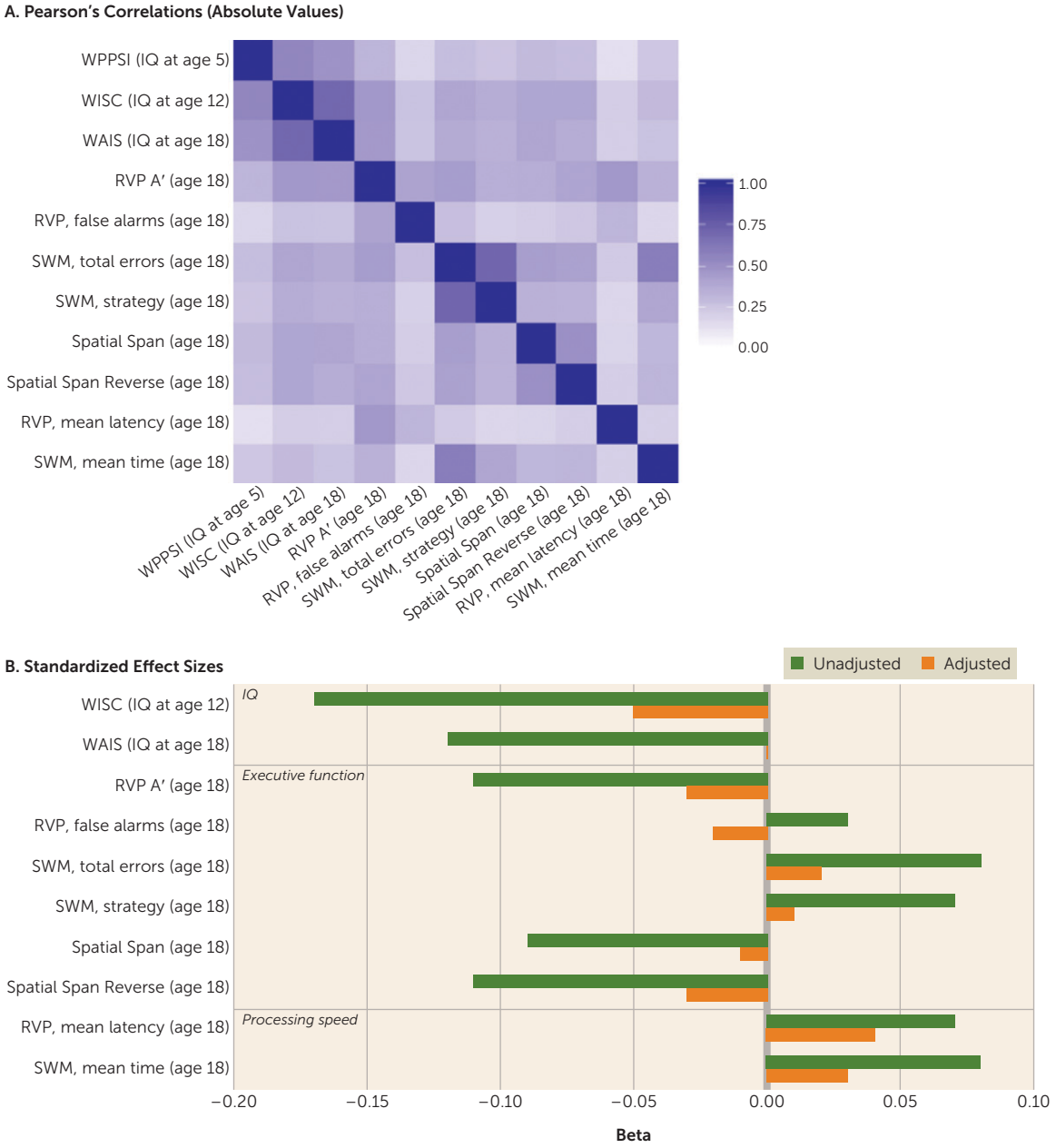
Study 1: The Environmental-Risk Longitudinal Twin Study

Sample. Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a birth cohort of 2,232 British children (Figure 1). Full details about the sample have been reported elsewhere (31) and can be found in the data supplement that accompanies the online edition of this article.

Childhood poly-victimization. Exposure to several types of victimization was assessed repeatedly when the children were 5, 7, 10, and 12 years of age, and dossiers have been compiled for each child with cumulative information about exposure to domestic violence between the mother and her partner, frequent bullying by peers, physical maltreatment by an adult, sexual abuse, emotional abuse, and physical neglect. Following Finkelhor et al. (30), for each child, our cumulative index counts the types of victimization experienced during the first 12 years of life. Details about these measurements have been reported previously (29). In addition to the above prospective measures of victimization, we assessed recall of victimization through the Childhood Trauma Questionnaire (32), completed by study members at the age-18 follow-up. Details about the victimization measurements are available in the online data supplement.

Cognitive testing. Figure 1 provides an overview of the cognitive testing in the E-Risk Study at ages 5, 12, and 18. Figure 2A provides a correlation matrix for all cognitive tests. Details are provided in the data supplement.

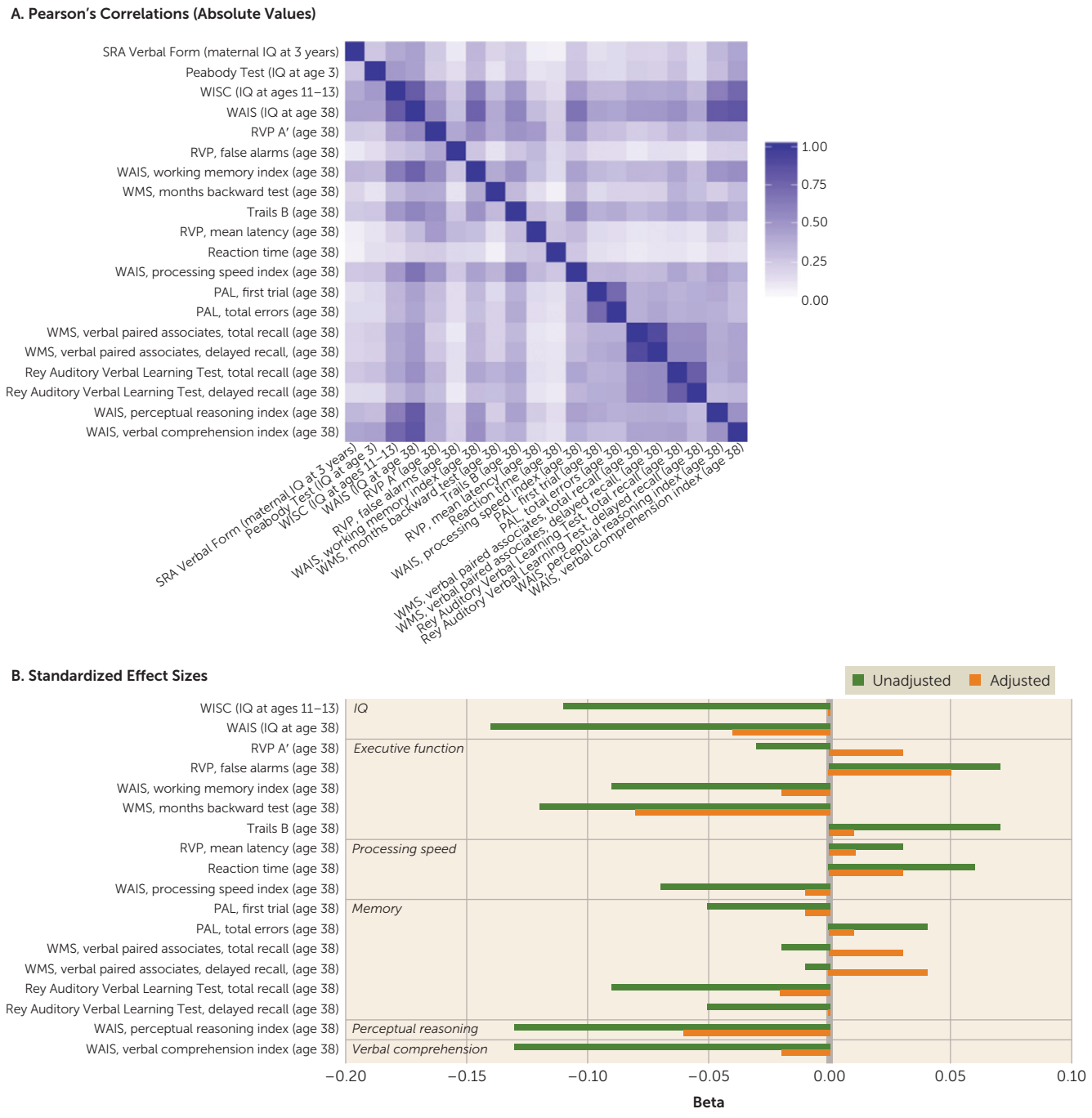
FIGURE 2. Association Between Childhood Victimization and Cognitive Functioning in the E-Risk Study[a]



[a] Panel A is a heat map displaying the absolute values of correlations across cognitive functions in the E-Risk Study. Darker pixels indicate stronger absolute values of correlations, and lighter pixels indicate weaker correlations. Exact correlation values are reported in Table S13 in the online data supplement. Panel B shows standardized effect sizes (beta coefficients) for the association between childhood victimization and different cognitive functions. Green bars indicate unadjusted associations, and orange bars indicate associations adjusted for cognitive functioning prior to the observational period for victimization (IQ at age 5) and family socioeconomic status. RVP=Cambridge Neuropsychological Test Automated Battery (CANTAB) Rapid Visual Processing; Spatial Span=CANTAB Spatial Span; Spatial Span Reverse=CANTAB Spatial Span Reverse; SWM=CANTAB Spatial Working Memory; WAIS=Wechsler Adult Intelligence Scale, 4th edition; WISC=Wechsler Intelligence Scale for Children–Revised; WPPSI=Wechsler Preschool and Primary Scale of Intelligence–Revised.

Statistical analysis. To test the associations between childhood victimization (independent variable) and cognitive measures (dependent variable), we ran a series of bivariate generalized estimating equation (GEE) linear regression models accounting for clustering of twins within families, using SAS, version 9.3 (SAS Institute, Cary, N.C.). To test whether observed associations were accounted for by preexisting cognitive vulnerabilities and nonspecific effects of socioeconomic disadvantage, we expanded the bivariate GEE models to include covariates for IQ at age 5 and family socioeconomic status (see the data supplement), respectively. To test for significant attenuation of the association by these covariates, we compared regression coefficients across models (33). To test whether the results based on the experience of poly-victimization could be generalized to all individual types of victimization, we reran the above analyses using in turn each type of victimization as the independent

FIGURE 3. Association Between Childhood Victimization and Cognitive Functioning in the Dunedin Study[a]



[a] Panel A is a heat map displaying the absolute values of correlations across cognitive functions in the Dunedin Study. Darker pixels indicate stronger absolute values of correlations, and lighter pixels indicate weaker correlations. Exact correlation values are reported in Table S14 in the online data supplement. Panel B shows standardized effect sizes (beta coefficients) for the association between childhood victimization and different cognitive functions. Green bars indicate unadjusted associations, and orange bars indicate associations adjusted for cognitive functioning prior to the observational period for victimization (maternal IQ and Peabody Picture Vocabulary Test at 3 years) and family socioeconomic status. PAL=Cambridge Neuropsychological Test Automated Battery (CANTAB) Paired Associates Learning; Peabody Test=Peabody Picture Vocabulary Test; reaction time=CANTAB reaction time index; RVP=CANTAB Rapid Visual Processing; Trails B=Trail Making Test, part B; WAIS=Wechsler Adult Intelligence Scale, 4th edition; WISC=Wechsler Intelligence Scale for Children–Revised; WMS=Wechsler Memory Scale–III.

variable. To test whether the above results depended on victimization in infancy or toddlerhood, we ran a sensitivity analysis excluding 307 study members with evidence of victimization before age 5. To test whether the association between childhood victimization and cognitive functioning was accounted for by unobserved genetic or environmental heterogeneity, we tested whether differences in cognitive functioning were associated with differences in poly-victimization within pairs of siblings sharing their early family environment and either some (dizygotic twins) or all

(monozygotic twins) genes. Finally, to test whether the results based on the study-specific, prospectively collected measure of maltreatment could be generalized to another more commonly used measure of childhood maltreatment, we reran the above analyses using the score on the retrospective Childhood Trauma Questionnaire as the independent variable. Details are provided in the data supplement.

Study 2: The Dunedin Longitudinal Study

Sample. Participants were members of the Dunedin Longitudinal Study, which tracks a 1972–1973 birth cohort of 1,037 children born in Dunedin, New Zealand (Figure 1). Full details about the sample have been reported elsewhere (34) and can be found in the data supplement.

Childhood victimization. As previously described (28), the measure of childhood maltreatment includes maternal rejection assessed at age 3 by observational ratings of mothers' interactions with the study children, harsh discipline assessed at ages 7 and 9 by parental report of disciplinary behaviors, two or more changes in the child's primary caregiver, and physical abuse and sexual abuse reported by study members once they reached adulthood (and were able to give informed consent). For each child, our cumulative index counts the number of maltreatment indicators during the first decade of life. When study members were 38 years old, they also completed the Childhood Trauma Questionnaire (32). Details about victimization measurements are available in the data supplement.

Cognitive testing. Figure 1 provides an overview of the cognitive testing in the Dunedin study at ages 3, 11–13, and 38. Figure 3A provides a correlation matrix for all cognitive tests. Details are provided in the data supplement.

Statistical analysis. To test the associations between childhood maltreatment (independent variable) and cognitive measures (dependent variable), we ran a series of bivariate ordinary least squares regression models. To test whether observed associations were accounted for by preexisting cognitive vulnerabilities and nonspecific effects of socioeconomic disadvantage (see the data supplement), we expanded the bivariate ordinary least squares models to include covariates for maternal IQ and Peabody Picture Vocabulary Test scores at age 3, and family socioeconomic status, respectively. To test for significant attenuation of the association by these covariates, we compared regression coefficients across models (33). To test whether the results based on the study-specific, prospectively collected measure of maltreatment could be generalized to another more commonly used measure of childhood maltreatment, we reran the above analyses using Childhood Trauma Questionnaire score as the independent variable.

RESULTS

Study 1: The E-Risk Study

Does childhood victimization predict low IQ in adolescence? We first used the E-Risk Study (Figure 1) to test whether child victimization had immediate effects on general intelligence in adolescence. Children who experienced poly-victimization between ages 5 and 12 had lower IQ test scores at age 12 than nonvictimized children (beta=−0.17, $p<0.01$) (Table 1A, model 1). However, these differences were significantly attenuated after preexisting differences in IQ at age 5 and family socioeconomic status were taken into account (beta=−0.05, p=0.02) (Table 1A, model 4; omitted variable bias test, $p<0.001$; Figure 2B).

These findings were replicated in analyses focusing on each of the specific types of victimization (see Tables S1–S7 in the online data supplement). For example, we found lower IQ at age 12 among children in the E-Risk Study who had been physically abused (beta=−0.09, $p<0.01$; Table S3A, model 1) or neglected (beta=−0.14, $p<0.01$; Table S6A, model 1). However, these differences, too, were significantly attenuated after preexisting differences in IQ at age 5 and family socioeconomic status were taken into account (beta=−0.03, p=0.13 and beta=−0.03, p=0.11, respectively; Tables S3A and S6A, model 4).

Does childhood victimization predict low IQ in young adulthood? Next, we tested whether childhood victimization had late-onset ("sleeper") effects on IQ in young adulthood. Children in the E-Risk Study who experienced poly-victimization between ages 5 and 12 had lower IQ at age 18 than nonvictimized children (beta=−0.12, $p<0.01$) (Table 1B, model 1). However, these differences were significantly attenuated after preexisting differences in IQ at age 5 and family socioeconomic status were taken into account (beta=0.00, p=0.82) (Table 1B, model 4; Figure 2B). Similar results emerged when we focused on each of the specific types of victimization (see Tables S1B–S7B in the data supplement).

Does childhood victimization predict impaired cognitive functions in young adulthood? Despite these limited residual effects on a broad measure of cognition, such as IQ, childhood victimization could have affected more specific cognitive functions that are only moderately correlated with IQ (Figure 2A). In particular, executive functions and processing speed hinge on functioning of the prefrontal cortex (35), which continues developing throughout childhood (36) and thus may be more sensitive to the effects of childhood victimization. Therefore, we tested the effects of victimization on these functions.

Children who experienced poly-victimization between ages 5 and 12 performed more poorly on executive function tests at age 18, such as the Cambridge Neuropsychological Test Automated Battery (CANTAB) Rapid Visual Information Processing A′, Spatial Working Memory total errors and strategy, and Spatial Span (Table 1C–H, model 1).

TABLE 1. Association of Childhood Poly-Victimization With IQ and Cognitive Functions in the E-Risk Study[a]

	Model 1			Model 2			Model 3			Model 4			Omitted Variable Bias		
Measure	b_1	SE	p	b_2	SE	p	b_3	SE	p	b_4	SE	p	b_1–b_4	SE	p
IQ															
A. WISC-R (IQ at age 12) (N=2,112)															
Poly-victimization	−0.17	0.02	<0.01	−0.10	0.02	<0.01	−0.09	0.02	<0.01	−0.05	0.02	0.02	−0.13	0.006	<0.01
IQ at age 5	0.45	0.02	<0.01	0.44	0.02	<0.01				0.38	0.02	<0.01			
Family SES	0.43	0.02	<0.01				0.41	0.03	<0.01	0.28	0.02	<0.01			
B. WAIS-IV (IQ at age 18) (N=2,045)															
Poly-victimization	−0.12	0.02	<0.01	−0.05	0.02	0.02	−0.03	0.02	0.13	0.00	0.02	0.82	−0.13	0.005	<0.01
IQ at age 5	0.42	0.02	<0.01	0.41	0.02	<0.01				0.34	0.02	<0.01			
Family SES	0.44	0.02	<0.01				0.43	0.02	<0.01	0.31	0.02	<0.01			
Executive function															
C. Rapid Visual Information Processing A′ (age 18) (N=2,042)															
Poly-victimization	−0.11	0.02	<0.01	−0.05	0.02	0.02	−0.06	0.02	0.02	−0.03	0.02	0.23	−0.08	0.005	<0.01
IQ at age 5	0.30	0.02	<0.01	0.29	0.02	<0.01				0.25	0.02	<0.01			
Family SES	0.25	0.02	<0.01				0.23	0.03	<0.01	0.15	0.03	<0.01			
D. Rapid Visual Information Processing, false alarms (age 18) (N=2,044)															
Poly-victimization	0.03	0.02	0.15	0.00	0.02	0.95	0.00	0.02	0.99	−0.02	0.02	0.46	—	—	—
IQ at age 5	−0.18	0.02	<0.01	−0.18	0.02	<0.01				−0.15	0.02	<0.01			
Family SES	−0.14	0.02	<0.01				−0.14	0.02	<0.01	−0.09	0.03	0.01			
E. Spatial Working Memory, total errors (age 18) (N=2,044)															
Poly-victimization	0.08	0.02	<0.01	0.03	0.02	0.15	0.04	0.03	0.08	0.02	0.02	0.45	0.06	0.006	<0.01
IQ at age 5	−0.26	0.02	<0.01	−0.25	0.02	<0.01				−0.23	0.02	<0.01			
Family SES	−0.18	0.03	<0.01				−0.17	0.03	<0.01	−0.09	0.03	0.01			
F. Spatial Working Memory, strategy (age 18) (N=2,044)															
Poly-victimization	0.07	0.02	<0.01	0.03	0.02	0.24	0.04	0.02	0.15	0.01	0.02	0.62	0.06	0.005	<0.01
IQ at age 5	−0.24	0.02	<0.01	−0.23	0.02	<0.01				−0.21	0.02	<0.01			
Family SES	−0.17	0.02	<0.01				−0.16	0.03	<0.01	−0.09	0.03	0.01			
G. Spatial Span (age 18) (N=2,041)															
Poly-victimization	−0.09	0.02	<0.01	−0.04	0.02	0.13	−0.04	0.02	0.12	−0.01	0.02	0.66	−0.08	0.005	<0.01
IQ at age 5	0.29	0.02	<0.01	0.28	0.02	<0.01				0.24	0.02	<0.01			
Family SES	0.24	0.02	<0.01				0.23	0.03	<0.01	0.14	0.03	<0.01			
H. Spatial Span Reversed (age 18) (N=2,034)															
Poly-victimization	−0.11	0.02	<0.01	−0.06	0.02	0.02	−0.06	0.02	0.02	−0.03	0.02	0.15	−0.07	0.005	<0.01
IQ at age 5	0.26	0.02	<0.01	0.25	0.02	<0.01				0.22	0.02	<0.01			
Family SES	0.22	0.02	<0.01				0.20	0.03	<0.01	0.13	0.03	<0.01			
Processing speed															
I. Rapid Visual Information Processing, mean latency (age 18) (N=2,042)															
Poly-victimization	0.07	0.02	<0.01	0.05	0.02	0.05	0.05	0.02	0.04	0.04	0.02	0.13	0.04	0.006	<0.01
IQ at age 5	−0.14	0.02	<0.01	−0.13	0.02	<0.01				−0.11	0.02	<0.01			
Family SES	−0.11	0.02	<0.01				−0.10	0.02	<0.01	−0.06	0.03	0.02			

continued

TABLE 1, *continued*

Measure	Model 1			Model 2			Model 3			Model 4			Omitted Variable Bias		
	b_1	SE	p	b_2	SE	p	b_3	SE	p	b_4	SE	p	b_1–b_4	SE	p
J. Spatial Working Memory, mean time (age 18) (N=2,044)															
Poly-victimization	0.08	0.02	<0.01	0.03	0.02	0.16	0.05	0.03	0.03	0.03	0.02	0.22	0.05	0.006	<0.01
IQ at age 5	−0.23	0.02	<0.01	−0.23	0.02	<0.01				−0.22	0.02	<0.01			
Family SES	−0.11	0.03	<0.01				−0.10	0.03	<0.01	−0.02	0.03	0.41			

[a] The table lists standardized regression coefficients (betas) for the association between childhood poly-victimization and cognitive measures using generalized estimating equation linear models and accounting for clustering within family. Model 1 presents bivariate (unadjusted) associations between all predictors and the cognitive measures. Model 2 is adjusted for the effect of IQ at age 5, model 3 for the effect of family socioeconomic status (SES), and model 4 for the effect of both IQ at age 5 and family socioeconomic status. "Omitted variable bias" presents the difference between the unadjusted and fully adjusted effect of poly-victimization on the cognitive measures when the unadjusted effects were statistically significant. WAIS-IV=Wechsler Adult Intelligence Scale, 4th edition; WISC-R=Wechsler Intelligence Scale for Children–Revised.

Furthermore, children who experienced poly-victimization performed more poorly on processing speed tests at age 18, such as CANTAB Rapid Visual Information Processing mean latency and Spatial Working Memory mean time (Table 1I–J, model 1). However, these differences were also significantly attenuated after preexisting differences in IQ at age 5 and family socioeconomic status were taken into account (Table 1C–J, model 4; Figure 2B). Similar results emerged when we focused on each of the specific types of victimization (see Tables S1C–J to S7C–J in the data supplement).

Does childhood victimization predict cognitive deficits in those not victimized before age 5? We considered that IQ tested at age 5 could have been influenced by earlier victimization and thus could be an inadequate baseline measure of cognitive function for some children, if they had been victimized early as infants or toddlers. There was evidence of victimization before age 5 for 307 children in the E-Risk Study. In analyses restricted to children without evidence of victimization before age 5, we found results similar to those in the overall sample (see the "omitted variable bias" columns in Table S8 in the data supplement and in Table 1), suggesting that the limited residual effects of childhood victimization on later cognitive functions were not simply a reflection of biased baseline measures of cognition.

Do differences in childhood victimization predict differences in cognitive function within sibling pairs? We also took advantage of the co-twin control method in the E-Risk Study to determine whether differences in poly-victimization were associated with differences in cognitive functions within pairs of twins who grew up in the same family and shared some (dizygotic twins) or all (monozygotic twins) of their genetic material (37). However, we did not find associations between poly-victimization and cognitive functions within sibling pairs except for IQ at age 12 in dizygotic twins (Table 2, and Table S9 in the data supplement), suggesting that the associations observed at the individual level (Table 1A–J, model 1) were likely explained by unmeasured familial (both genetic and environmental) factors.

Are retrospective reports of childhood victimization in young adulthood associated with low IQ and impaired cognitive functions? We extended our analysis to test whether the findings could be replicated when childhood victimization was measured at age 18 with the Childhood Trauma Questionnaire (32), a popular tool for retrospectively assessing childhood maltreatment history in adults. E-Risk Study members who reported having been maltreated as children performed more poorly on executive function tests (Spatial Working Memory total errors, Spatial Span) and processing speed tests (Rapid Visual Information Processing mean latency) but not IQ tests (see Table S10A–J, model 1, in the data supplement). However, these differences were significantly attenuated after preexisting differences in IQ at age 5 and family socioeconomic status were taken into account (see Table S10A–J, model 4). Furthermore, we did not find associations between differences in Childhood Trauma Questionnaire scores and differences in cognitive functions within pairs of siblings (see Table S11 in the data supplement).

Study 2: The Dunedin Study

Does childhood victimization predict low IQ in adolescence? Next, we tested whether the findings in the E-Risk Study could be replicated and expanded in an independent and older cohort. In the Dunedin Study (Figure 1), children who experienced maltreatment between ages 3 and 11 had lower IQ at ages 11–13 than nonmaltreated children (beta=−0.11, p<0.01) (Table 3A, model 1). However, these differences were again significantly attenuated after indicators of preexisting cognitive functioning, such as maternal and child IQ at age 3 and family socioeconomic status, were taken into account (beta=0.00, p=0.89) (Table 3A, model 4, and omitted variable bias test, p<0.01; Figure 3B).

Does childhood victimization predict low IQ in midlife? In the older Dunedin cohort, we tested whether childhood maltreatment exerted long-term "sleeper effects" on IQ into midlife. We found that children exposed to maltreatment between ages 3 and 11 had lower IQ scores at the study's latest assessment, at age 38, than nonmaltreated children (beta=−0.14, p<0.01) (Table 3B, model 1). These differences

TABLE 2. Association of Childhood Poly-Victimization With IQ and Cognitive Functions Within Twin Pairs[a]

	Dizygotic and Monozygotic Twin Pairs (N_{pairs}=1,003–1,061)		Monozygotic Twin Pairs (N_{pairs}=556–578)		Dizygotic Twin Pairs (N_{pairs}=447–483)	
Measure	r	p	r	p	r	p
IQ						
WISC-R (IQ at age 12)	−0.066	0.032	−0.020	0.636	−0.100	0.028
WAIS-IV (IQ at age 18)	−0.020	0.529	−0.066	0.120	0.016	0.737
Executive function						
Rapid Visual Information Processing A′ (at age 18)	−0.045	0.157	−0.039	0.363	−0.051	0.283
Rapid Visual Information Processing, false alarms (at age 18)	−0.021	0.515	−0.024	0.570	−0.016	0.741
Spatial Working Memory, total errors (at age 18)	−0.004	0.891	0.022	0.610	−0.028	0.548
Spatial Working Memory, strategy (at age 18)	−0.009	0.773	0.017	0.685	−0.035	0.458
Spatial Span (at age 18)	0.011	0.724	0.003	0.938	0.017	0.716
Spatial Span Reversed (at age 18)	−0.023	0.477	0.007	0.867	−0.048	0.309
Processing speed						
Rapid Visual Information Processing, mean latency (at age 18)	0.037	0.240	0.059	0.165	0.017	0.713
Spatial Working Memory, mean time (at age 18)	−0.023	0.457	−0.037	0.385	−0.013	0.776

[a] The table lists Pearson correlations between differences in childhood poly-victimization and differences in cognitive measures within twin pairs. WAIS-IV=Wechsler Adult Intelligence Scale, 4th edition; WISC-R=Wechsler Intelligence Scale for Children–Revised.

were significantly attenuated after indicators of preexisting cognitive functioning, such as maternal and child IQ at age 3 and family socioeconomic status, were taken into account (beta=−0.04, p=0.21) (Table 3B, model 4; Figure 3B).

Does childhood victimization predict impaired cognitive functions in midlife? To test more subtle and specific effects of childhood maltreatment on cognition, we used a comprehensive battery of neuropsychological tests, administered at age 38, that are only moderately correlated with IQ (Figure 3A). Children exposed to maltreatment between ages 3 and 11 performed more poorly in midlife on several tests of executive function (CANTAB Rapid Visual Information Processing, false alarms; WAIS working memory index; Wechsler Memory Scale–III, months backward test; Trail Making Test, part B), processing speed (WAIS processing speed index), memory (Rey Auditory Verbal Learning Test, total recall), perceptual reasoning (WAIS perceptual reasoning index), and verbal comprehension (WAIS verbal comprehension index) (Table 3C–R, model 1). These differences were significantly attenuated after indicators of preexisting cognitive functioning, such as maternal and child IQ at age 3 and family socioeconomic status, were taken into account (Table 3C–R, model 4; Figure 3B).

Are reports of childhood victimization in midlife associated with low IQ and impaired cognitive functions? Finally, we extended our analysis to test whether the findings could be replicated when childhood maltreatment was measured retrospectively at age 38 with the Childhood Trauma Questionnaire (32). Study members who reported having been maltreated as children performed more poorly on IQ tests administered in adolescence and midlife and on more specific cognitive tests administered in midlife (see Table S12A–R, model 1, in the data supplement). However, the link between childhood maltreatment and impaired cognitive performance was significantly attenuated after indicators of preexisting cognitive functioning, such as maternal and child IQ at age 3 and family socioeconomic status, were taken into account (see Table S12A–R, model 5).

DISCUSSION

We found that cognitive deficits previously described in individuals with a history of childhood victimization are largely explained by preexisting cognitive vulnerabilities and nonspecific effects of socioeconomic disadvantage. The results both strengthen the evidence for cognitive deficits in individuals with a history of childhood victimization and strongly challenge the conventional causal interpretation.

Consistent with previous research (16, 17), we found that adolescents and adults with a history of childhood victimization have pervasive deficits in clinically significant cognitive functions, including both general intelligence and more specific measures of executive function, processing speed, memory, perceptual reasoning, and verbal comprehension. We observed this in two population-representative birth cohorts totaling 3,000 individuals born 20 years and 20,000 km apart, and we reproduced the findings using multiple measures of victimization and cognitive assessments in childhood, adolescence, and adulthood.

In contrast to the conventional causal interpretation of these findings, our longitudinal prospective design revealed that cognitive deficits in victimized adolescents and adults were largely explained by cognitive deficits present before the observational period for childhood victimization and by

TABLE 3. Association Between Childhood Maltreatment and IQ and Cognitive Functions in the Dunedin Study[a]

	Model 1			Model 2			Model 3			Model 4			Model 5			Omitted Variable Bias		
Measure	b_1	SE	p	b_2	SE	p	b_3	SE	p	b_4	SE	p	b_5	SE	p	b_1–b_5	SE	p
IQ																		
A. WISC-R (IQ at ages 11–13) (N=899)																		
Child maltreatment	−0.11	0.03	<0.01	−0.06	0.03	0.06	−0.05	0.03	0.07	−0.04	0.03	0.17	0.00	0.03	0.89	−0.10	0.005	<0.01
Maternal IQ	0.40	0.03	<0.01	0.39	0.03	<0.01							0.23	0.03	<0.01			
IQ at age 3	0.48	0.03	<0.01				0.47	0.03	<0.01				0.36	0.03	<0.01			
Family SES	0.39	0.03	<0.01							0.38	0.03	<0.01	0.20	0.03	<0.01			
B. WAIS-IV (IQ at age 38) (N=913)																		
Child maltreatment	−0.14	0.03	<0.01	−0.08	0.03	<0.01	−0.08	0.03	<0.01	−0.08	0.03	0.01	−0.04	0.03	0.21	−0.10	0.005	<0.01
Maternal IQ	0.44	0.03	<0.01	0.43	0.03	<0.01							0.30	0.03	<0.01			
IQ at age 3	0.43	0.03	<0.01				0.42	0.03	<0.01				0.30	0.03	<0.01			
Family SES	0.38	0.03	<0.01							0.37	0.03	<0.01	0.17	0.03	<0.01			
Executive function																		
C. Rapid Visual Information Processing A′ (age 38) (N=890)																		
Child maltreatment	−0.03	0.03	0.44	0.01	0.03	0.85	0.00	0.03	0.99	0.00	0.03	0.95	0.03	0.03	0.41	—	—	—
Maternal IQ	0.24	0.03	<0.01	0.24	0.03	<0.01							0.18	0.04	<0.01			
IQ at age 3	0.22	0.03	<0.01				0.22	0.03	<0.01				0.16	0.04	<0.01			
Family SES	0.17	0.03	<0.01							0.17	0.03	<0.01	0.06	0.04	0.11			
D. Rapid Visual Information Processing, false alarms (age 18) (N=895)																		
Child maltreatment	0.07	0.03	0.04	0.06	0.03	0.09	0.05	0.03	0.13	0.06	0.03	0.08	0.05	0.03	0.17	0.02	0.006	<0.01
Maternal IQ	−0.09	0.03	<0.01	−0.09	0.03	0.01							−0.06	0.04	0.11			
IQ at age 3	−0.15	0.03	<0.01				−0.14	0.03	<0.01				−0.13	0.04	<0.01			
Family SES	−0.06	0.03	0.10							−0.05	0.03	0.18	0.01	0.04	0.71			
E. WAIS-IV, working memory index (age 38) (N=910)																		
Child maltreatment	−0.09	0.03	<0.01	−0.05	0.03	0.09	−0.06	0.03	0.07	−0.05	0.03	0.13	−0.02	0.03	0.56	−0.08	0.006	<0.01
Maternal IQ	0.34	0.03	<0.01	0.33	0.03	<0.01							0.23	0.03	<0.01			
IQ at age 3	0.31	0.03	<0.01				0.30	0.03	<0.01				0.21	0.03	<0.01			
Family SES	0.29	0.03	<0.01							0.28	0.03	<0.01	0.14	0.03	<0.01			
F. Wechsler Memory Scale–III, months backward test (age 38) (N=911)																		
Child maltreatment	−0.12	0.03	<0.01	−0.10	0.03	<0.01	−0.11	0.03	<0.01	−0.09	0.03	<0.01	−0.08	0.03	0.01	−0.04	0.006	<0.01
Maternal IQ	0.19	0.03	<0.01	0.18	0.03	<0.01							0.13	0.04	<0.01			
IQ at age 3	0.12	0.03	<0.01				0.11	0.03	<0.01				0.05	0.04	0.18			
Family SES	0.18	0.03	<0.01							0.16	0.03	<0.01	0.10	0.04	<0.01			
G. Trail Making Test, part B (age 38) (N=909)																		
Child maltreatment	0.07	0.03	0.05	0.04	0.03	0.25	0.04	0.03	0.27	0.04	0.03	0.23	0.01	0.03	0.67	0.05	0.006	<0.01
Maternal IQ	−0.24	0.03	<0.01	−0.24	0.03	<0.01							−0.17	0.03	<0.01			
IQ at age 3	−0.26	0.03	<0.01				−0.26	0.03	<0.01				−0.20	0.03	<0.01			
Family SES	−0.18	0.03	<0.01							−0.17	0.03	<0.01	−0.05	0.04	0.14			
Processing speed																		
H. Rapid Visual Information Processing, mean latency (age 38) (N=890)																		
Child maltreatment	0.03	0.03	0.45	0.02	0.03	0.65	0.01	0.03	0.74	0.02	0.03	0.55	0.01	0.03	0.80	—	—	—
Maternal IQ	−0.08	0.03	0.02	−0.07	0.03	0.03							−0.06	0.04	0.13			
IQ at age 3	−0.12	0.03	<0.01				−0.11	0.03	<0.01				−0.11	0.04	<0.01			
Family SES	−0.03	0.03	0.35							−0.03	0.03	0.42	0.02	0.04	0.51			

continued

TABLE 3, *continued*

	Model 1			Model 2			Model 3			Model 4			Model 5			Omitted Variable Bias		
Measure	b_1	SE	p	b_2	SE	p	b_3	SE	p	b_4	SE	p	b_5	SE	p	b_1–b_5	SE	p
I. Reaction time index (age 38) (N=895)																		
Child maltreatment	0.06	0.03	0.08	0.05	0.03	0.15	0.04	0.03	0.21	0.04	0.03	0.20	0.03	0.03	0.33	—	—	—
Maternal IQ	−0.08	0.03	0.02	−0.07	0.03	0.04							−0.03	0.04	0.47			
IQ at age 3	−0.13	0.03	<0.01				−0.13	0.03	<0.01				−0.11	0.04	<0.01			
Family SES	−0.10	0.03	<0.01							−0.09	0.03	<0.01	−0.05	0.04	0.18			
J. WAIS-IV, processing speed index (age 38) (N=912)																		
Child maltreatment	−0.07	0.03	0.04	−0.04	0.03	0.26	−0.03	0.03	0.29	−0.04	0.03	0.24	−0.01	0.03	0.73	−0.06	0.006	<0.01
Maternal IQ	0.25	0.03	<0.01	0.24	0.03	<0.01							0.18	0.03	<0.01			
IQ at age 3	0.27	0.03	<0.01				0.26	0.03	<0.01				0.21	0.03	<0.01			
Family SES	0.18	0.03	<0.01							0.17	0.03	<0.01	0.05	0.04	0.15			
Memory																		
K. Paired Associates Learning, first trial (age 38) (N=898)																		
Child maltreatment	−0.05	0.03	0.17	−0.03	0.03	0.41	−0.03	0.03	0.44	−0.03	0.03	0.37	−0.01	0.03	0.69	—	—	—
Maternal IQ	0.14	0.03	<0.01	0.14	0.03	<0.01							0.10	0.04	<0.01			
IQ at age 3	0.17	0.03	<0.01				0.17	0.03	<0.01				0.14	0.04	<0.01			
Family SES	0.10	0.03	<0.01							0.10	0.03	<0.01	0.02	0.04	0.57			
L. Paired Associates Learning, total errors (age 38) (N=898)																		
Child maltreatment	0.04	0.03	0.19	0.02	0.03	0.50	0.03	0.03	0.45	0.03	0.03	0.39	0.01	0.03	0.75	—	—	—
Maternal IQ	−0.17	0.03	<0.01	−0.16	0.03	<0.01							−0.13	0.04	<0.01			
IQ at age 3	−0.16	0.03	<0.01				−0.16	0.03	<0.01				−0.12	0.04	<0.01			
Family SES	−0.10	0.03	<0.01							−0.09	0.03	<0.01	−0.01	0.04	0.77			
M. Wechsler Memory Scale–III, verbal paired associates, total recall (age 38) (N=911)																		
Child maltreatment	−0.02	0.03	0.56	0.01	0.03	0.87	0.01	0.03	0.83	0.02	0.03	0.64	0.03	0.03	0.29	—	—	—
Maternal IQ	0.20	0.03	<0.01	0.20	0.03	<0.01							0.12	0.04	<0.01			
IQ at age 3	0.22	0.03	<0.01				0.22	0.03	<0.01				0.15	0.03	<0.01			
Family SES	0.22	0.03	<0.01							0.22	0.03	<0.01	0.13	0.04	<0.01			
N. Wechsler Memory Scale–III, verbal paired associates, delayed recall (age 38) (N=908)																		
Child maltreatment	−0.01	0.03	0.72	0.01	0.03	0.71	0.01	0.03	0.70	0.02	0.03	0.55	0.04	0.03	0.24	—	—	—
Maternal IQ	0.19	0.03	<0.01	0.19	0.03	<0.01							0.12	0.04	<0.01			
IQ at age 3	0.20	0.03	<0.01				0.20	0.03	<0.01				0.14	0.04	<0.01			
Family SES	0.20	0.03	<0.01							0.20	0.03	<0.01	0.12	0.04	<0.01			
O. Rey Auditory Verbal Learning Test, total recall (age 38) (N=910)																		
Child maltreatment	−0.09	0.03	<0.01	−0.06	0.03	0.08	−0.05	0.03	0.09	−0.05	0.03	0.14	−0.02	0.03	0.45	−0.06	0.006	<0.01
Maternal IQ	0.25	0.03	<0.01	0.25	0.03	<0.01							0.16	0.03	<0.01			
IQ at age 3	0.27	0.03	<0.01				0.26	0.03	<0.01				0.19	0.03	<0.01			
Family SES	0.25	0.03	<0.01							0.24	0.03	<0.01	0.13	0.04	<0.01			
P. Rey Auditory Verbal Learning Test, delayed recall (age 38) (N=911)																		
Child maltreatment	−0.05	0.03	0.15	−0.03	0.03	0.39	−0.03	0.03	0.38	−0.02	0.03	0.60	0.00	0.03	0.90	—	—	—
Maternal IQ	0.16	0.03	<0.01	0.16	0.03	<0.01							0.09	0.04	0.01			
IQ at age 3	0.16	0.03	<0.01				0.16	0.03	<0.01				0.10	0.04	<0.01			
Family SES	0.19	0.03	<0.01							0.19	0.03	<0.01	0.13	0.04	<0.01			

continued

TABLE 3, *continued*

	Model 1			Model 2			Model 3			Model 4			Model 5			Omitted Variable Bias		
Measure	b_1	SE	p	b_2	SE	p	b_3	SE	p	b_4	SE	p	b_5	SE	p	b_1–b_5	SE	p
Perceptual reasoning																		
Q. WAIS-IV, perceptual reasoning index (age 38) (N=911)																		
Child maltreatment	−0.13	0.03	<0.01	−0.09	0.03	<0.01	−0.09	0.03	<0.01	−0.09	0.03	<0.01	−0.06	0.03	0.05	−0.07	0.006	<0.01
Maternal IQ	0.33	0.03	<0.01	0.32	0.03	<0.01							0.24	0.03	<0.01			
IQ at age 3	0.29	0.03	<0.01				0.28	0.03	<0.01				0.20	0.03	<0.01			
Family SES	0.24	0.03	<0.01							0.23	0.03	<0.01	0.08	0.03	0.02			
Verbal comprehension																		
R. WAIS-IV, verbal comprehension index (age 38) (N=913)																		
Child maltreatment	−0.13	0.03	<0.01	−0.08	0.03	0.01	−0.07	0.03	0.01	−0.06	0.03	0.04	−0.02	0.03	0.39	−0.10	0.005	<0.01
Maternal IQ	0.42	0.03	<0.01	0.41	0.03	<0.01							0.26	0.03	<0.01			
IQ at age 3	0.44	0.03	<0.01				0.43	0.03	<0.01				0.30	0.03	<0.01			
Family SES	0.41	0.03	<0.01							0.40	0.03	<0.01	0.21	0.03	<0.01			

[a] The table lists standardized regression coefficients (betas) for the association between childhood maltreatment and cognitive measures from ordinary least squares (linear) regression models. Model 1 presents bivariate (unadjusted) associations between all predictors and the cognitive measures. Model 2 is adjusted for the effect of maternal IQ, model 3 for the effect of IQ at age 3, model 4 for the effect of family socioeconomic status (SES), and model 5 for the effect of all covariates. "Omitted variable bias" presents the difference between the unadjusted and fully adjusted effect of child maltreatment on the cognitive measures when the unadjusted effects were statistically significant. WAIS-IV=Wechsler Adult Intelligence Scale, 4th edition; WISC-R=Wechsler Intelligence Scale for Children–Revised.

nonspecific effects of childhood socioeconomic disadvantage. On the one hand, the results are consistent with the high heritability of cognitive functions (38), their strong continuity across the life course (22), and the stable cognitive deficits previously described in children exposed to adversity (39, 40). On the other hand, they are inconsistent with the causal effects of early-life stress on brain function reported in experimental animal models (41, 42). Although animal models show that early-life stress can have an effect on brain function, human studies, such as those reported here, are needed to test whether real-world exposures, such as childhood victimization, do typically affect clinically relevant brain functions in ordinary humans. We speculate that inconsistencies could arise for several reasons. First, differences in the effects of early-life stress could arise because of differences in life history and brain development timing across species (43, 44). Second, because of greater genetic heterogeneity in humans, individual differences may buffer the average effects of early-life stress on brain function to a greater extent in humans than in animal models (45). Third, universal interventions (e.g., schooling) and targeted interventions (e.g., child protection services, psychiatric treatment) in childhood may buffer the effect of early-life stress on brain function in humans but not in animal models. Finally, selective reporting of positive results may have biased scientific evidence (46).

We note a set of limitations. First, it is possible that our measures of childhood victimization have underestimated associations with cognitive functions. However, a comparison between our studies and previous studies suggests that this is not the case. For example, Perez and Widom (47) report standardized mean differences of −0.62 (95% CI= −0.77, −0.46) in IQ between court-substantiated cases of maltreatment and control subjects. By comparison, in the E-Risk Study, standardized mean differences in IQ between poly-victimized and nonvictimized study members were −0.68 (95% CI=−0.85, −0.50) at age 12 and −0.52 (95% CI=−0.70, −0.34) at age 18. In the Dunedin Study, standardized mean differences in IQ between definite maltreated and nonmaltreated study members were −0.29 (95% CI= −0.52, −0.06) at ages 11–13 and −0.43 (95% CI=−0.66, −0.20) at age 38. Confidence intervals for the estimates overlap, in line with expectations that there are no significant differences across the studies. This shows that, at the bivariate level, our studies have not underestimated the associations between childhood victimization and cognitive functions. However, our multivariate analyses suggest that these associations were significantly attenuated by the presence of cognitive deficits that predated childhood victimization and by confounding genetic and environmental risks. Second, the results may only be valid for childhood victimization within the age ranges described in our studies (3–12 years). It is possible that victimization of infants and toddlers (48) can cause immediate and stable changes in cognitive functions that we did not detect. To partly test for such effects, in the E-Risk Study we reran analyses excluding children who were victimized before the age-5 IQ assessment, but the results were unaltered. In the Dunedin Study we capitalized on a measure of maternal IQ, a proxy for the child's IQ (38) unbiased by the child's victimization experience. Cognitive deficits were similarly explained by differences in maternal IQ and differences in the child's IQ at age 3 (Table 3 and Table S12, models 2 and 3, respectively). These findings suggest that the limited residual effects of childhood victimization on later cognitive functions were unlikely to be due to early

victimization. Third, the results may only apply to the childhood victimization experiences measured here and not to more extreme and unusual experiences (e.g., institutional upbringing, head-injury-associated victimization). Fourth, the results may only apply to the clinically relevant cognitive measures used here and not to other brain functions that may be affected by victimization experiences (e.g., reward or threat processing). Fifth, there was evidence for a residual effect of childhood victimization on the Wechsler Intelligence Scale for Children at age 12 in one of our two samples. Therefore, we cannot conclusively rule out the presence of a small causal effect. Despite these limitations, the findings have implications for neuroscience and clinical practice.

With regard to neuroscience, these findings caution researchers to adopt a more circumspect approach to causal inference in human studies. Together with previous commentaries (18–20), these results highlight the fact that advances in neuroscience methods need to be accompanied by greater attention to study design. Experimental designs to test the effects of child victimization in humans are clearly unethical. Longitudinal designs like the ones used here are costly but essential for tracking within-individual changes (49). Twin and sibling designs are uncommon but can offer crucial insights in this area (50, 51). Neuroscience research capitalizing on these designs will be important to further test putative causal effects of child victimization on brain structure and function.

With regard to clinical practice, the present findings caution clinicians against simplistic case formulations for individuals with complex traumatic histories of child victimization. The results suggest that cognitive deficits should be conceptualized as children's individual risk factors for victimization (9, 21) as well as potential complicating features during treatment (52, 53). Interventions attempting to support and improve cognition (54, 55) in individuals with a history of childhood victimization can be useful to complement more commonly used interventions for emotional and behavioral disturbances in this population.

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REFERENCES

1. Danese A, McEwen BS: Adverse childhood experiences, allostasis, allostatic load, and age-related disease. Physiol Behav 2012; 106: 29–39
2. McCrory E, De Brito SA, Viding E: Research review: the neurobiology and genetics of maltreatment and adversity. J Child Psychol Psychiatry 2010; 51:1079–1095
3. Moffitt TE; Klaus-Grawe 2012 Think Tank: Childhood exposure to violence and lifelong health: clinical intervention science and stress-biology research join forces. Dev Psychopathol 2013; 25:1619–1634
4. Lim L, Radua J, Rubia K: Gray matter abnormalities in childhood maltreatment: a voxel-wise meta-analysis. Am J Psychiatry 2014; 171: 854–863
5. Sapolsky RM: Why stress is bad for your brain. Science 1996; 273: 749–750
6. Perry BD: Childhood experience and the expression of genetic potential: what childhood neglect tells us about nature and nurture. Brain Mind 2002; 3:79–100
7. Lupien SJ, McEwen BS, Gunnar MR, et al: Effects of stress throughout the lifespan on the brain, behaviour, and cognition. Nat Rev Neurosci 2009; 10:434–445
8. Tost H, Champagne FA, Meyer-Lindenberg A: Environmental influence in the brain, human welfare, and mental health. Nat Neurosci 2015; 18:1421–1431
9. Leppänen JM, Nelson CA: Tuning the developing brain to social signals of emotions. Nat Rev Neurosci 2009; 10:37–47
10. Susser E, Widom CS: Still searching for lost truths about the bitter sorrows of childhood. Schizophr Bull 2012; 38:672–675
11. Allen G, Smith ID: Early Intervention: Good Parents, Great Kids, Better Citizens. London, Centre for Social Justice and the Smith Institute, 2008 (http://www.centreforsocialjustice.org.uk/UserStorage/pdf/Pdf%20reports/EarlyInterventionFirstEdition.pdf)
12. Edwards R, Gillies V, Horsley N: Brain science and early years policy: hopeful ethos or "cruel optimism"? Crit Soc Policy 2015; 35:167–187
13. Bishop DVM: Research review: Emanuel Miller Memorial Lecture 2012: neuroscientific studies of intervention for language impairment in children: interpretive and methodological problems. J Child Psychol Psychiatry 2013; 54:247–259
14. Deary IJ, Whiteman MC, Starr JM, et al: The impact of childhood intelligence on later life: following up the Scottish mental surveys of 1932 and 1947. J Pers Soc Psychol 2004; 86:130–147
15. Schmidt FL, Hunter J: General mental ability in the world of work: occupational attainment and job performance. J Pers Soc Psychol 2004; 86:162–173
16. Pechtel P, Pizzagalli DA: Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology (Berl) 2011; 214:55–70
17. Hart H, Rubia K: Neuroimaging of child abuse: a critical review. Front Hum Neurosci 2012; 6:52
18. Open Science Collaboration: Psychology: estimating the reproducibility of psychological science. Science 2015; 349:aac4716
19. Falk EB, Hyde LW, Mitchell C, et al: What is a representative brain? Neuroscience meets population science. Proc Natl Acad Sci USA 2013; 110:17615–17622
20. Button KS, Ioannidis JPA, Mokrysz C, et al: Power failure: why small sample size undermines the reliability of neuroscience. Nat Rev Neurosci 2013; 14:365–376

21. Jones L, Bellis MA, Wood S, et al: Prevalence and risk of violence against children with disabilities: a systematic review and meta-analysis of observational studies. Lancet 2012; 380:899–907
22. Deary IJ, Pattie A, Starr JM: The stability of intelligence from age 11 to age 90 years: the Lothian birth cohort of 1921. Psychol Sci 2013; 24:2361–2368
23. Bradley RH, Corwyn RF: Socioeconomic status and child development. Annu Rev Psychol 2002; 53:371–399
24. Heckman JJ: Sample selection bias as a specification error. Econometrica 1979; 47:153
25. Duncan GJ, Magnuson KA, Ludwig J: The endogeneity problem in developmental studies. Res Hum Dev 2004; 1:59–80
26. Meier MH, Caspi A, Ambler A, et al: Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci USA 2012; 109:E2657–E2664
27. Gottfredson LS: Why g matters: The complexity of everyday life. Intelligence 1997; 24:79–132
28. Caspi A, McClay J, Moffitt TE, et al: Role of genotype in the cycle of violence in maltreated children. Science 2002; 297:851–854
29. Fisher HL, Caspi A, Moffitt TE, et al: Measuring adolescents' exposure to victimization: the Environmental Risk (E-Risk) Longitudinal Twin Study. Dev Psychopathol 2015; 27:1399–1416
30. Finkelhor D, Ormrod RK, Turner HA: Poly-victimization: a neglected component in child victimization. Child Abuse Negl 2007; 31:7–26
31. Moffitt TE; E-Risk Study Team: Teen-aged mothers in contemporary Britain. J Child Psychol Psychiatry 2002; 43:727–742
32. Bernstein DP, Fink L, Handelsman L, et al: Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am J Psychiatry 1994; 151:1132–1136
33. Clogg CC, Petkova E, Haritou A: Statistical methods for comparing regression coefficients between models. Am J Sociol 1995; 100: 1261–1293
34. Poulton R, Moffitt TE, Silva PA: The Dunedin Multidisciplinary Health and Development Study: overview of the first 40 years, with an eye to the future. Soc Psychiatry Psychiatr Epidemiol 2015; 50: 679–693
35. Luna B, Garver KE, Urban TA, et al: Maturation of cognitive processes from late childhood to adulthood. Child Dev 2004; 75: 1357–1372
36. Gogtay N, Giedd JN, Lusk L, et al: Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci USA 2004; 101:8174–8179
37. van Dongen J, Slagboom PE, Draisma HHM, et al: The continuing value of twin studies in the omics era. Nat Rev Genet 2012; 13: 640–653
38. Plomin R: Genetics and general cognitive ability. Nature 1999; 402(suppl):C25–C29
39. Richards M, Wadsworth MEJ: Long term effects of early adversity on cognitive function. Arch Dis Child 2004; 89:922–927
40. Pesonen A-K, Eriksson JG, Heinonen K, et al: Cognitive ability and decline after early life stress exposure. Neurobiol Aging 2013; 34: 1674–1679
41. Liu D, Diorio J, Day JC, et al: Maternal care, hippocampal synaptogenesis, and cognitive development in rats. Nat Neurosci 2000; 3:799–806
42. Brunson KL, Kramár E, Lin B, et al: Mechanisms of late-onset cognitive decline after early-life stress. J Neurosci 2005; 25: 9328–9338
43. Clancy B, Finlay BL, Darlington RB, et al: Extrapolating brain development from experimental species to humans. Neurotoxicology 2007; 28:931–937
44. Workman AD, Charvet CJ, Clancy B, et al: Modeling transformations of neurodevelopmental sequences across mammalian species. J Neurosci 2013; 33:7368–7383
45. van der Worp HB, Howells DW, Sena ES, et al: Can animal models of disease reliably inform human studies? PLoS Med 2010; 7: e1000245
46. Ioannidis JPA, Munafó MR, Fusar-Poli P, et al: Publication and other reporting biases in cognitive sciences: detection, prevalence, and prevention. Trends Cogn Sci 2014; 18:235–241
47. Perez CM, Widom CS: Childhood victimization and long-term intellectual and academic outcomes. Child Abuse Negl 1994; 18: 617–633
48. US Department of Health and Human Services, Administration for Children and Families, Administration on Children, Youth and Families, Children's Bureau: Child Maltreatment 2013 (http://www.acf.hhs.gov/cb/resource/child-maltreatment-2013)
49. Kraemer HC, Yesavage JA, Taylor JL, et al: How can we learn about developmental processes from cross-sectional studies, or can we? Am J Psychiatry 2000; 157:163–171
50. Gilbertson MW, Shenton ME, Ciszewski A, et al: Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. Nat Neurosci 2002; 5:1242–1247
51. Ouellet-Morin I, Danese A, Bowes L, et al: A discordant monozygotic twin design shows blunted cortisol reactivity among bullied children. J Am Acad Child Adolesc Psychiatry 2011; 50: 574–582.e3
52. Nanni V, Uher R, Danese A: Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. Am J Psychiatry 2012; 169:141–151
53. Agnew-Blais J, Danese A: Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. Lancet Psychiatry 2016; 3:342–349
54. 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; 11:141–168
55. Harvey AG, Lee J, Williams J, et al: Improving outcome of psychosocial treatments by enhancing memory and learning. Perspect Psychol Sci 2014; 9:161–179