

Childhood adversities and adult psychopathology in the National Comorbidity Survey Replication (NCS-R) III: associations with functional impairment related to DSM-IV disorders

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Background. Despite evidence that childhood adversities (CAs) are associated with increased risk of mental disorders, little is known about their associations with disorder-related impairment. We report the associations between CAs and functional impairment associated with 12-month DSM-IV disorders in a national sample.

Method. We used data from the US National Comorbidity Survey Replication (NCS-R). Respondents completed diagnostic interviews that assessed 12-month DSM-IV disorder prevalence and impairment. Associations of 12 retrospectively reported CAs with impairment among cases ($n=2242$) were assessed using multiple regression analysis. Impairment measures included a dichotomous measure of classification in the severe range of impairment on the Sheehan Disability Scale (SDS) and a measure of self-reported number of days out of role due to emotional problems in the past 12 months.

Results. CAs were positively and significantly associated with impairment. Predictive effects of CAs on the SDS were particularly pronounced for anxiety disorders and were significant in predicting increased days out of role associated with mood, anxiety and disruptive behavior disorders. Predictive effects persisted throughout the life course and were not accounted for by disorder co-morbidity. CAs associated with maladaptive family functioning (MFF; parental mental illness, substance disorder, criminality, family violence, abuse, neglect) were more consistently associated with impairment than other CAs. The joint effects of co-morbid MFF CAs were significantly subadditive. Simulations suggest that CAs account for 19.6% of severely impairing disorders and 17.4% of days out of role.

Conclusions. CAs predict greater disorder-related impairment, highlighting the ongoing clinical significance of CAs at every stage of the life course.

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Key words: Childhood adversity, disability, functional impairment, severity.

Introduction

High rates of mental disorders have been documented consistently among individuals exposed to childhood adversities (CAs) in community and epidemiologic studies (Kessler *et al.* 1997; Phillips *et al.* 2005; Collishaw *et al.* 2007). Until recently, however, the effects of CAs on risk for initial disorder onset and disorder course have not been differentiated. Recent evidence from the National Comorbidity Survey Replication (NCS-R), a nationally representative survey of the US household population, documents substantial

CA effects on initial onset of psychiatric disorders (Afifi *et al.* 2008; Green *et al.*, in press). Although several studies have reported associations between CAs and the chronicity of major depression (Brown & Moran, 1994; Riso *et al.* 2002), results from the NCS-R indicate fairly trivial effects of CAs on disorder persistence (McLaughlin *et al.*, in press). These findings raise questions about whether CAs, although associated with increased risk of initial disorder onset, might not have as much to do with the manifestation of disorders once they emerge.

Prior evidence, however, suggests that mental disorders that develop in individuals exposed to CAs are associated with high levels of functional impairment. CAs have been found to predict increased risk for mental health disability (Tommyr *et al.* 2007), greater perceived need for mental health treatment (Sareen

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et al. 2005), and greater functional impairment among individuals with mood disorders (Klein *et al.* 2008). However, the extent to which co-morbidity underlies these associations remains unclear. Co-morbidity is an important predictor of disorder impairment (Kessler *et al.* 2005), and high rates of co-morbidity have been documented among individuals exposed to CAs (Levitin *et al.* 2003). As such, the reported associations between CAs and functional impairment may be attributable to high rates of co-morbidity among individuals exposed to CAs. To our knowledge, this possibility has never been examined directly in the literature. We do so in the current report, where we extend the previous NCS-R analyses by examining the effects of CAs on impairment related to 12-month DSM-IV mental disorders.

Method

Sample

The NCS-R is a face-to-face household survey of 9282 English-speaking respondents aged ≥ 18 years carried out by the professional interview staff of the Institute for Social Research at the University of Michigan between February 2001 and April 2003 in a nationally representative multi-stage clustered area probability sample of the US household population (Kessler & Merikangas, 2004). The response rate was 70.9%. Recruitment began with a letter and study fact brochure followed by an in-person interviewer visit to explain study aims and procedures and obtain informed consent. Respondents were paid US\$50 for participation. The NCS-R recruitment and consent procedures were approved by human subjects committees of Harvard Medical School and the University of Michigan.

The survey was administered in two parts. Part I included a core diagnostic assessment ($n = 9282$). Part II included questions about risk factors, consequences and other correlates along with assessments of additional disorders that were administered to all Part I respondents who met lifetime criteria for any Part I disorder plus a probability subsample of other respondents ($n = 5692$). The Part I sample was weighted to adjust for differential probabilities of selection within households, and for differences in intensity of recruitment effort among hard-to-recruit cases. The Part II sample was also weighted to adjust for the lower selection probabilities for Part II respondents without a mental disorder. A final weight adjusted the Part II sample to match the 2000 census population on a cross-classification of geographic and sociodemographic variables. All analyses reported in this paper used these weights. More complete information about

the NCS-R sampling design and weighting is reported elsewhere (Kessler *et al.* 2004).

Diagnostic assessment

NCS-R diagnoses are based on Version 3.0 of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI; Kessler & Üstun, 2004), a fully structured lay-administered interview that generates diagnoses according to the definitions and criteria of both the ICD-10 and DSM-IV diagnostic systems. DSM-IV criteria are used here. The 12-month diagnoses considered here include three broad classes of disorders that encompass the 15 specific disorders included in the analysis: mood disorders [major depressive disorder, dysthymic disorder, bipolar I disorder (BP-I), BP-II and subthreshold BPD], anxiety disorders (panic disorder, agoraphobia without a history of panic disorder, generalized anxiety disorder, specific phobia, social phobia, post-traumatic stress disorder and separation anxiety disorder) and disruptive behavior disorders (intermittent explosive disorder, attention-deficit/hyperactivity disorder and oppositional-defiant disorder). Diagnostic hierarchy rules and organic exclusion rules were used in making diagnoses. As detailed elsewhere (Kessler *et al.* 2004), blinded clinical reappraisal interviews with a probability subsample of NCS-R respondents generally found good concordance between DSM-IV diagnoses based on the CIDI and those based on the Structured Clinical Interview for DSM-IV (SCID; First *et al.* 2002).

Childhood adversities

Twelve dichotomously measured CAs occurring before age 18 were assessed in the NCS-R. These 12 CAs include three types of interpersonal loss (parental death, parental divorce and other loss of contact with parents), four types of parental maladjustment (mental illness, substance abuse, criminality and violence), three types of harsh parenting (physical abuse, sexual abuse and neglect) and two other CAs (serious respondent physical illness and family economic adversity). The interpersonal losses were assessed with measures developed for the baseline NCS about parental death, divorces and other parental separations lasting ≥ 6 months (adoption, foster placement and living with other relatives instead of parents). Parental criminality, family economic adversity and sexual abuse were also assessed with measures developed for the baseline NCS. Parental mental illness (major depression, generalized anxiety disorder, panic disorder and antisocial personality disorder) and substance abuse were assessed with the

Family History Research Diagnostic Criteria (FHRDC) Interview (Endicott *et al.* 1978) and its extensions (Kendler *et al.* 1991). Family violence and physical abuse of the respondent by parents were assessed with a modified version of the Conflict Tactics Scale (Straus, 1979). Finally, neglect was assessed using a battery of questions commonly used in studies of child welfare (Courtney *et al.* 1998).

Impairment

Functional impairment associated with DSM-IV disorders was assessed among 12-month cases using two methods that were designed to assess disorder-specific role impairment. First, the Sheehan Disability Scale (SDS; Leon *et al.* 1997) was used to ask respondents the extent to which each of their 12-month disorders led to impairment in their role performance in work, household maintenance, social life and intimate relationships. These questions were asked separately for each 12-month disorder. Respondents were asked to think of the month in the past year when the focal disorder was most severe and to rate on a 0–10 visual analog scale (with associated scale scores of none, 0; mild, 1–3; moderate, 4–6; severe, 7–9; and very severe, 10) the extent to which the focal disorder created impairment during that month in each of the four role domains. Respondents who received a score of severe or very severe in any of the four domains were classified as ‘severe’ for the current analyses. After completing the SDS ratings, respondents were asked to estimate the total number of days out of 365 in the past 12 months when they were ‘totally unable to work or carry out any of your other normal daily activities’ because of the focal disorder. These questions were administered separately for 15 different mental disorders, in each case administering the questions only to respondents who met criteria for the disorder at some time in the past 12 months.

Data analysis

The predictive effects of CAs on functional impairment were first examined using an overall data array (i.e. a data file that stacked the 15 separate files for the DSM-IV/CIDI disorders and included 14 dummy variables that distinguished among these files). Each of the 12 CAs was entered separately as a covariate to determine the independent predictive effect of each CA on impairment. Logistic regression models were estimated to predict the probability of being classified as ‘severe’ on any of the four subscales of the SDS. Poisson regression models were estimated to predict days out of role. These models controlled for age at

interview, gender and race-ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other).

A series of multivariate models that controlled for number and type of CA were estimated: an additive model that included separate variables for each of the 12 CAs, a model that included variables for number of CAs without information about type, and an interactive model that included variables for type and number of CAs. In previous factor analysis of CAs in the NCS-R (Green *et al.*, in press), a primary underlying dimension of maladaptive family functioning (MFF) emerged that included parent mental illness, substance abuse, criminality, physical and sexual abuse, neglect and family violence. Several CAs did not load onto this factor including parent death, divorce or other loss, serious physical illness, and economic adversity. The best-fitting multivariate model in analysis of CA effects on disorder onset included variables for type and number of CAs, and differentiated CAs into MFF and other adversities. This best-fitting model was estimated to predict impairment using the data array, and again in subsamples defined by age at interview and class of disorder. These models also included controls for lifetime co-morbidity, defined as disorder onsets temporally prior to the focal disorder, in addition to the sociodemographic controls included in bivariate CA models.

We assessed the overall impact of all CAs on functional impairment using simulation methods to generate individual-level predicted probabilities of impairment twice from the coefficients in the most complex multivariate model, the first time using all the coefficients in the model and the second time assuming that the coefficients associated with the CAs were all zero. The ratio of the predicted estimates of the prevalence of severe impairment associated with disorders in the two specifications was then used to calculate the percentage of severely impairing disorders that would be prevented if none of the CAs had occurred and the odds ratios (ORs) in the model were due to causal effects of CAs. We assessed the impact of CAs on days out of role in a second set of simulations using the same two model specifications described above.

The logistic regression coefficients and their standard errors were exponentiated and are reported in the form of ORs with 95% confidence intervals (CIs). Exponentiated Poisson regression coefficients are reported as rate ratios (RRs) with 95% CIs. All significance tests for coefficients were evaluated using 0.05-level two-sided tests. Because the NCS-R data are clustered and weighted, the design-based Taylor series method (Wolter, 1985) implemented in the SUDAAN software system (Research Triangle Institute, 2002) was used to estimate standard errors of

Table 1. Bivariate and multivariate associations (odds ratios) between childhood adversities (CAs) and severe impairment related to NCS-R/DSM-IV disorders with controls^a

	Bivariate ^b		Multivariate					
			Additive ^c		Number of CAs ^b		Interactive ^d	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
I. MFF								
Parent Mental Illness	1.5*	1.1–2.0	1.2	0.9–1.5			1.5*	1.1–1.9
Parent Substance	1.3	0.9–1.9	0.8	0.5–1.2	–	–	1.1	0.7–1.9
Parent Criminal	1.7*	1.2–2.4	1.1	0.8–1.7	–	–	1.6*	1.0–2.5
Family Violence	2.0*	1.6–2.5	1.6*	1.2–2.1	–	–	2.0*	1.3–3.0
Physical Abuse	2.2*	1.6–2.9	1.3*	1.0–1.7	–	–	1.8*	1.2–2.7
Sexual Abuse	1.7*	1.2–2.3	1.2	0.9–1.7	–	–	1.6*	1.1–2.4
Neglect	2.6*	1.7–3.9	1.7*	1.1–2.6	–	–	2.5*	1.6–4.0
$\chi^2(7)$ (<i>p</i> value)				41.2 (<0.001)*				25.9 (0.001)*
II. Other CAs								
Parent Died	1.2	0.9–1.7	1.0	0.7–1.5	–	–	1.3	0.9–1.9
Parent Divorce	1.1	0.8–1.5	0.9	0.6–1.2	–	–	1.1	0.7–1.5
Other Parent Loss	1.8*	1.4–2.3	1.3	1.0–1.6	–	–	1.7*	1.2–2.4
Serious Physical Illness	1.5*	1.1–2.3	1.5	1.0–2.2	–	–	1.9*	1.1–3.1
Family Economic Adversity	1.6*	1.1–2.2	1.3	0.9–1.8	–	–	1.8*	1.2–2.7
$\chi^2(5)$ (<i>p</i> value)				9.7 (0.08)				19.3 (0.002)*
$\chi^2(12)$ (<i>p</i> value)				79.8 (<0.001)*				46.5 (<0.001)*
III. Number of CAs								
0	–	–	–	–	–	–	–	–
1	–	–	–	–	1.6*	1.2–2.0	–	–
2	–	–	–	–	1.9*	1.3–2.7	0.8	0.5–1.3
3	–	–	–	–	2.0*	1.4–2.9	0.5	0.3–1.1
4	–	–	–	–	2.3*	1.5–3.7	0.4*	0.1–0.9
5	–	–	–	–	5.3*	2.8–10.1	0.5	0.1–1.6
6	–	–	–	–	3.9*	1.9–7.8	0.2*	0.1–0.9
7	–	–	–	–	2.7*	1.5–5.1	0.1*	0.0–0.4
χ^2 (<i>p</i> value)						$\chi^2(7) = 55.6 (<0.001)*$		$\chi^2(6) = 20.3 (0.002)*$

NCS-R, National Comorbidity Survey Replication; MFF, maladaptive family functioning; OR, odds ratio; CI, confidence interval.

^a Severe impairment defined as a score of 7–10 on any of the four subscales on the Sheehan Disability Scale (SDS) among those with a 12-month diagnosis.

^b Model controlled for age of onset, time since onset, age category, sex, race, diagnosis category and co-morbid conditions prior to onset of disorder in question.

^c Model controlled for age of onset, time since onset, age category, sex, race, diagnosis category, co-morbid conditions and type of adversity.

^d Model controlled age of onset, time since onset, age category, sex, race, diagnosis category, co-morbid conditions, type of adversity and number of adversities.

* Significant at the 0.05 level, two-tailed.

ORs and RRs and to evaluate the statistical significance of coefficients.

Results

The predictive effects of CAs on impairment related to DSM-IV/CIDI disorders

We used logistic regression to examine the predictive effects of CAs on functional impairment associated

with the 15 pooled DSM-IV/CIDI disorders, controlling for lifetime co-morbidity. In bivariate models, 85.7% of the MFF CAs positively and significantly predict the odds of being classified in the severe range on the SDS with ORs in the range of 1.5–2.6, and 60% of other CAs positively and significantly predict severe impairment with ORs in the range of 1.5–1.8 (Table 1). The ORs associated with other CAs become insignificant in a multivariate model that includes

all CAs. Three MFF CAs remain significant in the multivariate additive model (physical abuse, family violence and neglect) with ORs in the range of 1.3–1.7. The multivariate model that considers only the number of CAs shows that ORs generally increase with increasing number of CAs, from an OR of 1.6 associated with having exactly one CA to ORs of 2.7–5.3 associated with having 5, 6 or ≥ 7 CAs. The test for the joint effects of the seven number-of-CA predictors is significant [$\chi^2(7)=55.6, p<0.001$]. The multivariate model that controls for both type and number of CAs shows an effect of type of CA on disorder-related impairment after controlling for number of CAs [$\chi^2(12)=46.5, p<0.001$], with both MFF and other CAs having significant predictive effects, and an effect of number of CAs on impairment after controlling for type of CA [$\chi^2(6)=20.3, p=0.002$].

In the most complex multivariate model, which includes separate predictors for type of CA (i.e. one predictor for each of the 12 CAs) and number of CAs (i.e. separate predictors for respondents who were exposed to exactly one, exactly two, exactly three, ..., etc. CAs) and distinguishes between MFF CAs and other CAs, 75% of ORs for type of CA are positive and significant, ranging from 1.6 to 2.7 (Table 2). The test for the effects of type of CA controlling for number is significant [$\chi^2(12)=70.2, p<0.001$] and both MFF and other CAs are significantly associated with functional impairment. The test for variation in ORs is also significant, indicating that the ORs are not the same for all CAs [$\chi^2(11)=35.4, p<0.001$]. Although the odds of being classified in the severe range on the SDS increase with an increasing number of CAs (as shown in the simple number-of-CAs model), the odds increase at a significantly decreasing rate with increases in the number of CAs. This subadditive interaction is significant for MFF CAs [$\chi^2(6)=13.7, p=0.03$] but not for other CAs [$\chi^2(3)=7.5, p=0.06$].

Differential predictive effects on impairment by class of DSM-IV/CIDI disorders and age at interview

Disaggregation of the best-fitting model reveals differential effects of CAs in predicting impairment related to the broad disorder classes (mood, anxiety, disruptive behavior). CAs are associated with increased odds of having a severely impairing anxiety disorder [$\chi^2(12)=37.8, p<0.001$] but are not associated with impairment due to mood or disruptive behavior disorders (Table 2). More than half of the MFF CAs predict impairment related to anxiety disorders (ORs in the range of 1.7–2.5), as do 40% of the other CAs (serious physical illness and economic adversity, ORs 2.1 and 1.9 respectively). The ORs associated with number of MFF CAs in predicting severe anxiety

disorder-related impairment become increasingly negative as the number of CAs increases, documenting significant subadditive interactions [$\chi^2(6)=19.5, p=0.003$]. No subadditive interaction is present for other CAs [$\chi^2(3)=5.6, p=0.13$]. The number of MFF CAs also predict impairment related to disruptive behavior disorders [$\chi^2(6)=14.1, p=0.03$]. This means that, even though none of the MFF CAs, when occurring alone, significantly predict severely impairing disruptive behavior disorders, the odds of having a severely impairing disorder are significantly greater among respondents who experienced a number of these CAs.

Disaggregation of the best-fitting model by respondent age at interview shows that the effects of CAs on functional impairment are most pronounced among the middle-aged [ages 30–44, $\chi^2(12)=40.0, p<0.001$; ages 45–59, $\chi^2(12)=31.1, p=0.002$] but are still significant among adolescents and early adults [ages 18–29, $\chi^2(12)=23.4, p=0.02$] and among older respondents [ages ≥ 60 , $\chi^2(12)=35.9, p<0.001$]. (Results not shown but available upon request.) MFF CAs significantly predict impairment among respondents aged 30–44 [$\chi^2(7)=26.1, p<0.001$] whereas other CAs predict impairment among respondents aged 45–59 [$\chi^2(5)=21.2, p<0.001$].

Population-level predictive effects of CAs on prevalence of severely impairing mental disorders

We estimated the proportion of disorders involving severe impairment in the population that are associated with CAs based on the best-fitting model. These estimates can be interpreted as the proportion of severely impairing disorders that would not have occurred in the absence of the CAs if the coefficients in the model represent causal effects of CAs. Although this assumption is unlikely to be accurate, these estimates nonetheless provide useful data on the strength of associations between CAs and functional impairment (Table 3). The results show that CAs explain 19.6% of all severely impairing disorders, 25.3% of anxiety disorders, 11.0% of mood disorders and 13.4% of disruptive behavior disorders.

The predictive effects of CAs on days out of role associated with DSM-IV/CIDI disorders

We used Poisson regression to examine the predictive effects of CAs on days out of role associated with outcome disorders in the past 12 months using the overall data array. In bivariate analyses, 71.4% of MFF CAs positively and significantly predict days out of role, with RRs ranging from 1.5 to 2.2 (Table 4). Most of these effects become non-significant in the

Table 2. Multivariate associations (odds ratios) between childhood adversities (CAs) and severe impairment related to NCS-R/DSM-IV classes of disorders^a

	Mood ^b		Anxiety ^c		Disruptive behavior ^d		Any disorder ^e	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
I. MFF								
Parent Mental Illness	1.2	0.8–1.8	1.7*	1.1–2.5	1.4	0.6–3.4	1.6*	1.2–2.1
Parent Substance	1.6	0.9–2.9	1.3	0.7–2.2	0.8	0.3–2.3	1.2	0.8–2.1
Parent Criminal	1.2	0.6–2.1	1.5	0.9–2.7	1.9	0.6–6.5	1.7*	1.0–2.8
Family Violence	1.5	0.8–3.0	2.5*	1.5–4.1	2.3	0.8–6.9	2.2*	1.4–3.4
Physical Abuse	2.3*	1.0–5.0	2.1*	1.3–3.5	1.5	0.6–4.3	2.1*	1.4–3.2
Sexual Abuse	1.9*	1.1–3.1	1.3	0.8–2.2	2.0	0.5–7.1	1.7*	1.1–2.8
Neglect	1.2	0.6–2.1	2.3*	1.4–3.9	1.5	0.5–4.6	2.7*	1.8–3.9
$\chi^2(7)$ (<i>p</i> value)	11.8 (0.11)		22.6 (0.002)*		5.5 (0.60)		36.0 (<0.001)*	
$\chi^2(6)$ (<i>p</i> value)	8.6 (0.20)		12.1 (0.059)		4.4 (0.62)		12.5 (0.052)	
II. Other CAs								
Parent Died	1.7	0.8–3.5	1.3	0.7–2.3	0.6	0.2–1.6	1.3	0.8–1.9
Parent Divorce	1.2	0.8–2.0	1.2	0.8–1.8	0.4*	0.2–0.8	1.0	0.8–1.3
Other Parent Loss	1.5	0.7–3.4	1.4	0.9–2.0	0.6	0.2–1.6	1.7*	1.3–2.2
Serious Physical Illness	1.2	0.7–2.2	2.1*	1.3–3.3	0.9	0.3–2.9	1.9*	1.2–2.9
Family Economic Adversity	1.6	0.8–3.4	1.9*	1.2–3.1	0.8	0.3–1.8	1.9*	1.2–3.0
$\chi^2(5)$ (<i>p</i> value)	6.3 (0.28)		13.5 (0.02)*		8.0 (0.16)		22.9 (<0.001)*	
$\chi^2(12)$ (<i>p</i> value)	20.2 (0.060)		37.8 (<0.001)*		10.1 (0.610)		70.2 (<0.001)*	
III. Number of MFF CAs								
0–1	–	–	–	–	–	–	–	–
2	0.5	0.2–1.2	0.5*	0.2–1.0	1.3	0.4–3.9	0.6	0.3–1.0
3	0.3*	0.1–0.8	0.4	0.1–1.1	0.7	0.1–5.8	0.4*	0.2–0.9
4	0.2	0.1–1.2	0.2	0.0–0.6	0.2	0.0–2.9	0.2*	0.1–0.6
5	0.1*	0.0–0.5	0.4	0.1–3.2	0.7	0.0–24.6	0.3	0.0–1.4
6	0.0*	0.0–0.6	0.1	0.0–1.1	0.2	0.0–30.9	0.0*	0.0–0.3
7	–	–	0.1*	0.0–0.6	0.4	0.0–192.6	0.0*	0.0–0.6
χ^2 (<i>p</i> value)	$\chi^2(5) = 10.8$ (0.054)		$X^2(6) = 19.5$ (0.003)*		$X^2(6) = 14.1$ (0.030)*		$\chi^2(6) = 13.7$ (0.030)*	
IV. Number of other CAs								
0–1	–	–	–	–	–	–	–	–
2	1.2	0.5–2.8	0.5	0.3–1.0	1.8	0.5–6.0	0.6*	0.4–1.0
3	0.8	0.2–2.6	0.3*	0.1–0.9	5.4	0.7–44.5	0.4*	0.2–0.8
≥4	0.1	0.0–26.3	0.1	0.0–2.8	–	–	0.1	0.0–1.5
χ^2 (<i>p</i> value)	$\chi^2(3) = 1.7$ (0.64)		$\chi^2(3) = 5.6$ (0.13)		$\chi^2(2) = 2.8$ (0.25)		$\chi^2(3) = 7.5$ (0.06)	
$\chi^2(21)$ (<i>p</i> value)	43.9 (0.002)*		183.8 (<0.001)*		52.1 (<0.001)*		165.0 (<0.001)*	

NCS-R, National Comorbidity Survey Replication; MFF, maladaptive family functioning; OR, odds ratio; CI, confidence interval.

^a Severe impairment defined as a score of 7–10 on any of the four subscales on the Sheehan Disability Scale (SDS) among those with a 12-month diagnosis.

^{b–e} Model 3 controlling for age of onset, time since onset, age category, sex, race, diagnosis category, co-morbid conditions, type of adversity, number of MFF adversities, and number of other adversities.

^c Disruptive behavior disorders are restricted to those ≤44 years of age at interview.

* Significant at the 0.05 level, two-sided test.

multivariate model that includes all CAs, with the exception of family violence and physical abuse (RRs 1.4 and 1.7 respectively). Economic adversity is the only other CA that predicts days out of role in bivariate analysis (RR 1.4), and this association is no longer significant in the multivariate additive model. In the multivariate model that considers only the number of

CAs, RRs generally increase with increasing number of CAs, from an RR of 1.4 associated with having exactly one CA to ORs of 2.9–3.4 among respondents who experienced 6 or ≥7 CAs. The test for the joint effects of the seven number-of-CA predictors is significant [$\chi^2(7) = 77.3$, $p < 0.001$]. In the multivariate model that controls for both type and number of CAs,

Table 3. Simulated effects of childhood adversities (CAs) on severe disorder-related impairment and days out of role in subsamples defined by the cross-classification of disorder type and respondent age at interview

	Overall			Ages 18–29 years			Ages 30–44 years			Ages 45–59 years			Ages ≥60 years		
	Mean _u	Mean _r	Diff.	Mean _u	Mean _r	Diff.	Mean _u	Mean _r	Diff.	Mean _u	Mean _r	Diff.	Mean _u	Mean _r	Diff.
			%			%			%			%			
I. SDS															
Mood	0.64	0.57	11.0	0.59	0.41	30.1	0.70	0.65	7.2	0.63	0.56	12.0	0.63	0.59	5.3
Anxiety	0.48	0.36	25.3	0.49	0.28	41.6	0.50	0.41	18.1	0.50	0.39	21.9	0.35	0.25	26.8
Disruptive behavior ^a	0.42	0.37	13.4	0.38	0.33	11.2	0.46	0.37	18.4	–	–	–	–	–	–
Any disorder	0.59	0.48	19.6	0.58	0.40	30.3	0.63	0.53	15.6	0.60	0.49	17.2	0.49	0.41	16.0
II. Days out of role															
Mood	50.8	46.2	9.1	36.8	32.2	12.4	58.4	54.4	6.8	62.3	57.8	7.2	40.6	33.5	17.6
Anxiety	48.2	38.9	19.2	40.1	29.3	26.8	57.5	45.3	21.1	56.8	49.9	12.1	23.4	21.3	9.1
Disruptive behavior ^a	27.9	22.7	18.8	16.9	13.1	22.5	43.3	35.6	17.9	–	–	–	–	–	–
Any disorder	59.2	48.8	17.4	44.2	34.3	22.5	73.5	60.3	17.9	65.3	58.4	10.5	37.1	30.6	17.6

SDS, Sheehan Disability Scale; Mean_u, mean predicted probability of severe disorder-related impairment in the unrestricted model (Part I) and mean number of days out of role in the unrestricted model (Part II); Mean_r, mean predicted probability of severe disorder-related impairment in the restricted model (Part I), and mean number of days out of role in the restricted model (Part II); Diff. %, percentage difference between the restricted and unrestricted model.

^a Disruptive behavior disorders are restricted to those ≤44 years of age at interview.

MFF CAs predict days out of role [$\chi^2(7)=22.4$, $p=0.002$], but not other CAs [$\chi^2(5)=3.3$, $p=0.65$] or number of CAs [$\chi^2(6)=9.6$, $p=0.14$].

In the interactive multivariate model that controls for type of CAs and number of MFF and other CAs, only the RRs for parent criminality and physical abuse are positive and significant (RR=1.6 for both) (Table 5). A test for variation in RRs is significant, indicating that the RRs are not the same for all CAs [$\chi^2(11)=31.4$, $p<0.001$]. The test for the effects of MFF CAs controlling for number is statistically significant [$\chi^2(7)=38.2$, $p<0.001$] but the test for the effects of other CAs is not [$\chi^2(5)=5.2$, $p=0.39$]. In contrast to the findings for disorder severity based on the SDS, we find no evidence for subadditive interaction for MFF [$\chi^2(5)=2.6$, $p=0.77$] or other CAs [$\chi^2(2)=1.9$, $p=0.38$].

Differential predictive effects on days out of role by class of DSM-IV/CIDI disorders and age at interview

Disaggregation of the most complex multivariate model by disorder class revealed differentiation in the effects of CAs across mood, anxiety and disruptive behavior disorders (Table 5). Forty percent of other CAs were associated with days out of role for both mood and anxiety disorders, with RRs in the range of 1.7–1.8. Of the MFF CAs, physical abuse predicts

days out of role for mood disorders (RR 1.8), and family violence has a strong association with days out of role for disruptive behavior disorders (RR 3.4). The number of CAs is not associated with days out of role for any of the disorder classes. A test of the joint effects of the 21 type and number CA variables on disorder persistence across the three disorder classes is not significant [$\chi^2(63)=38.4$, $p=0.45$], indicating no differential CA effects by disorder type.

Disaggregation of the interactive model by respondent age at interview shows that the effects of CAs on days out of role are significant and similar in magnitude at all stages of the life course: adolescence and early adulthood [ages 18–29, $\chi^2(12)=49.8$, $p<0.001$], mid-adulthood [ages 30–44, $\chi^2(12)=41.3$, $p<0.001$; ages 45–59, $\chi^2(12)=45.4$, $p<0.001$] and later adulthood [ages ≥60, $\chi^2(12)=56.8$, $p<0.001$]. (Results not shown but available upon request.) MFF CAs significantly predict days out of role among all age groups with the exception of respondents aged 45–59, whereas other CAs predict days out of role among all age groups with the exception of respondents aged 30–44.

Population-level predictive effects of CAs on days out of role

We estimated the population percentage of days out of role per year that would not have occurred in the

Table 4. Bivariate and multivariate associations (rate ratios) between childhood adversities (CAs) and days out of role associated with NCS-R/DSM-IV disorders with controls^a

	Bivariate ^b		Multivariate					
			Additive ^c		Number of CAs ^b		Interactive ^d	
	RR	95% CI	RR	95% CI			RR	95% CI
I. MFF								
Parent Mental Illness	1.1	0.8–1.4	0.8	0.6–1.0	–	–	0.8	0.5–1.3
Parent Substance	1.4	1.0–2.0	1.0	0.7–1.3	–	–	1.0	0.6–1.8
Parent Criminal	1.9*	1.3–2.8	1.4	0.9–2.2	–	–	1.6	0.9–3.0
Family Violence	1.9*	1.4–2.5	1.4*	1.0–1.8	–	–	1.4	0.9–2.3
Physical Abuse	2.2*	1.7–2.8	1.7*	1.2–2.3	–	–	1.6	1.0–2.9
Sexual Abuse	1.5*	1.1–2.0	1.1	0.8–1.6	–	–	1.2	0.7–2.1
Neglect	1.8*	1.3–2.5	1.1	0.7–1.7	–	–	1.3	0.7–2.3
$\chi^2(7)$ (<i>p</i> value)			54.9 (<0.001)*				22.4 (0.002)*	
II. Other CAs								
Parent Died	1.5	0.9–2.4	1.2	0.8–2.0	–	–	1.6	0.9–2.9
Parent Divorce	1.1	0.8–1.5	0.9	0.7–1.2	–	–	1.1	0.7–1.5
Other Parent Loss	1.3	0.8–1.9	1.0	0.6–1.5	–	–	1.2	0.8–1.9
Serious Physical Illness	1.3	0.9–1.8	1.2	0.9–1.6	–	–	1.5	1.0–2.1
Family Economic Adversity	1.4*	1.0–1.9	1.1	0.8–1.5	–	–	1.4	0.9–2.2
$\chi^2(5)$ (<i>p</i> value)			3.1 (0.68)				3.3 (0.65)	
$\chi^2(12)$ (<i>p</i> value)			92.9 (<0.001)*				31.4 (0.002)*	
III. Number of CAs								
0	–	–	–	–	–	–	–	–
1	–	–	–	–	1.4*	1.0–1.9	–	–
2	–	–	–	–	1.3	0.9–1.9	0.8	0.3–1.8
3	–	–	–	–	2.4*	1.6–3.5	1.2	0.3–4.1
4	–	–	–	–	1.9*	1.2–2.9	0.7	0.1–3.4
5	–	–	–	–	3.2*	1.9–5.3	0.8	0.1–7.4
6	–	–	–	–	3.4*	2.3–4.9	0.8	0.1–9.4
7	–	–	–	–	2.9*	1.5–5.3	0.4	0.0–10.3
χ^2 (<i>p</i> value)					$\chi^2(7) = 77.3$ (0.001)*		$\chi^2(6) = 9.6$ (0.14)	

NCS-R, National Comorbidity Survey Replication; MFF, maladaptive family functioning; RR, rate ratio; CI, confidence interval.

^a Models were estimated in a Poisson regression framework with one adversity and controls used to predict number of days out of role associated with the outcome disorders.

^b Model controlled for age of onset, time since onset, age category, sex, race, diagnosis category, and co-morbid conditions prior to onset of disorder in question.

^c Model controlled for age of onset, time since onset, age category, sex, race, diagnosis category, co-morbid conditions, and type of adversity.

^d Model controlled for age of onset, time since onset, age category, sex, race, diagnosis category, co-morbid conditions, type of adversity, and number adversities.

* Significant at the 0.05 level, two-tailed.

absence of the CAs if the coefficients in the best-fitting model represent causal effects of CAs (Table 3). The results show that eliminating the effects of CAs would result in a 17.4% reduction of days out of role per year for all disorders, 19.2% for anxiety disorders, 9.1% for mood disorders and 18.8% for disruptive behavior disorders.

Discussion

The results of this study should be interpreted in the light of several limitations. Our assessment of CAs may have been subject to recall bias and was not exhaustive (Green *et al.*, in press). For example, we did not assess emotional abuse, which has been associated

Table 5. Multivariate associations (rate ratios) between childhood adversities (CAs) and days out of role associated with NCS-R/DSM-IV classes of disorders^a

	Mood ^b		Anxiety ^c		Disruptive behavior ^{d,f}		Any disorder ^e	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
I. MFF								
Parent Mental Illness	0.6	0.4–1.0	0.9	0.5–1.7	0.4	0.2–1.3	0.8	0.5–1.3
Parent Substance	1.3	0.8–2.1	0.8	0.4–1.7	0.9	0.3–2.8	1.0	0.6–1.7
Parent Criminal	1.5	0.8–2.6	1.6	0.8–3.0	1.8	0.5–6.3	1.6*	1.0–2.6
Family Violence	1.2	0.7–2.0	1.3	0.8–2.3	3.4*	1.4–8.3	1.4	0.9–2.1
Physical Abuse	1.8*	1.2–2.8	1.6	0.9–2.8	0.7	0.2–2.3	1.6*	1.0–2.5
Sexual Abuse	1.1	0.7–1.6	1.2	0.6–2.6	1.4	0.4–4.2	1.2	0.7–2.1
Neglect	1.1	0.6–1.9	1.1	0.5–2.2	1.6	0.5–5.1	1.2	0.7–2.0
$\chi^2(7)$ (<i>p</i> value)	19.3 (0.007)*		19.3 (0.007)*		14.2 (0.049)*		38.2 (<0.001)*	
$\chi^2(6)$ (<i>p</i> value)	23.3 (<0.001)*		19.8 (0.003)*		12.7 (0.049)*		34.1 (<0.001)*	
II. Other CAs								
Parent Died	1.8*	1.1–2.9	1.9	0.9–3.8	1.2	0.3–4.7	1.6	0.9–2.9
Parent Divorce	1.0	0.6–1.7	1.2	0.8–1.8	1.1	0.5–2.6	1.1	0.7–1.5
Other Parent Loss	1.1	0.7–1.7	1.7*	1.0–2.9	0.7	0.2–2.0	1.2	0.8–1.9
Serious Physical Illness	1.7*	1.1–2.8	1.8*	1.1–3.0	0.7	0.2–1.8	1.5	1.0–2.1
Family Economic Adversity	1.7	0.9–3.2	1.4	0.8–2.4	1.0	0.3–2.9	1.4	0.9–2.2
$\chi^2(5)$ (<i>p</i> value)	8.1 (0.15)		8.5 (0.13)		2.0 (0.85)		5.2 (0.39)	
$\chi^2(12)$ (<i>p</i> value)	60.4 (<0.001)*		38.5 (<0.001)*		33.0 (<0.001)*		71.3 (<0.001)*	
III. Number of MFF CAs								
0–1	–		–		–		–	
2	1.1	0.5–2.3	1.3	0.4–3.9	0.7	0.2–3.1	1.2	0.5–2.9
3	1.3	0.5–3.7	1.6	0.4–6.6	0.6	0.1–5.0	1.6	0.5–5.1
4	0.9	0.2–4.7	1.4	0.2–10.6	0.8	0.0–13.5	1.5	0.3–8.5
5	0.6	0.1–4.7	1.4	0.1–21.7	0.9	0.0–24.7	1.5	0.2–12.5
6	0.6	0.0–6.9	2.2	0.1–58.2	0.6	0.0–67.9	1.6	0.1–23.1
$\chi^2(5)$ (<i>p</i> value)	4.6 (0.460)		2.0 (0.860)		0.9 (0.970)		2.6 (0.77)	
IV. Number of other CAs								
0–1	–		–		–		–	
2	0.9	0.4–1.8	0.8	0.5–1.3	1.1	0.3–4.4	0.8	0.5–1.3
3	0.5	0.2–1.5	0.4	0.1–1.3	2.5	0.2–30.8	0.5	0.2–1.4
$\chi^2(2)$ (<i>p</i> value)	3.0 (0.22)		2.6 (0.28)		1.2 (0.54)		1.9 (0.38)	
$\chi^2(19)$ (<i>p</i> value)	85.1 (<0.001)*		150.8 (<0.001)*		116.5 (<0.001)*		140.4 (<0.001)*	

MFF, Maladaptive family functioning; RR, rate ratio; CI, confidence interval.

^a Models were estimated in a Poisson regression framework with one adversity and controls used to predict number of days out of role associated with the outcome disorders.

^{b–e} Model controlling for age of onset, time since onset, age category, sex, race, diagnosis category, co-morbid conditions, type of adversity, number of MFF adversities, and number of other adversities.

^f Disruptive behavior disorders are restricted to those ≤ 44 years of age at interview.

* Significant at the 0.05 level, two-sided test.

with adult psychopathology in prior research (Brown *et al.* 2007). Our analysis of the effects of CAs on functional impairment was limited to 12-month cases because the SDS and days out of role assessments were administered only to respondents who met criteria for 12-month disorders. These measures were not administered to respondents with substance use

disorders. Because this analysis excluded a substantial portion of lifetime cases, it is likely that our findings underestimate the impact of CAs on impairment related to mental disorders. Respondent reports of days out of role associated with psychiatric disorders are subjective and may have been biased by mood-dependent recall among individuals with current

disorders (Clark & Teasdale, 1982). Because individuals exposed to CAs are more likely to have disorder onsets (Green *et al.*, in press), mood-dependent recall may have been more common among respondents with a history of CAs, potentially inflating our estimates of associations between CAs and days out of role. Finally, individual characteristics (e.g. hopelessness or negative attributional style) probably influenced judgments about the degree to which disorders interfered with role functioning. Because CAs are associated with such characteristics (Alloy *et al.* 2001; Garber & Flynn, 2001), respondents with CA exposure may have reported more functional impairment than respondents without CA exposure, potentially inflating associations between CAs and disorder-related impairment.

Within the context of these limitations, our findings extend the previous literature on CAs and psychiatric morbidity in several important ways. First, we document predictive effects of CAs on disorder-related impairment after controlling for lifetime co-morbidity, providing novel evidence suggesting direct effects of CAs on functional impairment associated with adult disorders. Second, we find evidence for differential effects of CAs on impairment. CAs involving MFF had the strongest effects on impairment, and among the MFF CAs, we find little evidence that one or more types of CAs are more important in predicting disorder-related impairment than others. Prior research has reported strong effects of these specific adversities on psychiatric morbidity and disability (Sareen *et al.* 2005; Tommyr *et al.* 2007), and they also have strong associations with disorder onset and course (Green *et al.*, in press; McLaughlin *et al.*, in press). These CAs may have the greatest effects on impairment because they were ongoing, as opposed to a single event or disruption, or occurred more frequently or for a longer duration than other CAs (Clemmons *et al.* 2007). Alternatively, they may serve as a risk factor for subsequent stressors that increase risk for disorder severity and functional impairment (Horwitz *et al.* 2001; Hazel *et al.* 2008), a possibility that warrants investigation in future research.

Third, we document differential CA effects on impairment across the disorder classes. A majority of CAs predicted impairment based on the SDS when we examined an overall data array. However, these effects resulted from the strong and consistent associations between CAs and impairment related to anxiety disorders. Early adverse experiences may create a cognitive predisposition to perceive events as outside an individual's control, generating a lasting psychological vulnerability to the development of anxiety (Chorpita & Barlow, 1998; Bolger & Patterson, 2001). In particular, this cognitive style may predispose

individuals exposed to CAs to the development of post-traumatic stress disorder in response to subsequent stressors (Brewin *et al.* 2000; Copeland *et al.* 2007), a disorder associated with high levels of impairment (Kessler *et al.* 2005).

In contrast to the SDS findings, we find little evidence for differential CA effects on days out of role associated with the disorder classes. CAs predicted days out of role for mood, anxiety and disruptive behavior disorders with little meaningful variation, indicating an effect of CAs on the duration of functional impairment associated with adult disorders. Overall, our findings that CAs predict impairment across two distinct measures highlights the ongoing clinical significance of adverse childhood experiences at all stages of the life course.

The effects of cumulative MFF CAs on impairment are largely non-additive, consistent with findings on disorder onset and persistence (Green *et al.*, in press; McLaughlin *et al.*, in press). Of the 35 models in which we examined these effects, they were significant, with a negative pattern of ORs approximately 65% of the time for severe impairment on the SDS and approximately 35% of the time for days out of role. This generally subadditive pattern of interactions indicates that the joint effects of multiple CAs are less than the product of their individual ORs, suggesting that impairment increases at a decreasing rate as the number of MFF CAs increases. It is possible that individuals who develop a severely impairing disorder following one CA represent a more vulnerable population, whereas those who do not develop a severe disorder are more resilient. Subsequent CAs thus have a lower incremental effect because they occur to a more resilient population. Together with findings of non-additive effects of MFF CAs on disorder onset and persistence, these results argue against the use of a simple summative index to investigate CA effects (Schilling *et al.* 2008).

Finally, we find differentiation in CA effects on impairment at different points in the life course. The results of our simulations reveal that CAs are most strongly associated with functional impairment and days out of role among young adults (ages 18–29). CA effects are likely to be weaker in older individuals because the effects of CAs attenuate over time (Kessler *et al.* 1997). What is most striking about these results, however, is that CAs predict disorder-related impairment and days out of role at every stage of the life course, with clear effects in late middle age, and significant effects into late life. Because these analyses control for lifetime co-morbidity, removing any indirect effects of CAs on impairment through onset of co-morbid disorders, our findings suggest direct and lasting effects of CAs on impairment at every stage

of the life course. Furthermore, because we also control for temporally prior disorder onsets, we are identifying active effects of CAs in middle and later life, decades after their occurrence in childhood.

We provide evidence for the role of CAs in predicting greater impairment related to anxiety disorders and increased days out of role for mood, anxiety and disruptive behavior disorders. A substantial proportion of mental disorders in the community are attributable to CAs (Afifi *et al.* 2008; Green *et al.*, in press), and our findings suggest that CAs also increase functional impairment across the life course. We build on prior work, which has failed to account for co-morbidity in examining predictive effects of CAs on impairment and has neglected to examine differential CA effects across disorder type. We find evidence for a greater role of MFF CAs in predicting degree and duration of functional impairment than other CAs and for non-additive effects of multiple MFF CAs. Although several mechanisms linking CAs to psychopathology onset have been identified, such as affect dysregulation and insecure attachment (Toth *et al.* 1992; Maughan & Cicchetti, 2002), the extent to which these factors underlie the associations between CAs and disorder severity remains unclear. Further identification of such mechanisms and specification of their associations with functional impairment represents a crucial step in the development of interventions aimed at reducing the mental health consequences of CAs. We believe this work will proceed most clearly and fruitfully by beginning with a clear descriptive characterization of the differential effects of CAs on disorder onset, course and impairment of the type we have provided in the current study and in prior work (Green *et al.*, in press; McLaughlin *et al.*, in press).

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Declaration of Interest

Dr Kessler has been a consultant for GlaxoSmithKline Inc., Kaiser Permanente, Pfizer Inc., Sanofi-Aventis, Shire Pharmaceuticals, and Wyeth-Ayerst; has served on advisory boards for Eli Lilly & Company and Wyeth-Ayerst; and has had research support for his epidemiological studies from Bristol-Myers Squibb, Eli Lilly & Company, GlaxoSmithKline, Johnson & Johnson Pharmaceuticals, Ortho-McNeil Pharmaceuticals Inc., Pfizer Inc., and Sanofi-Aventis.

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