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Adverse Childhood Experience and Vulnerability to Mood and Anxiety Disorders During the COVID-19 Pandemic

Scott B. Patten

University of Calgary, Mathison Centre for Mental Health Education & Research, Cal Wenzel Precision Health Building, 3280 Hospital Drive NW, Calgary, AB, Canada. T2N4Z6. Cuthbertson & Fischer Chair in Pediatric Mental Health. patten@ucalgary.ca; patten@ucalgary.ca, +1-403-220-8752

Abstract: The COVID-19 pandemic had a global impact on mental health. Identification of individuals at higher or lower risk of mental health issues may assist with targeting prevention, support and treatment efforts during future pandemics. Using a Canadian national mental health survey that collected data (March 2022 – December 2022) during the pandemic period, this study examined vulnerability of participants reporting exposure to child abuse or neglect by examining the risk of mood, anxiety and substance use disorders over a one year period. Psychiatric disorders were identified using the Composite International Diagnostic Interview (CIDI). Because childhood adversities are well-known risk factors for mental disorders, the analysis focused on interactions between childhood adversities and pandemic stressors by estimating the relative excess risk due to interaction (RERI). RERIs provide evidence of synergy based on the occurrence of greater than additive interactions. Evidence of synergy was consistently found between physical and sexual abuse and mood and anxiety disorders. There was no such evidence for substance use disorders. Childhood adversities increase vulnerability to stressors and may be useful for identification of individuals with greater mental health needs during public health emergencies.

Keywords: Major depressive disorder; generalized anxiety disorder

1. Introduction

Childhood adversities, including physical and sexual abuse [1], are risk factors for mood and anxiety disorders [2]. Neurobiological mechanisms may underpin this association and may include developmental effects of childhood adversities on the hypothalamic–pituitary–adrenal axis, immune/inflammatory systems, anatomical brain development and epigenetic changes [3]. These effects often persist into adulthood [4,5], including older adulthood [6]. Childhood adversities are associated with differential susceptibility to environmental stressors, such that while they are viewed as risk factors for adult mental disorders in their own right, their impact on risk occurs at least partially through increased reactivity to life events [7-10].

Individuals exposed to childhood adversities may be particularly vulnerable to adverse mental health effects of pandemic stressors. If true, this knowledge would allow better targeting of mental health supports during public health emergencies. Several studies, for example, have suggested that youth, particularly adolescent and young adult women, were at higher risk of mental health difficulties during the pandemic [11-21]. Childhood adversities represent another potential indicator of vulnerabiltiy, a question that has been examined by some prior studies [22-24]. However, these studies only examined whether childhood adversities were associated with mental health outcomes, not whether they interacted synergistically with pandemic-related stressors. Also, none of these studies included measures of depressive disorders, they used symptom ratings, which do not have the same clinical implications as a diagnosis.

The goal of this study was examine whether a set of important childhood adversities, physical and sexual abuse, interacted synergistically with pandemic-related stressors to increase the

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prevalence of mood, anxiety and substance use disorders. In keeping with epidemiological theory about causation, synergy was defined as greater than additive effect [25] and evaluated using the RERI.

2. Materials and Methods

2.1. Data Source

This study used data from the Mental Health and Access to Care Survey (MHACS), a national survey conducted by Canada's national statistical agency, Statistics Canada. Data were collected during an interval spanning March to July 2022 [26]. MHACS included a research diagnostic interview, a Canadian adaptation of the World Mental Health Composite International Diagnostic Interview (CIDI) [27], which was administered via computer assisted telephone interviews. MHACS included measures of various pandemic-related stressors and demographic variables.

The MHACS target population consisted of the household population over the age of 15. This population consists of residents of private dwellings, resulting in the exclusion of residents of institutions, homeless people, people living on indigenous reservations, members of the armed forces and residents of some remote areas. A multiphase sampling strategy produced clustering and unequal selection probabilities, design effects that must be addressed during analysis using specialized variance estimation strategies and sampling weights. Master weights are provided to investigators by Statistics Canada, as well as a set of 1000 replicate bootstrap weights, which are used with a Fay adjustment for accurate variance estimation.

2.2. Assessment of Pandemic-Related Stressors

MHACS included a set of items assessing pandemic-related stressors. Each of these items had binary yes/no scoring. They included:

1. Loss of job or income
2. Difficulty meeting financial obligations or essential needs (e.g., rent or mortgage payments, utilities and groceries)
3. Difficulty accessing required childcare services
4. Difficulty accessing required medications
5. Difficulty accessing required health care services
6. Diagnosed with COVID-19
7. Hospitalized due to COVID-19
8. Severe illness of a family member, friend or someone you care about
9. Death of a family member, friend or someone you care about
10. Feelings of loneliness or isolation
11. Emotional distress (e.g., grief, anger, worry, etc.)
12. Physical health problems (e.g., weight gain or loss, high blood pressure, headaches, sleep problems, etc.)
13. Challenges in personal relationships with members of your household (e.g., children, spouse, parent, grandparents, etc.)
14. Other

Item 11 was not included in the analysis because, within the context of the current study, distress is a component of the outcome rather than an exposure. Item 14 referred to unspecified "other stressors" and was excluded because its unclear meaning. The association of each of the stressors with the mental disorder categories included in the study (see below) was explored in preliminary analyses using logistic regression models including each of the stressors listed above simultaneously in each model. In age and sex-adjusted models with major depression as the dependent variable, financial difficulties, physical health problems and challenges with personal relationships all had statistically significant associations whereas the remainder of stressors did not. Identical results were found for substance used disorders. For anxiety disorders the same three stressors showed signficant associations as did one other, difficulty accessing health care. Based on these analyses, a dichotomous

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variable representing one or more of the three key stressors (financial difficulties, physical health problems and challenges with personal relationships) was derived for use in the analysis.

2.3. Measurement of Abuse-Related Adversities

The MHACS interview included several items from the Childhood Experiences of Violence Questionnaire (CEVQ) [28] as well as two additional items (field tested and implemented in severeal prior Statistics Canada surveys) to assess sexual abuse. In each case, the response options referenced number of occurrences, ranging from 0 to 10+. Inclusion of all of these items as a scale was considered, but confirmatory factor analysis using a structural equation model having a single underlying latent characteristic (abuse) had a poor fit (Root Mean Squared Error of Approximation 0.334, Comparative Fit Index 0.541, Tucker-Lewis Index 0.235). However, a two factor model representing physical and sexual abuse by separate but correlated factors had a good fit (Root mean squared error of approximation 0.064, Comparative fit index 0.985, Tucker–Lewis index 0.972). Therefore, two separate scales were created, one for physical abuse and one for sexual abuse, noting that items for witnessing violence between adults in the household were included in the physical abuse scale along with items referring to personal receipt of physical abuse, a decision supported by the results of the factor analysis. Cronbach's alpha for the physical and sexual abuse scales were: 0.76 and 0.84, respectively.

Because calculation of the RERI requires a categorical exposure variable, these scales were dichotomized at the 90th percential for calculation of this parameter.

2.4. Assessment of Mental Health

As noted above, a Canadian adaptation of the CIDI was used in the MHACS survey. The CIDI included assessment of Major Depressive Episode, Social Anxiety Disorder, Generalized Anxiety Disorder and Substance Use Disorders. This version of the CIDI interview is based on DSM-IV rather than DSM-5 diagnostic criteria. The DSM-5 revision did not include substantial changes to the DSM-IV modules for Major Depression, Social Anxiety Disorder or Generalized Anxiety Disorder, however, DSM-5 replaced the DSM-IV concepts of Substance Abuse and Dependence with a single diagnoses, Substance Use Disorder, subcategorized as mild, moderate or severe [29]. The current study combined the Abuse and Dependence categories into a single Substance Use Disorder category, roughly approximating the DSM-5 approach. This category included disorders related to alcohol, cannabis and other drugs (not including nicotine). The CIDI generates both lifetime and past-year diagnoses. The current study used past year diagnoses, ensuring that the disorders were present during the pandemic time frame, and avoiding concerns about the validity of lifetime diagnoses, e.g. [30].

2.5. Statistical Analysis

The analysis used Stata 18 [31], which is the first version of Stata to support RERI estimation. The RERI estimates were derived from logistic regression equations, which incorporated the master survey weights. However, the recommended variance estimation procedures could not be employed in Stata's "reri" command. For this reason, greater than additive interactions were also explored where possible using generalized linear models (binomial family, identity link) in order to explore the implications of possible underestimation of the variance of the RERI. The analysis took place at the Prairie Regional Research Data Centre at the University of Calgary.

3. Results

The selected MHACS sample included n = 39,485 households identified by the sampling strategy. After application of two stages of selection (household and individual respondent, one from each sampled residence), the final sample size was 9,861, resulting in an overall response rate of 25%. However, the weighted sample was representative of the Canadian household population despite the low overall response rate. A tabulation of (weighted) features of the MHACs sample is presented in Table 1.

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Table 1. Weighted sample characteristics, MHACS.

Age (mean, in years)	47.6
Sex at birth	
Male	48.9%
Female	51.1%
Pandemic-related stressors	
Loss of job or income	18.9%
Difficulty meeting financial obligations or essential needs	13.5%
Difficulty accessing required childcare services	4.1%
Difficulty accessing required medications	4.60%
Difficulty accessing required health care services	19.2%
Diagnosed with COVID19	22.1%
Hospitalized due to COVID19	0.5%
Severe illness of a family member, friend or someone you care about	22.7%
Physical health problems	22.5%
Challenges in personal relationships with members of your household	18.5%
Childhood adversity (or more experiences before age 16 years)	
Saw/heard parent hit other adult in your home	15.0%
Slapped/hit/spanked	40.9%
Pushed/grabbed/shoved/threw things at you	20.2%
Physically attacked	9.8%
Forced unwanted sexual activity	6.1%
Forced unwanted sexual touching	10.6%
Any childhood adversity (one or more of above)	49.2%

The past-year prevalence of the targeted conditions in MHACS has been reported previously [32]. Past year major depression prevalence was 7.6% (95% CI 6.9 - 8.3), generalized anxiety disorder was 5.2% (95% CI 4.7 - 5.8), social anxiety disorder was 7.1% (95% CI 6.4 – 7.7) and substance use disorders, 16.7% (95% CI 15.7 – 17.7) for alcohol, 6.8% (95% CI 6.2 – 7.6) for cannabis, and 3.6% (95% CI 3.1 – 4.3) [32] for other drugs.

Both forms of abuse were associated with all three types of disorders, see Table 2. Age and sex did not confound these associations as the adjusted and unadjusted estimates in Table 2 are similar to one another.

Table 2. Odds ratios for physical and sexual abuse as risk factors for major depression, anxiety disorders and substance use disorders*.

	Physical abuse		**Sexual abuse**	
	Crude OR (95% CI)	Adjusted OR** (95% CI)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Major depression	1.14 (1.11 - 1.17)	1.16 (1.13 - 1.19)	1.24 (1.17 - 1.32)	1.26 (1.18 - 1.34)
Anxiety disorders	1.11 (1.09 - 1.14)	1.14 (1.11 - 1.16)	1.22 (1.12 - 1.33)	1.32 (1.21 - 1.45)
Substance use disorders	1.09 (1.06 - 1.12)	1.10 (1.07 - 1.13)	1.22 (1.14 - 1.30)	1.23 (1.15 - 1.32)

* p-values associated with all of the reported ORs < 0.001. **adjusted for sex and age, the latter included as a continuous variable in the model.

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Table 2 presents odds ratios for the both physical and sexual abuse scales. The scale scores are included in these models as continuous variables such that the OR depicts a change in the odds of each disorder for each unit change in the scale score.

The composite pandemic-related stressor variable was also found to be associated with each of the mental disorders. Age and sex adjusted odds ratios for major depression (OR = 4.14, 95% CI 3.30 - 5.19), anxiety disorders (OR = 3.25, 95% CI 2.68 - 3.95) and substance use disorders (OR = 2.32, 95% CI 1.71 - 3.14) were all significantly elevated.

In models including both the indicator for pandemic-related stress and for both forms of abuse simultaneously, all of the ORs remained signficiantly elevated.

Analysis of the age and sex adjusted RERIs showed subtantial and statistically significant greater than additive effects for major depression and anxiety disorders, see Table 3.

Table 3. RERI values for physical and sexual abuse interacting with pandemic stressors.

	Physical abuse & pandemic stress RERI (95% CI, p-value)	Sexual abuse & pandemic stress RERI (95% CI, p-value)
Major depression	5.29 (1.99-8.59, p = 0.002)	4.32 (1.44 – 7.21) p = 0.003
Anxiety disorders	2.77 (0.66 - 4.88, p = 0.010)	3.31 (1.38 – 5.23) p = 0.001
Substance use disorders	0.28 (-1.60 – 2.16) p = 0.29	2.24 (-0.03 - 4.53) p = 0.053

Because of concerns about the lack of control for clustering in the RERI analyses, generalized linear models were also fit, as described above. These models included the recommended replicate bootstrap method to ensure correct estimation of the standard errors. To examine interactions on an additive scale, these models used the identity link function. The binomial family was specified because of the binary outcome. Models containing the exposures, interactions and age and sex did not converge, so the same models were fit without the age and sex adjustments, which seemed unimportant as sources of confounding at any rate, e.g. see Table 2. In models containing physical abuse, pandemic stressors and the interaction, coefficients for the interaction term were signficant when the dependent varaible was past year major depression ($p = 0.002$) and when it was anxiety disorders ($p = 0.022$), but in keeping with the RERI analysis, not for substance use disorders ($p = 0.814$). The same result was seen in models including sexual abuse rather than physical abuse, where p-values for the interaction terms were: $p = 0.004$, $p < 0.001$ and $p = 0.061$, respectively.

4. Discussion

The connection between statistical risk additivity and insight into biological causation arises from the sufficient-component cause of etiology. This model, originally put forward by Rothman, states that most health issues are caused by multiple combinations of component causes, that together comprise causal mechanisms for those health issues [33]. Both childhood adversities and life stressors are known to contribute to the etiology of mental disorders, but neither is in itself a sufficient cause since some persons exposed to these factors do not develop mental disorders. These exposures may combine with other unknown factors to comprise a set of causal mechanisms. If no causal mechanisms involve both factors acting together, then the risk of disease in the jointly exposed group will arise from various mechanisms that involve each of them separately and will be equal to the sum of the individual exposures. On the other hand, if there are causal mechanisms that require both child abuse and adult stressors, the risk of disease in people with the joint exposure will be greater than the sum of the individual exposure groups. In essence, exceeding additivity indicates that some

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people exposed to pandemic-related stressors would only have developed a mood or anxiety disorder if they had earlier experienced abuse, and some people with a history of abuse would only have experienced a mood or anxiety disorder if they were exposed to pandemic stressors.

Perhaps the most widely discussed biological mechanism interactions with childhood adversities is Meaney's concept that early life experience can "program" stress responses through epigenetic mechanisms, potentially leading to elevated vulnerability to mental disorders with subsequent stress exposures [34]. This idea has since been extended by studies examining multiple neurobiological sequelae of adversity and abuse that may contribute to sensitization of stress response systems [35,36]. While epidemiological data cannot confirm such hypotheses, these results confirm the expected existence of greater than additive synergy in a general population sample.

A key finding from this study is the specificity of the greater than additive synergy for depression and anxiety disorders. Although child abuse was a risk factor for substance use disorders, as were pandemic-related stressors, there was no evidence of greater than additive synergy, suggesting that the mechanisms linking these two exposures to these outcomes are independent of one another. This observation may help to inform neurobiological hypotheses about the etiology of substance use disorders.

From a clinical and public health perspective these results may be useful for preparedness for future public health emergencies. Even though child abuse is a risk factor for many disorders, the impact of future pandemics may be especially strong in clinical settings managing mood and anxiety disorders due to the synergisms reported here. These results suggest that demand for substance use disorders may increase during pandemics, but that this would occur proportionally to increased stress exposures. Given that the current study reports epidemiological data, such interpretations should be viewed as hypotheses to be confirmed or refuted by future studies.

There may also be implications of these results for primary prevention. The three types of pandemic-related stressor that were associated with these disorders are all potentially modifiable: financial hardships, physical health issues, and relationship issues. Programs designed to reduce the impact of such stressors can be expected to lessen the impact of future pandemics. Given the reported synergies, it will be important that people with a history of child abuse have access to such programs and that such programs are able to deliver trauma-informed care.

The study has several limitations. One of these is the cross-sectional nature of the MHACS. The concepts of etiology and interaction are usually based on incidence or risk rather than the prevalence estimates. In this case, while one expects that child abuse would usually precede the emergence of mental disorders, this may not always be the case. The timing of pandemic-related stressors in relation to the mental health outcomes can similarly not be clarified by the cross-sectional data used in this study. All of the measures used in the current study were self-reported items and modules, which are subject to error, and measurement error has the potential to introduce bias into the studies estimates. Similarly, despite the use of sophisticated sampling weights that included adjustments for non-response, the low (25%) overall response rate creates a vulnerability to selection bias.

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Institutional Review Board Statement: According to Article 2.2 of the Canadian Tri-council Statement on Research, this research was exempted from Ethics Review as the data are made available through a mechanism set out by legislation or regulation and that is protected by law, see https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2022.html.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The dataset used in this analysis cannot be released publicly by investigators. However, access can be obtained through an application process, details may be found here: https://www.statcan.gc.ca/en/microdata/data-centres/access .

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