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Prediction of depressive symptoms in young adults by polygenic score and childhood maltreatment: Results from a population-based birth cohort

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Abstract

Childhood maltreatment is linked with later depressive symptoms, but not every maltreated child will experience symptoms later in life. Therefore, we investigate whether genetic predisposition for depression (i.e., polygenic score for depression, PGS_{DEP}) modifies the association between maltreatment and depressive symptoms, while accounting for different types of maltreatment and whether it was evaluated through prospective and retrospective reports. The sample included 541–617 participants from the Quebec Longitudinal Study of Child Development with information on maltreatment, including threat, deprivation, assessed prospectively (5 months–17 years) and retrospectively (reported at 23 years), PGS_{DEP} and self-reported depressive symptoms (20–23 years). Using hierarchical linear regressions, we found that retrospective, but not prospective indicators of maltreatment (threat/deprivation/cumulative) were associated with later depressive symptoms, above and beyond the PGS_{DEP}. Our findings also show the presence of gene–environment interactions, whereby the association between maltreatment (retrospective cumulative maltreatment/threat, prospective deprivation) and depression was strengthened among youth with higher PGS_{DEP} scores. Consistent with the Diathesis-Stress hypothesis, our findings suggest that a genetic predisposition for depression may exacerbate the putative impact of maltreatment on later depressive symptoms, especially when maltreatment is retrospective. Understanding the gene–environment interplay emerging in the context of maltreatment has the potential to guide prevention efforts.

Keywords: Childhood maltreatment; depression; polygenic risk score; prospective; retrospective

Introduction

Depression is a common disease among young adults and a recognized leading cause of disability globally, affecting up to 21% individuals aged 18–25 years (Ferrari et al., 2022; Thapar et al., 2022; Villarroel & Terlizzi, 2020; WHO, 2023). Symptoms of depression tend to emerge in childhood, to steadily increase during adolescence, and to peak in early adulthood (Thapar et al., 2022).

Adverse life events, particularly childhood maltreatment, occurring in early life, are well-documented risk factors for depression (LeMoult et al., 2020). Childhood maltreatment, encompassing any form of abuse (e.g., physical, sexual, or psychological abuse) or neglect (e.g., physical, emotional neglect) by a caregiver (Leeb et al., 2008, p.11), has been prospectively

associated with a range of mental health problems, including depression (Danese & Widom, 2020; Kessler et al., 2010; Spatz Widom et al., 2007; Strathearn et al., 2020). Furthermore, individuals with a history of childhood maltreatment are more likely to be diagnosed with depression, to manifest more severe symptoms (Humphreys et al., 2020), and to have more treatment-resistant depression (Nanni et al., 2012).

Gene–environment interactions

While some individuals report depressive symptoms following experiences of childhood maltreatment, others do not (Jaffee, 2017). This interindividual variability may be partly accounted by genetically inherited vulnerability for depression (Kendall et al., 2021). Depressive symptoms have been found to be moderately heritable (ranging between 30-50%) (Kendall et al., 2021). This raises the possibility that interindividual variability may be a result of the interaction between genetic and environmental influences, such as genetic vulnerability for depression and childhood maltreatment (Arnau-Soler et al., 2019; Belsky et al., 2007). There is a need to further examine the potential role of genetic

factors in either exacerbating or buffering the occurrence of depressive symptoms in the aftermath of adversity (i.e., gene–environment interactions: GxEs). Gene–environment interactions refer to the dynamic interplay between genetic factors and environmental influences, whereby the strength of the association linking pathogenic environments on disease varies according to individual's genetic predispositions (Ottman, 1996). Among the many form GxEs may take (e.g., Differential Susceptibility, Social Push) (Boardman et al., 2013), the Diathesis-Stress model is the most commonly reported in the context of depression. This model proposes that mental health problems arise from the interaction between dispositional factors (diathesis, e.g., genes) and environmental factors (stress, e.g., maltreatment). Thereby, individuals with genetic vulnerabilities for depression may be more at-risk for the depressogenic effect of adverse environments. Yet, this diathesis is hypothesized to remain latent in the absence of adversity (Broerman, 2020).

Prior studies that examined the independent and joint roles of genetic vulnerability and childhood maltreatment in depressive symptoms have mainly focused on single candidate genes, with inconsistent findings (McIntosh et al., 2019; Ripke et al., 2013). For instance, a systematic review conducted by Li et al., (2020) on studies testing GxE between childhood maltreatment and candidate genes (i.e., SLC6A4, CRHR1, BDNF, FKBP5, CREB1, NTRK2, OXTR, IL 6, CRP, TNF, TNFR1, TNFR2, IL1B) in the prediction of depression showed mixed findings ($n = 29$ studies). For the serotonin transporter (i.e., 5-HTTLPR; $n = 15$ studies) gene, two out of five studies reported a significant interaction with childhood maltreatment predicting later depressive *symptoms* among those carrying the S allele, and eight of out ten studies reported such an interaction for a *diagnosis of major depression*. Other genetic variants more consistently interacted with maltreatment, including the variant CREB1-rs2253206 and the variant CRHR1 haplotypes, which respectively strengthened and attenuated depressive symptoms in the presence of childhood maltreatment. Candidate gene approaches have strengths, such as focusing on genes that are involved in known biological processes related to depression (i.e., hypothesis-driven approach); but indirectly exclude all other potential polymorphisms. The issues of limited power and low estimates of variance explained constraint current evidence related to the candidate gene approach in the prediction of complex polygenic disorders (i.e., involving several genes), such as depression (Belsky & Israel, 2014).

The consideration of genome wide association studies (GWAS) has become widespread to account for genetic variants associated to phenotypes of interest. Information derived from GWAS can be used to calculate polygenic risk scores (PGS), which address the highly polygenic nature of depression in GxEs. PGS represent the participants' cumulative genetic propensity for a complex phenotype (e.g., depressive symptoms) encompassing several common single nucleotide polymorphisms (SNPs) located across the genome. These genetic variants are weighted according to the strength of their association with the phenotype according to previously documented GWAS (Abdellaoui et al., 2023; Howard et al., 2019; McIntosh et al., 2019). However, the few studies that have investigated the interplay between the polygenic risk for depression (PGS_{DEP}) and childhood maltreatment in the prediction of depression found inconsistent results. For instance, Peyrot et al. (2014) reported that retrospective childhood maltreatment was associated with higher risk for major depressive disorder only for participants with higher PGS_{DEP} scores,

supporting the Diathesis-Stress model. Conversely, Mullins et al. (2016) found that higher genetic risk was associated with major depression only in the absence, rather than in the presence, of childhood maltreatment. This result echoes the Social Push model (Boardman et al., 2013), whereby individuals carrying lower genetic risk for depression may lose their genetic advantage for lower levels of depression in the presence of childhood maltreatment. A meta-analysis of nine cohorts from the Psychiatric Genomics Consortium ($n = 5765$, <18 years), including those from Mullins et al. (2016) and Peyrot et al. (2014), did not find a consistent pattern of an interactive contribution of retrospectively reported childhood maltreatment and the PGS_{DEP} (i.e., diagnosed based on DSM-IV or self-reported symptoms) (Peyrot et al., 2018). However, the evidence of GxE (Mullins et al., 2016; Peyrot et al., 2014) taking distinct forms (i.e., interactions in different directions) certainly complicates the overall interpretation of these findings.

Several factors may account for these inconsistencies. Earlier GWAS (Ripke et al., 2013) have tended to consider genetic variants associated with a diagnosis of major depressive disorder, while more recent GWAS (Howard et al., 2019; Wray et al., 2018) have included continuously distributed depression phenotypes, especially in the general population (e.g., self-reported symptoms). The PGS derived from these more recent GWAS may be more predictive of the continuum of depressive symptoms, including subclinical levels. More recent GWAS also include a larger number of participants, increasing the power to detect variants with smaller effects (Howard et al., 2019; Wray et al., 2018), including those that may interact with adverse experiences. For instance, Wray et al. (2018) (135, 458 cases and 344, 901 controls) uncovered 44 genetic variants (SNP-based heritability $= 0.087$, SE $= 0.004$) associated with major depression based on self-reported depressive symptoms in the general population. Howard et al. (2019) (246, 363 cases and 561, 190 controls) found 102 genetic variants (SNP-based heritability $= 0.089$, SE $= 0.003$) associated with diagnosed major depression, self-reported depressive symptoms, or help-seeking for depressive symptoms. One study investigating the GxE between PGS_{DEP} (based on Wray et al., 2018) and childhood abuse on depression in clinical and epidemiological adolescent cohorts found independent effects of childhood abuse and PGS_{DEP} to depression, but no significant interaction effect (Halldorsdottir et al., 2019). More studies relying on recent GWAS are needed to further examine if GxE arise between PGS_{DEP} and childhood maltreatment in the prediction of depressive symptoms.

Assessment and types of childhood maltreatment

Another factor contributing to the inconclusive set of findings in GxE studies is the inconsistency in measuring childhood maltreatment (e.g., single vs. repeated, dimensional vs cumulative, and types of maltreatment). Prior studies that have investigated the role of polygenic risk in the context of maltreatment (Mullins et al., 2016; Peyrot et al., 2018) have exclusively relied on retrospective reports. However, associations between maltreatment and psychopathology have been shown to differ depending on whether maltreatment was evaluated through prospective versus retrospective reports (Baldwin et al., 2019; Danese & Widom, 2020). Notably, retrospective reports are more strongly associated with psychopathology, including depression, than prospective reports, perhaps due to the retrospective evaluation being done in temporal proximity to the outcome, in addition to potential methodological

biases (e.g., shared method variance) (Danese & Widom, 2020). In addition, a weak concordance between prospective and retrospective estimates has been reported (continuous or dichotomous) (Baldwin et al., 2019; Danese & Widom, 2020; Scardera et al., 2023), which raises the question on whether we should anticipate differential GxE findings with these distinct measures. To the best of our knowledge, no studies have tested this possibility.

Childhood maltreatment encompasses several subtypes (e.g., physical abuse, sexual abuse, and neglect). However, existing studies have typically focused on cumulative maltreatment (Lacey et al., 2020; Putnam et al., 2013), while others investigated isolated subtypes (Jackson et al., 2019). More recently, a dimensional model of adversity and psychopathology proposes to examine subtypes according to two dimensions: deprivation and threat (McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). While deprivation refers to the "absence of expected environmental inputs" (e.g., neglect), threat refers to the presence of "an atypical or unexpected experience characterized by actual or threatened death, injury [. . .] or other harm to one's physical integrity" (e.g., abuse) (McLaughlin et al., 2014). Both dimensions are hypothesized to affect development through distinct cognitive, emotional, and neurophysiological mechanisms (McLaughlin et al., 2019). While both deprivation- and threat-based exposures have been associated with mental health outcomes, including depression (Geoffroy et al., 2016; Humphreys et al., 2020; Lin et al., 2023; Schäfer et al., 2023; Wang et al., 2022; van Dam et al., 2015), many studies found stronger associations for threat-based (e.g., (Schäfer et al., 2023; Wang et al., 2022)), but not all (Lin et al., 2023). Moreover, experiences of threat and deprivation may differentially affect gene expression, including DNA methylation (Parade et al., 2021; Sarro et al., 2014; Sumner et al., 2019). To the best of our knowledge, no prior studies have yet tested whether differential GxE findings emerge in the prediction of depressive symptoms according to these two dimensions of childhood maltreatment.

The objectives of this study were threefold: (1) to test whether prospective and retrospective measures of childhood maltreatment (i.e., cumulative maltreatment, threat or deprivation) and PGS_{DEP} independently predict depressive symptoms in young adults, (2) to examine whether associations differ by threat and deprivation experiences, and (3) examine whether PGS_{DEP} moderated the association between childhood maltreatment and depressive symptoms. Since no prior studies had examined this GxE according to prospective and retrospective, as well as threat and deprivation, no a priori hypothesis were posited.

Methods

Participants

Participants were from the Québec Longitudinal Study of Child Development (QLSCD), an ongoing population-based cohort, managed by Institut de la Statistique du Québec, collecting data annually or biennially from 2120 singletons born in the Canadian Province of Québec in 1997–1998. When the participants were 10 years old, blood or saliva samples were collected from 992 participants and 978 were successfully genotyped, from which 721 passed quality control and could be used for the calculation of the PGS_{DEP} score (see Appendix S1 for further details). From those 721 individuals, participants with measures of childhood maltreatment and depressive symptoms were included in the final analyses (*n* ranging from 541 to 617). Each data collection was approved by Ethical committees of Institut de la Statistique du Québec and the

CHU Sainte-Justine Hospital Research Centre. The 2021 Special Round data collection (23 years) was also approved by the Douglas Research Center Ethics Committee. Written informed consent or assent was obtained from participants (and/or their parents, when minor) at each data collection. Further details about the cohort can be found online at https://jesuisjeserai.stat.gouv.qc.ca (Orri et al., 2021).

Measures

Childhood maltreatment
Prospective measures. The QLSCD did not administer an existing childhood maltreatment questionnaire to assess prospective childhood maltreatment. Our prospective indices of childhood maltreatment relied on information collected prospectively, from infancy to the end of adolescence (14 time points), across multiple informants (mothers, children, teachers, and home observations) regarding the many experiences the child may have been subjected to. Following a procedure described by Scardera et al. (2023), relevant information collected over time was first screened by two independent raters based on definitions from the Quebec Youth Protection Act (2021) and supporting resources (Grounds for Reporting a Situation, 2022). From the 462 items considered for inclusion, two maltreatment experts independently selected these items and identified cutoffs for dichotomization, while considering the developmental period of the child. The process of item selection and identifying cutoff scores was guided by the premise that a single item could signal concerns about potential maltreatment. For example, the question "how often do you tell him/her that he/she is bad or not as good as others?" was recoded at 5 months as "absence" if parents replied "never" or "about once a week or less," while responses of "a few times a week" or more were deemed "probable maltreatment." At 17 months, however, the same item was recoded as "absence" if parents answered "never," "about once a week or less," or "a few times a week," and considered "probable maltreatment" if parents reported saying it "once or twice a day" or more (Scardera et al., 2023). Any disagreements between the maltreatment experts were then resolved, and 251 items were included. Three indicators of probable maltreatment have been selected for this study, including (1) *cumulative maltreatment* by the end of adolescence represented the exposure to various types of maltreatment (physical abuse, sexual abuse, psychological abuse, emotional neglect, physical neglect, and family violence; 0, 1, 2, or 3+ types of maltreatment); (2) the presence (vs. absence) of maltreatment taking the form of *threat* (physical, sexual, or psychological abuse, and family violence from birth to 17 years); and (3) the presence (vs. absence) of maltreatment taking the form of *deprivation* (emotional or physical neglect). The category of supervisory/educational neglect was excluded from our indicators given the high rate of endorsement (Scardera et al., 2023).

Retrospective measures. Self-reported childhood maltreatment was collected at age 23 years using a seven-item scale assessing physical abuse, sexual abuse, psychological abuse, emotional neglect, physical neglect, and exposure to domestic violence. All subtypes of retrospective maltreatment, except sexual abuse, were measured using items from the Adverse Childhood Experiences International Questionnaire (ACE-IQ) (Christoforou & Ferreira, 2020), developed by the World Health Organization to measure adverse experiences that occur before 18 years of age. Exposure to

sexual abuse was evaluated using two items derived from the recombination of the six items from the Early Trauma Inventory Self-Report Short Form (ETI) (Bremner et al., 2007). The ACE-IQ and ETI reliably measure childhood maltreatment (Bremner et al., 2007; Tarquinio Camille et al., 2023). Similar coding procedures for the retrospective variables (cumulative, threat, deprivation) as for the prospective measures.

Polygenic risk score for depression. We calculated a PGS$_{DEP}$ based on previously reported GWAS (Howard et al., 2019) using PGS-CS software. PGS-CS is a Bayesian estimation method that applies a continuous shrinkage prior to SNP weighting (Ge et al., 2019). The PGS-CS approach has been shown to be superior to other methods (e.g., clumping and thresholding) (Ge et al., 2019). We used a global shrinkage parameter phi set to 0.01. PGS$_{DEP}$ was computed by using a linear combination of the genotype data and the adjusted summary statistics in PLINK 1.90 (Chang et al., 2015). PGS$_{DEP}$ was adjusted for population stratification using the first ten principal factor components derived from the pairwise genetic relationship matrix during quality control. The resulting standardized residuals were used in all analyses.

Depressive symptoms at 20–23 years. Past-week depressive symptoms were evaluated at 20, 22, and 23 years using the Center for Epidemiological Studies-Depression scale (CES-D) short-form (Poulin et al., 2005; Radloff, 1977) administered through a web-based questionnaire link. The CES-D short form includes 12 statements (e.g., "*I felt depressed*"). Response options ranged from 0 = *rarely/none of the time* to 3 = *most/all of the time* with total scores ranging from 0-36. Higher response options indicated higher symptom severity. Cronbach's alpha was .85, .87 and .87 at 20, 22 and 23 years, and correlations across measurement points were moderate to high ($r_s = .511$–$.667$ $p < .001$). To capture overall depressive symptoms in early adulthood, we computed a mean score, which serves as our primary outcome variable.

Potential confounders. All regression analyses were adjusted for sex and socioeconomic status (averaged from 5 months to 5 years; 6 assessments) (Willms & Shields, 1996), known for its association with childhood maltreatment (Table S1) (Gallo et al., 2018; Merrick et al., 2017; WHO, 2022). To account for possible gene–environment correlations (rGE), whereby genetic influences may be confounded with the exposure to specific environments (Quinn & D'Onofrio, 2020), we also examined whether each of the maltreatment indicators was associated with the PGS$_{DEP}$ according to a liberal threshold ($p < .10$). When associations were detected, standardized residuals accounting for this covariance were derived prior to the main analyses.

Statistical analyses

First, we used t-tests and chi-square tests to evaluate if mean differences on key child/family characteristics were present between participants with and without a valid PGS score. Second, we examined the bivariate associations between the childhood maltreatment indicators, PGS$_{DEP}$, and depressive symptoms, which allowed to examine for the presence of possible gene–environment correlations. Third, independent hierarchical linear regressions tested the main and interaction effects of the maltreatment indicators and PGS$_{DEP}$ on depressive symptoms by

first including one of the maltreatment indicators (step 1), PGS$_{DEP}$ (step 2), and their interaction term (step 3). Analyses were performed separately for each prospective and retrospective indicator of maltreatment, and all analyses were adjusted for sex and socioeconomic status. All continuous variables were converted into z-scores to ease interpretation. Significant interactions were illustrated by using the simple slopes analysis, which depicts the association between childhood maltreatment and depressive symptoms at the mean and at one standard deviation above and below the sample's PGS$_{DEP}$ mean.

Results

Participants excluded (vs. included) in the study subsample were more likely to be males, have higher internalizing symptoms at 29 months, have younger mother at birth, come from non-intact families of lower socioeconomic status at age 5 months (Table S2). To adjust for selective attrition that may have affected our study sample, we conducted analyses with and without inverse probability weights, representing participants' probabilities of being included in the study sample conditional on sex, socioeconomic status, family structure, internalizing symptoms at 29 months, and maternal age at birth. The general pattern of results with and without weights did not differ (data not shown); thus, only the weighted results are presented here. The descriptive characteristics for key variables of interest (child/family characteristics, prospective and retrospective maltreatment indicators, PGS$_{DEP}$, and depressive symptoms from 20 to 23 years) are presented in Table 1. Overall, our participants came from an intact family of average socioeconomic status and were of Canadian descent. Interestingly, 67% of the sample was flagged as exposed to any type of prospectively measured maltreatment. Specifically, about one third of sample was flagged as exposed to one type of maltreatment, and another third was flagged as exposed to 2, 3 or more types of maltreatment (cumulative score distribution: 0 (32.9), 1 (35.6), 2 (20.8), 3+ (10.6)) (Table 1). Retrospective self-reports were obtained across seven items and had lower estimates of any maltreatment (cumulative distribution score: 0 (71.9), 1 (18.7), 2 (5.1), 3+ (5.1)) compared to prospective reports.

Bivariate associations showed that PGS$_{DEP}$ had a low correlation with each prospective maltreatment (cumulative: $r = .162$, $p < .001$; deprivation: $r = .122$, $p = .002$; threat: $r = .084$, $p = .029$) and retrospective maltreatment indicator (cumulative: $r = .138$, $p < .001$; deprivation: $r = .108$, $p = .008$; threat: $r = .104$, $p = .010$), suggesting the possibility of rGE and the need to account for them in analyses. PGS$_{DEP}$ was also significantly associated with depressive symptoms at age 20–23 years ($\beta = .146$, $p < .001$, adjusted $r^2 = .019$). Finally, the associations between prospective maltreatment and depressive symptoms were small and non-significant ($r_s = .040$–$.074$, $p_s = .022$–$.444$), while moderate significant associations were noted for retrospective maltreatment ($r_s = .262$–$.369$, $p_s < .001$).

Additional analyses revealed low correlations between deprivation and threat when prospectively recorded ($r = .171$, $p < .001$) and retrospectively recorded ($r = .295$, $p < .001$), suggesting distinct experiences. Similarly to what was shown in the larger QLSCD sample (Scardera et al., 2023), the agreement between the prospective and retrospective reports of maltreatment were generally small and varied in magnitude across indicators: cumulative maltreatment ($\kappa = .056$, $p = .020$), deprivation ($\kappa = .056$, $p = .097$), and threat ($\kappa = .083$, $p < .001$).

Table 1. Descriptive statistics for study's key variables

	total N	n(%) or M(SD)
Child/Family characteristics (age 5 months)		
Male, No., (%)	721	323(44.8)
Non-Canadian[a]	715	144(20.1)
Non-intact family (single or blended), No., (%)	718	128(17.8)
Family socioeconomic status	719	0.11(.95)
PGS-depression (range 113.98–115.56)	721	114.76(.25)
Depressive symptoms at 20–23 years (range 0–31)	647	9.85(5.81)
Prospective maltreatment		
Cumulative Maltreatment	541	
0		178(32.9)
1		193(35.6)
2		112(20.8)
3+		58(10.6)
Any lifetime deprivation	592	271(45.9)
Any lifetime threat	617	347(56.2)
Retrospective maltreatment		
Cumulative Maltreatment	585	
0		420(71.9)
1		109(18.7)
2		25(4.3)
3+		30(5.1)
Any lifetime deprivation	584	87(14.9)
Any lifetime threat	585	120(20.5)

Data were compiled from the final master file of the Quebec Longitudinal Study of Child Development (1998–2021), © Gouvernement du Quebec, Institut de la Statistique du Quebec. All variables are based on maximum available samples.
[a]Non-Canadian refers to ancestry of non-Canadian descent.

Main and interaction effects of cumulative maltreatment with the PGS_DEP

Prospective reports of cumulative maltreatment significantly predicted depressive symptoms at 20–23 years ($\beta = .101$, $p = .024$), while controlling for socioeconomic status and sex (Table 2). This association was also significant and stronger in magnitude when maltreatment was reported retrospectively ($\beta = .322$, $p < .001$). However, only retrospective reports of cumulative maltreatment remained significantly associated with depressive symptoms once PGS_DEP was added to the regression model ($\beta = .322$, $p < .001$). A significant interaction between the retrospective cumulative maltreatment and PGS_DEP was also found ($\beta = .094$, $p = .031$). That is, as participants' scores of cumulative maltreatment increased, their depressive symptoms showed a steeper increase if they carried a high genetic risk for depression (at $+ 1$ SD) in comparison to those who were at the sample's mean or lower levels (-1 SD) (see Figure 1). No significant interaction was noted for prospective cumulative maltreatment ($\beta = .092$, $p = .152$).

Main and interaction effects of deprivation with the PGS_DEP

The presence of any experiences of deprivation, as measured retrospectively, was associated with depressive symptoms at 20–23
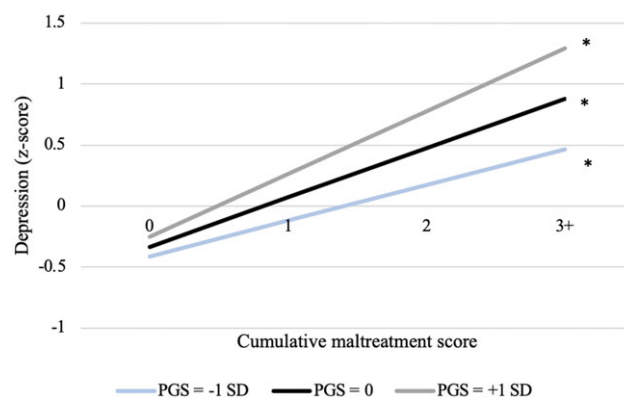

Figure 1. Association between the retrospectively reported presence of cumulative maltreatment and depressive symptoms (20–23 years), according to the PGS-depression. PGS "Polygenic risk score"; SD "Standard deviation". The asterisk indicates a significant (simple slope) association between childhood maltreatment and depressive symptoms at each level of PGS. Data were compiled from the final master file of the Quebec longitudinal study of child development (1998–2021), © gouvernement du Quebec, institut de la statistique du Quebec.

years ($\beta = .312$, $p < .001$), an association that remained significant when PGS_DEP was included in the model, of which the main effect was also significant ($\beta = .299$, $p < .001$). The prospective measure of deprivation, however, did not predict depressive symptoms ($\beta = -.005$, $p = .912$; Table 3). Only the interaction between PGS_DEP and the prospective measure was significant ($\beta = .106$, $p = .044$; retrospective measure: $\beta = .054$, $p = .198$). While none of the simple slopes were significant, the decomposition of this significant interaction suggested that participants identified as having experienced prospective deprivation (vs. no deprivation) seemed to have higher depressive symptomatology at higher levels of genetic risk. Meanwhile, those identified as having deprivation had decreasing depressive symptoms at low PGS_DEP levels. Individuals carrying mean levels of genetic risk had stable depressive scores across both groups (deprivation vs absence) (see Figure 2). However, none of the simple slopes were significant (see Figure 2).

Main and interaction effects of threat with the PGS_DEP

The presence of any threat, as measured retrospectively, was associated with depressive symptoms at 20–23 years ($\beta = .200$, $p < .001$) and remained significant when the PGS_DEP was simultaneously considered ($\beta = .200$, $p < .001$; Table 4). A significant interaction between retrospective reports of threat and PGS_DEP was also found ($\beta = .098$, $p = .028$). That is, individuals perceiving exposure to any threat (birth to 17 years) had a higher level of depressive symptoms when they carried a higher genetic risk for depression ($+1$ SD) in comparison to those who were at the sample's mean and lower levels (-1 SD) (see Figure 3). No significant main and interaction contribution were detected for prospective reports of maltreatment (main: $\beta = .052$, $p = .202$; interaction: $\beta = .014$, $p = .816$). Since small but significant associations were noted between deprivation and threat using prospective ($r = .171$, $p < .001$) and retrospective ($r = .295$, $p < .001$) indices, we reran the analyses while statistically controlling for the deprivation in the models conducted for threat. The patterns of findings for main effects and interactions remained unchanged.

Table 2. Hierarchical linear regression predicting depressive symptoms (20–23 years) according to cumulative childhood maltreatment, prospective and retrospective reports, and PGS-depression

		Prospective reports (n = 541)		Retrospective reports (n = 585)	
		Beta	*P-value*	Beta	*P-value*
Model 1	Cumulative CM	.101	.024	.322	< .001
Model 2	Cumulative CM	.081	.070	.322	< .001
	PGS-depression	.141	< .001	.124	.001
Model 3	Cumulative CM *PGS-depression	.092	0.152	.094	.031

Note. Max *N* based on data available for reports of prospective (birth to 17 years) and retrospective maltreatment, PGS-depression and depressive symptoms. Cumulative child maltreatment (CM) was coded as 0, 1, 2, 3+ types. Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2021), © Gouvernement du Québec, Institut de la Statistique du Québec. For PGS-depression we used the standardized residual scores that account for the 10 principal components and covariance with childhood maltreatment. All models were adjusted for sex and socioeconomic status. The main effects of Cumulative CM and PGS-depression are not presented in Model 3 but were included.

Table 3. Hierarchical linear regression predicting depressive symptoms (20-23 years) according to prospective and retrospective reports of *deprivation* and PGS-depression

		Prospective reports (n = 592)		Retrospective reports (n = 584)	
		Beta	*p-value*	Beta	*P-value*
Model 1	Deprivation	−.008	.849	.312	< .001
Model 2	Deprivation	−.005	.912	.299	< .001
	PGS-depression	.164	< .001	.135	< .001
Model 3 *Interaction*	Deprivation*PGS-depression	.106	0.044	.054	0.198

Note. Max *N* based on data available for reports of prospective (birth to 17 years) and retrospective maltreatment, PGS-depression and depressive symptoms. Any deprivation was coded as "yes" or "no". Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2021), © Gouvernement du Québec, Institut de la Statistique du Québec. For PGS-depression we used the standardized residual scores that account for the 10 principal components and covariance with childhood maltreatment. All models were adjusted for sex and socioeconomic status. The main effects of deprivation and PGS-depression are not presented in Model 3 but were included.

Discussion

Childhood maltreatment is one of the most studied and robust risk factors for depression (Jaffee, 2017; Kessler et al., 2010; Nanni et al., 2012). However, our understanding of the interplay between genetic risk for depression and childhood maltreatment in predicting depressive symptoms remains limited. Given prior evidence for associations of distinct magnitude between prospective and retrospective reports of maltreatment with mental health (Baldwin et al., 2019; Danese & Widom, 2020; Reuben et al., 2016), we also tested the moderating role of a PGS for depression (Howard et al., 2019) on depressive symptoms in young adults according to threat and deprivation experiences prospectively and retrospectively reported.

Retrospective versus prospective maltreatment measurements

First, the prevalence of exposure to at least one type of maltreatment varied depending on prospective vs. retrospective
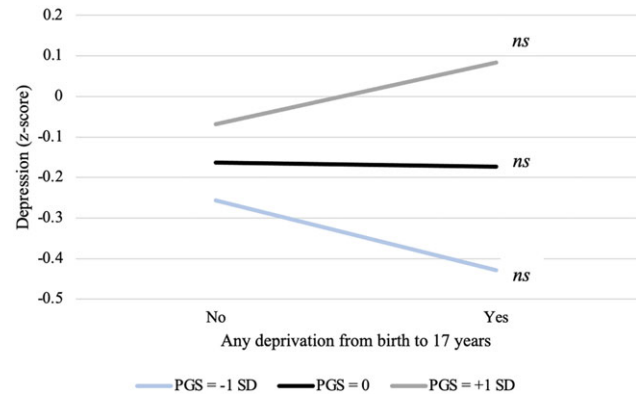

Figure 2. Association between the prospectively reported presence of deprivation and depressive symptoms (20–23 years), according to the PGS-depression. PGS "Polygenic risk score"; SD "Standard deviation". *ns* indicates that the (simple slope) association between childhood maltreatment and depressive symptoms are non-significant at each level of PGS. Data were compiled from the final master file of the Quebec longitudinal study of child development (1998–2021), © gouvernement du Quebec, institut de la statistique du Quebec.

reports, with approximately two-thirds (67%) of participants being assigned to probable maltreatment according to the prospective measures, as compared to one third (29%) for the retrospective measure. We speculate that the use of prospective reports relying on multiple informants and timepoints (n = 14) across several items (n = 251) may partly account for these higher rates in comparison to measures derived from seven items completed retrospectively by only one informant at only one timepoint. This additional difference in the measures of maltreatment obtained from retrospective versus prospective reports provides another argument for examining GxEs according to both types of measure.

Second, as previously mentioned, several studies and a meta-analysis have shown a low concordance between prospective and retrospective maltreatment (Baldwin et al., 2019; Danese & Widom, 2020; Scardera et al., 2023). Indeed, the poor agreement between these measures in this study (k = 0.056), as well as in a meta-analysis (k = 0.19) conducted by Balwin et al (2019), indicates that prospective and retrospective maltreatment measures, to a certain extent, identify different groups of individuals, and thus cannot be used interchangeably, but rather in a complementary approach. Further findings from Danese & Widom (2020) showed that subjective accounts of maltreatment may help to study the association between maltreatment and psychopathology. To illustrate, participants with retrospective reports of maltreatment only were more likely to meet diagnostic criteria for a psychopathology, along with participants with both court-recorded maltreatment and retrospective reports. However, participants with court-recorded maltreatment only were not at higher risk of psychopathology (Danese & Widom, 2020). This may be partly due to a recall bias, which refers to a negative bias on autobiographical memory related to one's current mental health. Retrospective reports may also provide additional insight through the subjective account of the childhood environment, which may be relevant to understand the etiology of depression.

Prospective versus retrospective maltreatment and depression

Our first objective was to investigate the associations between retrospective and prospective indicators of maltreatment with later

Table 4. Hierarchical linear regression predicting depressive symptoms (20-23 years) according to prospective and retrospective reports of *threat* and PGS-depression

		Prospective reports (*n* = 617)		Retrospective reports (*n* = 585)	
		Beta	*p-value*	Beta	*p-value*
Model 1	Threat	.062	0.135	.200	< .001
Model 2	Threat	.052	0.202	.200	< .001
	PGS-depression	.140	< .001	.145	< .001
Model 3 *Interaction*	Threat*PGS-depression	.014	0.816	.098	.028

Note. Max *N* based on data available for reports of prospective (birth to 17 years) and retrospective maltreatment, PGS-depression and depressive symptoms. Any threat was coded as "yes" or "no". Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2021), © Gouvernement du Québec, Institut de la Statistique du Québec. For PGS-depression, we used the standardized residual scores that account for the 10 principal components and covariance with childhood maltreatment. All models were adjusted for sex and socioeconomic status. The main effects of threat and PGS-depression are not presented in Model 3 but were included.
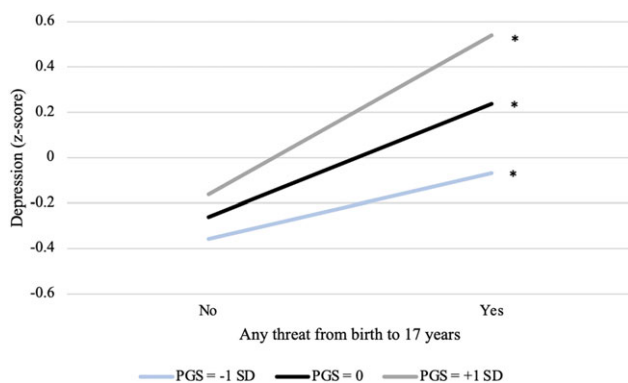

Figure 3. Association between the retrospectively reported presence of threat and depressive symptoms (20–23 years), according to the PGS-depression. PGS 'Polygenic risk score'; SD 'Standard deviation'. *indicates a significant association between childhood maltreatment and depressive symptoms at each level of PGS. Data were compiled from the final master file of the Quebec longitudinal study of child development (1998–2021), © gouvernement du Quebec, institut de la statistique du Quebec.

depressive symptoms. Our findings indicate that retrospective reports of maltreatment were consistently associated with depressive symptoms in young adulthood, even after controlling for the potential confounding effects of sex and parental socioeconomic status. Specifically, young adults who retrospectively reported a history of childhood maltreatment (according to all three indicators) were more likely to also report depressive symptoms in later years. Meanwhile, prospective reports of cumulative maltreatment only modestly predicted higher levels of depressive symptoms (and only marginally after controlling for PGS_DEP). These results are consistent with previous studies showing stronger associations between maltreatment reported retrospectively and mental health problems, including depression, in comparison to prospective official records (Baldwin et al., 2019; Humphreys et al., 2020; Newbury et al., 2018). Associations between prospective reports and psychopathology is generally weak (Danese & Widom, 2020).

Given the previously reported low agreement between the retrospective and prospective reports (Baldwin et al., 2019; Danese & Widom, 2020; Scardera et al., 2023), one could speculate that the stronger associations between retrospective maltreatment and depressive symptoms may partly arise due to differences in cognitive appraisal of life experiences. Notably, depressive symptoms can induce or exacerbate negative biases, attributions, and ruminations about oneself, including one's past experiences (Mennen et al., 2019), which in turn increases or maintains depressive symptomatology (i.e., reciprocal effects). The hopelessness theory of depression further postulates that the experiences of repeated exposure to adverse or inescapable life circumstances, such as childhood maltreatment, leads to negative inferential styles (Liu et al., 2015). As such, experiences of maltreatment may induce or exacerbate cognitive vulnerabilities for depression through a general negative outlook on past, present, and future life (Liu et al., 2015). It is thus difficult to tease apart these genuine sources of influence from the bias (e.g., shared methods and informants) that may inflate the estimates of the association between maltreatment and depression. Furthermore, in the absence of a significant association with prospective measures, these findings provide limited support for a causal relationship between maltreatment exposure and depression. Additional studies including both prospective and retrospective measures of maltreatment would help further understand this discrepancy in findings.

Threat versus deprivation and depression

The significant main effects noted between the retrospective indicators of deprivation and threat with depressive symptoms are consistent with another study showing that both types of experiences retrospectively reported in adulthood are associated with depressive symptoms (Lin et al., 2023). However, we did not find that retrospectively reported threat was more associated to depressive symptoms, as other studies have (Schäfer et al., 2023; Wang et al., 2022). Some differences in our study designs may partly explain this inconsistency. For example, Schäfer et al. (2023) reported an association between parent reports of threat and internalizing symptoms (including depressive symptoms), but not with deprivation. Their measure of deprivation did not include accounts of emotional deprivation (Schäfer et al., 2023), even though emotional neglect has been shown to more robustly associated with depression than physical neglect (Grummitt et al., 2022). Conversely, Wang et al. (2022) described high rates of retrospectively reported threat experienced in childhood which were associated with depression measured in college students, although the difference between the magnitude of the association between threat/deprivation and depression was not formally tested. Thus, we remain cautious in the interpretation of the distinct findings related to deprivation vs. threat and suggest that future studies investigate these experiences more systematically with depression.

PGS_DEP and depressive symptoms

Our study showed that the retrospective reports of childhood maltreatment were significantly associated with depressive symptoms in early adulthood, above and beyond the genetic vulnerability captured by our PGS_DEP indicator (Howard et al., 2019). Inversely, and similarly to all other studies that controlled for adverse experiences (e.g., peer victimization, childhood abuse, trauma) (Halldorsdottir et al., 2019; Perret et al., 2023; Thorp et al.,

2023), PGS$_{DEP}$ also predicted depressive symptoms after controlling for all childhood maltreatment indicators. However, the PGS$_{DEP}$ alone accounted for only 1.9% of variance in depressive symptoms measured in young adulthood (20–23 years). This estimate is similar to the variance in depression accounted for by this PGS in previous studies conducted in adolescence and adulthood (∼1.0%–2.0%) (Halldorsdottir et al., 2019; Perret et al., 2023; Wray et al., 2018). This contrasts with the variance related to the genetic factors estimated using twin and family study designs (∼40%) (Kendler et al., 2006; Ormel et al., 2019). In light of this "missing heritability" problem, Matthews and Turkheimer (2022) highlight the need to better understand how and in which contexts genes translate into a greater proportion of the targeted phenotype (e.g., depression). Advances made on these complementary fronts will help to further elucidate the complexity underlying the unfolding of the genetic etiology of depressive symptoms.

Interaction between PGS$_{DEP}$ and childhood maltreatment

Our second objective was to investigate the moderating role of PGS$_{DEP}$ in the association between childhood maltreatment and depressive symptoms. In this study, we present some evidence for GxEs emerging between childhood maltreatment and PGS$_{DEP}$ in the prediction of depressive symptoms in young adulthood. These interactions are in line with the Diathesis-Stress model (Broerman, 2020), whereby individuals who had (retrospectively) reported a history of maltreatment (cumulative maltreatment and threat) reported more depressive symptoms if they had a higher genetic predisposition for depression. Nevertheless, it is important to note that significant associations between these indicators of childhood maltreatment and depressive symptoms are reported at all levels of genetic vulnerability; the magnitude of these associations only varying in strength. Our findings thus align with a study by Peyrot et al. (2014) who showed that individuals with a history of childhood trauma, measured using the Childhood Trauma Questionnaire (i.e., retrospective report), were at a higher risk for major depressive disorder if they had a higher PGS$_{DEP}$ (calculated based on Ripke et al. (2013)). Similar evidence of GxEs has also been reported while using general trauma exposure (i.e., beyond youth) (Coleman et al., 2020; Thorp et al., 2023). However, other studies have reported GxE in opposite directions (Mullins et al., 2016; Peyrot et al., 2014), or no interaction at all (Halldorsdottir et al., 2019). This falls in line with a meta-analysis indicating no robust evidence for a genetic moderation (although no studies based their PGS on the most recent GWAS (Howard et al., 2019)) (Peyrot et al., 2018). Another study that relied on a GWAS including self-reported depressive symptoms (Wray et al., 2018) also did not detect a GxE between the PGS and childhood maltreatment in an epidemiological sample of adolescents (Halldorsdottir et al. (2019)). Testing GxE associations using more recent GWAS building on more participants and a greater variety of measures of depression may help to clarify this finding.

Although we found significant GxEs across retrospectively reported cumulative maltreatment and threat, this genetic moderation was not detected in the context of past deprivation. The only significant GxE for deprivation was uncovered for prospective reports and the simple slopes were not significant (i.e., individuals within each PGS$_{DEP}$ level did not report more depressive symptoms when exposed to deprivation versus those who did not). We speculate that these distinct results between retrospective versus prospective deprivation can be attributed to the specific items used via both methods and the saliency of

experiences. For the derivation of the prospective measure, there were more items covering acts of deprivation, emotional and physical neglect, compared to the information comprised in self-report items (Scardera et al., 2023). It is possible that the informants, including the caregivers, are more willing to disclose omission acts than commission acts (i.e., threat). In comparison, self-reported deprivation may be less accurate (or refer to less salient experiences) than self-reported threat compared to adult prospective reports. Thus, the saliency of threat experiences ultimately increases recall of events and the power to detect interactions with retrospective reports, compared prospective reports. More studies investigating GxE according to prospective and retrospective CM for both threat and deprivation experiences may shed more light on these preliminary findings.

The main effects noted between the retrospective indicators of both deprivation and threat with depressive symptoms are consistent with another study showing that both threat and deprivation are associated with depressed mood (Wang et al., 2022). However, only (retrospective) threat significantly interacted with PGS$_{DEP}$, which aligns with prior evidence that threat and deprivation affect later functioning through distinct pathways (Milojevich et al., 2019; Sheridan & McLaughlin, 2014). For example, in a brain imaging study involving young adults, distinct brain reactivity patterns were observed for retrospectively reported threat and deprivation. Threat was associated with higher activity in the ventral amygdala, while deprivation was linked to higher reactivity in the cortical fronto-parietal network, as well as in the dorsal amygdala (Puetz et al., 2020). Another study found that deprivation can result in major structural changes to the brain, which can lead to impaired executive functioning (Milojevich et al., 2019; Sheridan & McLaughlin, 2014). Meanwhile, early threat exposure is proposed to induce changes in neural circuits responsible for threat detection and emotional learning, which may further align to and exacerbate the genetic vulnerability for depression captured in Howard et al. (2019) GWAS. Milojevich et al. (2019) showed that individuals exposed to childhood threat are more likely to engage in avoidance strategies in adolescence which, in turn, partially mediated the association between threat and later internalizing problems. This association was not detected for deprivation. Previous studies have also suggested that avoidance strategies, common among people experiencing depressive symptoms, carry a genetic basis (Fleurkens et al., 2018; Smederevac et al., 2022). Moreover, Sumner et al. (2019) found that exposure to threat, not deprivation, was associated with altered gene expression (i.e., DNA methylation) and accelerated biological aging (Sumner et al., 2019). Furthermore, the indicator of accelerated biological aging moderated the association between threat exposure and later depression (Sumner et al., 2019). While we cannot rely on prior GxE studies that have specifically examined threat in the prediction of depressive symptoms, our preliminary findings suggest that threat, vs deprivation, and genes involved in the risk of depression exacerbate more robustly (or homogeneously) the risk of depression. Replication studies should therefore systematically examine this possibility rather than relying on broader indices of maltreatment.

Gene–environment correlation

We uncovered associations between PGS$_{DEP}$ and all our retrospective and prospective maltreatment indicators, pointing to possible gene–environment correlations (*r*GE) that can, if overlooked, increase the risk of inflated error rate (i.e., type 1 or

type 2) in the test of GxE interactions. Although indications of gene–environment correlations were not found in Peyrot et al. (2014)'s meta-analysis and in Mullins et al. (2016), other studies (Perret et al., 2023; Peyrot et al., 2018) have found significant (albeit weak) indications of association between PGS_{DEP} and retrospective measures of childhood neglect and abuse, as well as peer victimization. We extend these findings by showing that these patterns of covariance are also detected in prospective measures of maltreatment. These findings indicate that maltreatment experiences may not be random. Genetic vulnerabilities may be passed down from parents to children, along with the risk of facing neglectful or hostile environments (i.e., passive rGE), or to trigger negative patterns of interaction with caregivers (i.e., evocative rGE; (Quinn & D'Onofrio, 2020)). Future studies are needed to examine how these processes unfold during development and contribute to explain the intergenerational transmission of depression.

Methodological considerations

Our study's strengths include the use of a contemporary cohort followed from birth to 23 years, with prospective childhood maltreatment data across multiple informants (e.g., mother, teacher, self, observations). While several studies rely on strictly official records, less than 10% of maltreatment cases are reported to authority, to which cases not severe enough to be flagged are also missed (Statistics Canada, 2021). Our approach complemented the use of retrospective reports to test whether distinct pattern of GxE would emerge according to prospective measures of maltreatment.

Although we did not have access to depression diagnostics, depressive symptoms were measured at three occasions according to continuously distributed self-reports, aligning with the broad assessment of depression in Howard et al.'s (2019) GWAS. Second, we did not account for the severity, chronicity, or timing of maltreatment experiences even though these characteristics have been shown to modulate the estimated effect of maltreatment on development (Cicchetti & Toth, 1995; Li et al., 2022). Indeed, Peyrot et al. (2014) found that those exposed to more severe maltreatment while carrying higher genetic susceptibility had higher depression scores. While our cumulative maltreatment indicator encompassed various types of maltreatment experiences, it did not specifically assess severity. Third, our sample was relatively small to test interactions, which may have led to higher risk of type II error, considering the small predictive capacity of the PGS further constrained by variable patterns of interaction across the genome. Nonetheless, we detected several interactions, pointing to the relevance of GxE in the etiology of depression. Fourth, our results may not be generalizable to diverse populations as our sample was primarily composed of White European descendants. Finally, while our sample suffered from non-random longitudinal attrition, the use inverse probability weighting limited its impact on the generalization of our finding to the population.

Conclusion

Our study replicated earlier findings showing that retrospective reports of childhood maltreatment were consistently associated with depressive symptoms in early adulthood, beyond the estimated genetic vulnerability for depression, as well as sex and parental socioeconomic status. We found evidence for gene–environment interactions between two of three retrospective indicators of maltreatment. Consistent with the Diathesis-Stress model, participants exposed to maltreatment reported higher depressive symptoms if they had a higher genetic risk for depression. Although a similar pattern of GxE was uncovered with the prospectively measured deprivation, caution is warranted in the interpretation of this isolated finding. Future studies using both prospectively and retrospectively measured maltreatment experiences could help to further examine the distinct patterns of GxE arising in the context of threat vs deprivation, as well as for retrospective vs. prospective measures of maltreatment. If replicated, our findings may indicate that some children possess a heightened genetic susceptibility to the depressogenic effects of maltreatment, and that self-reported experiences may better capture these joint negative sources of influence. Research on the interplay between genetic and environmental factors is crucial in gaining a more comprehensive understanding of the complex nature of depression and eventually guide prevention efforts to offset this psychopathology in the context of childhood maltreatment.

References

Abdellaoui, A., Yengo, L., Verweij, K. J. H., & Visscher, P. M. (2023). 15 years of GWAS discovery: Realizing the promise. *The American Journal of Human Genetics*, 110(2), 179–194. https://doi.org/10.1016/j.ajhg.2022.12.011

Arnau-Soler, A., Adams, M. J., Clarke, T.-K., MacIntyre, D. J., Milburn, K., Navrady, L., McIntosh, A., & Thomson, P. A. (2019). A validation of the diathesis-stress model for depression in generation Scotland. *Translational Psychiatry*, 9(1), 25. https://doi.org/10.1038/s41398-018-0356-7

Baldwin, J. R., Reuben, A., Newbury, J. B., & Danese, A. (2019). Agreement between prospective and retrospective measures of childhood maltreatment: A systematic review and meta-analysis. *JAMA Psychiatry*, 76(6), 584–593. https://doi.org/10.1001/jamapsychiatry.2019.0097

Belsky, D. W., & Israel, S. (2014). Integrating genetics and social science: Genetic risk scores. *Biodemography and Social Biology*, 60(2), 137–155. https://doi.org/10.1080/19485565.2014.946591

Belsky, J., Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2007). For better and for worse: Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, 16(6), 300–304. https://doi.org/10.1111/j.1467-8721.2007.00525.x

Boardman, J. D., Daw, J., & Freese, J. (2013). Defining the environment in gene-environment research: Lessons from social epidemiology. *American Journal of Public Health*, 103(Suppl 1), S64–72. https://doi.org/10.2105/ajph. 2013.301355

Bremner, J. D., Bolus, R., & Mayer, E. A. (2007). Psychometric properties of the early trauma inventory-self report. *The Journal of Nervous and Mental Disease*, 195(3), 211. https://doi.org/10.1097/01.nmd.0000243824.84651.6c

Broerman, R. (2020). Diathesis-stress model. In V. Zeigler-Hill, & T. K. Shackelford (Ed.), *Encyclopedia of personality and individual differences* (pp. 1107–1109). Springer International Publishing. https://doi.org/10.1007/978-3-319-24612-3_891

Statistics Canada (2021). *Childhood maltreatment and the link with victimization in adulthood: Findings from the 2019 general social survey*. Stats Can. https://www150.statcan.gc.ca/n1/pub/11-627-m/11-627-m2021064-eng.htm.

Chang, C. C., Chow, C. C., Tellier, L. C., Vattikuti, S., Purcell, S. M., & Lee, J. J. (2015). Second-generation PLINK: Rising to the challenge of larger and richer datasets. *Gigascience*, 4(1), s13742-015. https://doi.org/10.1186/s13742-015-0047-8.

Christoforou, R., & Ferreira, N. (2020). Psychometric assessment of adverse childhood experiences international questionnaire (ACE-IQ) with adults engaging in non-suicidal self-injury. *Mediterranean Journal of Clinical Psychology*, 8(3), 1–23. https://doi.org/10.6092/2282-1619/mjcp-2601

Cicchetti, D., & Toth, S. L. (1995). A developmental psychopathology perspective on child abuse and neglect. *Journal of American Academy of Child Adolescent & Psychiatry*, 34(5), 541–565. https://doi.org/doi:0.1097/00004583-199505000-00008

Coleman, J. R. I., Peyrot, W. J., Purves, K. L., Davis, K. A. S., Rayner, C., Choi, S. W., Hübel, C., Gaspar, Héléna A., Kan, C., Van der Auwera, S., Adams, M. J., Lyall, D. M., Choi, K. W., Ripke, S., Mattheisen, M., Trzaskowski, M., Byrne, E. M., Abdellaoui, A., Adams, M. J., Agerbo, E., Air, T. M., Andlauer, T. F. M., Bacanu, S.-A., Bækvad-Hansen, M., Beekman, A. T. F., Bigdeli, T. B., Binder, E. B., Bryois, J., Buttenschøn, H. N., Bybjerg-Grauholm, J., Cai, N., Castelao, E., Christensen, J. H., Clarke, T.-K., Coleman, J. R. I., Colodro-Conde, L. D.;a, Couvy-Duchesne, B., Craddock, N., Crawford, G. E., Davies, G., Deary, I. J., Degenhardt, F., Derks, E. M., Direk, N., Dolan, C. V., Dunn, E. C., Eley, T. C., Escott-Price, V., Kiadeh, F. F. H., Finucane, H. K., Foo, J. C., Forstner, A. J., Frank, J., Gaspar, Héléna A., Gill, M., Goes, F. S., Gordon, S. D., Grove, J., Hall, L. S., Hansen, C. Søholm, Hansen, T. F., Herms, S., Hickie, I. B., Hoffmann, P., Homuth, G., Horn, C., Hottenga, J.-J., Hougaard, D. M., Howard, D. M., Ising, M., Jansen, R., Jones, I., Jones, L. A., Jorgenson, E., Knowles, J. A., Kohane, I. S., Kraft, J., Kretzschmar, W. W., Kutalik, Zán, Li, Y., Lind, P. A., MacIntyre, D. J., MacKinnon, D. F., Maier, R. M., Maier, W., Marchini, J., Mbarek, H., McGrath, P., McGuffin, P., Medland, S. E., Mehta, D., Middeldorp, C. M., Mihailov, E., Milaneschi, Y., Milani, L., Mondimore, F. M., Montgomery, G. W., Mostafavi, S., Mullins, N., Nauck, M., Ng, B., Nivard, M. G., Nyholt, D. R., O'Reilly, P. F., Oskarsson, H., Owen, M. J., Painter, J. N., Pedersen, C. B.øcker, Pedersen, M. G.ørtz, Peterson, R. E., Pettersson, E., Peyrot, W. J., Pistis, G., Posthuma, D., Quiroz, J. A., Qvist, P., Rice, J. P., Riley, B. P., Rivera, M., Mirza, S. S., Schoevers, R., Schulte, E. C., Shen, L., Shi, J., Shyn, S. I., Sigurdsson, E., Sinnamon, G. C. B., Smit, J. H., Smith, D. J., Stefansson, H., Steinberg, S., Streit, F., Strohmaier, J., Tansey, K. E., Teismann, H., Teumer, A., Thompson, W., Thomson, P. A., Thorgeirsson, T. E., Traylor, M., Treutlein, J., Trubetskoy, V., Uitterlinden, Aés G., Umbricht, D., Van der Auwera, S., van Hemert, A. M., Viktorin, A., Visscher, P. M., Wang, Y., Webb, B. T., Weinsheimer, S. M., Wellmann, J. C.;rgen, Willemsen, G., Witt, S. H., Wu, Y., Xi, H. S., Yang, J., Zhang, F., Arolt, V., Baune, B. T., Berger, K., Boomsma, D. I., Cichon, S., Dannlowski, U., de Geus, E. J. C., DePaulo, J. R., Domenici, E., Domschke, K., Esko, Tõnu, Grabe, H. J., Hamilton, S. P., Hayward, C., Heath, A. C., Kendler, K. S., Kloiber, S., Lewis, G., Li, Q. S., Lucae, S., Madden, P. A. F., Magnusson, P. K., Martin, N. G., McIntosh, A. M., Metspalu, A., Mors, O., Mortensen, P. B., Müller-Myhsok, B., Nordentoft, M., Nöthen, M. M., O'Donovan, M. C., Paciga, S. A., Pedersen, N. L., Penninx, B. W. J. H., Perlis, R. H., Porteous, D. J., Potash, J. B., Preisig, M., Rietschel, M., Schaefer, C., Schulze, T. G., Smoller, J. W., Stefansson, K., Tiemeier, H., Uher, R., Völzke, H.,

Weissman, M. M., Werge, T., Lewis, C. M., Levinson, D. F., Breen, G., Børglum, A. D., Sullivan, P. F., Dunn, E. C., Vassos, E., Danese, A., Maughan, B., Grabe, H. J., Lewis, C. M., O'Reilly, P. F., McIntosh, A. M., Smith, D. J., Wray, N. R., Hotopf, M., Eley, T. C., & Breen, G. (2020). Genome-wide gene-environment analyses of major depressive disorder and reported lifetime traumatic experiences in UK biobank. *Molecular Psychiatry*, 25(7), 1430–1446. https://doi.org/10.1038/s41380-019-0546-6

Danese, A., & Widom, C. S. (2020). Objective and subjective experiences of child maltreatment and their relationships with psychopathology. *Nature Human Behaviour*, 4(8), 1–8. https://doi.org/10.1038/s41562-020-0880-3

Ferrari, A. J., Santomauro, D. F., Mantilla Herrera, A. M., Shadid, J., Ashbaugh, C., Erskine, H. E., Charlson, F. J., & Whiteford, H. A. (2022). Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. *The Lancet Psychiatry*, 9(2), 137–150. https://doi.org/10.1016/S2215-0366(21)00395-3

Fleurkens, P., van Minnen, A., Becker, E. S., van Oostrom, I., Speckens, A., Rinck, M., & Vrijsen, J. N. (2018). Automatic approach-avoidance tendencies as a candidate intermediate phenotype for depression: Associations with childhood trauma and the 5-HTTLPR transporter polymorphism. *PLoS One*, 13(3), e0193787. https://doi.org/10.1371/journal.pone.0193787

Gallo, E. A. G., Munhoz, T. N., de Mola, C. L., & Murray, J. (2018). Gender differences in the effects of childhood maltreatment on adult depression and anxiety: A systematic review and meta-analysis. *Child Abuse & Neglect*, 79, 107–114. https://doi.org/10.1016/j.chiabu.2018.01.003

Ge, T., Chen, C.-Y., Ni, Y., Feng, Y.-C. A., & Smoller, J. W. (2019). Polygenic prediction via Bayesian regression and continuous shrinkage priors. *Nature Communications*, 10(1), 1–10. https://doi.org/10.1038/s41467-019-09718-5

Geoffroy, M.-C., Pinto Pereira, S., Li, L., & Power, C. (2016). Child neglect and maltreatment and childhood-to-adulthood cognition and mental health in a prospective birth cohort. *Journal of the American Academy of Child & Adolescent Psychiatry*, 55(1), 33–40.e33. https://doi.org/10.1016/j.jaac.2015.10.012

Grounds for Reporting a Situation (2022). *Gouvernement du Quebec*. Quebec Director of Youth Protection. https://www.quebec.ca/en/family-and-support-for-individuals/childhood/services-youth-difficulty-families/youth-protection/reporting-a-situation-to-the-director-of-youth-protection/grounds-for-reporting-a-situation.

Grummitt, L. R., Kelly, E. V., Barrett, E. L., Lawler, S., Prior, K., Stapinski, L. A., & Newton, N. C. (2022). Associations of childhood emotional and physical neglect with mental health and substance use in young adults. *Australian & New Zealand Journal of Psychiatry*, 56(4), 365–375.

Halldorsdottir, T., Piechaczek, C., Soares de Matos, A. P., Czamara, D., Pehl, V., Wagenbuechler, P., Feldmann, L., Quickenstedt-Reinhardt, P., Allgaier, A.-K., & Freisleder, F. J. (2019). Polygenic risk: Predicting depression outcomes in clinical and epidemiological cohorts of youths. *American Journal of Psychiatry*, 176(8), 615–625. https://doi.org/10.1176/appi.ajp.2019 1809. 1014.

Howard, D. M., Adams, M. J., Clarke, T.-K., Hafferty, J. D., Gibson, J., Shirali, M., Coleman, J. R., Hagenaars, S. P., Ward, J., & Wigmore, E. M. (2019). Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. *Nature Neuroscience*, 22(3), 343–352. https://doi.org/10.1038/s41593-018-0326-7

Humphreys, K. L., LeMoult, J., Wear, J. G., Piersiak, H. A., Lee, A., & Gotlib, I. H. (2020). Child maltreatment and depression: A meta-analysis of studies using the childhood trauma questionnaire. *Child Abuse & Neglect*, 102, 104361. https://doi.org/10.1016/j.chiabu.2020.104361

Jackson, Y., McGuire, A., Tunno, A. M., & Makanui, P. K. (2019). A reasonably large review of operationalization in child maltreatment research: Assessment approaches and sources of information in youth samples. *Child Abuse & Neglect*, 87, 5–17. https://doi.org/10.1016/j.chiabu.2018

Jaffee, S. R. (2017). Child maltreatment and risk for psychopathology in childhood and adulthood. *Annual Review of Clinical Psychology*, 13(1), 525–551. https://doi.org/10.1146/annurev-clinpsy-032816-045005

Kendall, K. M., Van Assche, E., Andlauer, T. F. M., Choi, K. W., Luykx, J. J., Schulte, E. C., & Lu, Y. (2021). The genetic basis of major depression.

Psychological Medicine, *51*(13), 2217–2230. https://doi.org/10.1017/S0033291721000441

Kendler, K. S., Gatz, M., Gardner, C. O., & Pedersen, N. L. (2006). A swedish national twin study of lifetime major depression. *American Journal of Psychiatry*, *163*(1), 109–114. https://doi.org/10.1176/appi.ajp.163.1.109

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., Aguilar-Gaxiola, S., Alhamzawi, A. O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., de Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O., Haro, J. M., Hu, C.-Y., Karam, E. G., Kawakami, N., Lee, S., Lépine, J.-P., Ormel, J., Posada-Villa, Jé, Sagar, R., Tsang, A., Üstün, T. B., Vassilev, S., Viana, M. C., & Williams, D. R. (2010). Childhood adversities and adult psychopathology in the WHO world mental health surveys. *The British Journal of Psychiatry*, *197*(5), 378–385. https://doi.org/10.1192/bjp.bp.110.080499

Lacey, R. E., Pereira, S. M. P., Li, L., & Danese, A. (2020). Adverse childhood experiences and adult inflammation: Single adversity, cumulative risk and latent class approaches. *Brain, Behavior, and Immunity*, *87*, 820–830. https://doi.org/10.1016/j.bbi.2020.03.017

Leeb, R. T., Paulozzi, L. J., Melanson, C., Simon, T. R., & Arias, I. (2008). *Child maltreatment surveillance; uniform definitions for public health and recommended data elements* (pp. 11–16). Centers for Disease Control and Prevention 1.0.

LeMoult, J., Humphreys, K. L., Tracy, A., Hoffmeister, J. A., Ip, E., & Gotlib, I. H. (2020). Meta-analysis: Exposure to early life stress and risk for depression in childhood and adolescence. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(7), 842–855. https://doi.org/10.1016/j.jaac.2019.10.011

Li, M., Gao, T., Su, Y., Zhang, Y., Yang, G., D'Arcy, C., & Meng, X. (2022). The timing effect of childhood maltreatment in depression: A systematic review and meta-analysis. *Trauma, Violence, & Abuse*, *24*(4), 2560–2580. https://doi.org/10.1177/15248380221102558

Lin, L., Cao, B., Chen, W., Li, J., Zhang, Y., & Guo, V. Y. (2023). Association of childhood threat and deprivation with depressive symptoms and the moderating role of current economic status among middle-aged and older adults in China. *Social Psychiatry and Psychiatric Epidemiology*, *58*(8), 1227–1236. https://doi.org/10.1007/s00127-022-02384-x

Liu, R. T., Kleiman, E. M., Nestor, B. A., & Cheek, S. M. (2015). The hopelessness theory of depression: A quarter century in review. *Clinical Psychology (New York)*, *22*(4), 345–365. https://doi.org/10.1111/cpsp

Matthews, L. J., & Turkheimer, E. (2022). Three legs of the missing heritability problem. *Studies in History and Philosophy of Science*, *93*, 183–191. https://doi.org/10.1016/j.shpsa.2022.04.004

McIntosh, A. M., Sullivan, P. F., & Lewis, C. M. (2019). Uncovering the genetic architecture of major depression. *Neuron*, *102*(1), 91–103. https://doi.org/10.1016/j.neuron.2019.03.022

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience & Biobehavioral Reviews*, *47*(2014), 578–591. https://doi.org/10.1016/j.neubiorev.2014.10.012

McLaughlin, K. A., Weissman, D., & Bitrán, D. (2019). Childhood adversity and neural development: A systematic review. *Annual Review of Developmental Psychology*, *1*(1), 277–312. https://doi.org/doi:0.1146/annurev-devpsych-121318-084950

Mennen, A. C., Norman, K. A., & Turk-Browne, N. B. (2019). Attentional bias in depression: Understanding mechanisms to improve training and treatment. *Current Opinion in Psychology*, *29*, 266–273. https://doi.org/10.1016/j.copsyc.2019.07.036

Merrick, M. T., Ports, K. A., Ford, D. C., Afifi, T. O., Gershoff, E. T., & Grogan-Kaylor, A. (2017). Unpacking the impact of adverse childhood experiences on adult mental health. *Child Abuse & Neglect*, *69*, 10–19. https://doi.org/10.1016/j.chiabu.2017.03.016

Milojevich, H. M., Norwalk, K. E., & Sheridan, M. A. (2019). Deprivation and threat, emotion dysregulation, and psychopathology: Concurrent and longitudinal associations. *Development and Psychopathology*, *31*(3), 847–857. https://doi.org/10.1017/s0954579419000294

Mullins, N., Power, R. A., Fisher, H. L., Hanscombe, K. B., Euesden, J., Iniesta, R., Levinson, D. F., Weissman, M. M., Potash, J. B., & Shi, J. (2016). Polygenic interactions with environmental adversity in the aetiology

of major depressive disorder. *Psychological Medicine*, *46*(4), 759–770. https://doi.org/10.1017/S0033291715002172

Nanni, V., Uher, R., & Danese, A. (2012). Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: A meta-analysis. *American Journal of Psychiatry*, *169*(2), 141–151. https://doi.org/10.1176/appi.ajp.2011

Newbury, J. B., Arseneault, L., Moffitt, T. E., Caspi, A., Danese, A., Baldwin, J. R., & Fisher, H. L. (2018). Measuring childhood maltreatment to predict early-adult psychopathology: Comparison of prospective informant-reports and retrospective self-reports. *Journal of Psychiatric Research*, *96*, 57–64.

Ormel, J., Hartman, C. A., & Snieder, H. (2019). The genetics of depression: Successful genome-wide association studies introduce new challenges. *Translational Psychiatry*, *9*(1), 114. https://doi.org/10.1038/s41398-019-0450-5

Orri, M., Boivin, M., Chen, C., Ahun, M. N., Geoffroy, M.-C., Ouellet-Morin, I., Tremblay, R. E., & Côté, S. M. (2021). Cohort profile: Quebec longitudinal study of child development (QLSCD). *Social Psychiatry and Psychiatric Epidemiology*, *56*(5), 883–894. https://doi.org/10.1007/s00127-020-01972-z

Ottman, R. (1996). Gene-environment interaction: Definitions and study designs. *Preventative Medicine*, *25*(6), 764–770. https://doi.org/10.1006/pmed.1996.0117

Parade, S. H., Huffhines, L., Daniels, T. E., Stroud, L. R., Nugent, N. R., & Tyrka, A. R. (2021). A systematic review of childhood maltreatment and DNA methylation: Candidate gene and epigenome-wide approaches. *Translational Psychiatry*, *11*(1), 134. https://doi.org/10.1038/s41398-021-01207-y

Perret, L. C., Boivin, M., Morneau-Vaillancourt, G., Andlauer, T. F., Paquin, S., Langevin, S., Girard, A., Turecki, G., O'Donnell, K., & Tremblay, R. E. (2023). Polygenic risk score and peer victimisation independently predict depressive symptoms in adolescence: Results from the Quebec longitudinal study of children development. *Journal of Child Psychology and Psychiatry*, *64*(3), 388–396. https://doi.org/10.1111/jcpp.13706

Peyrot, W. J., Milaneschi, Y., Abdellaoui, A., Sullivan, P. F., Hottenga, J. J., Boomsma, D. I., & Penninx, B. W. (2014). Effect of polygenic risk scores on depression in childhood trauma. *The British Journal of Psychiatry*, *205*(2), 113–119. https://doi.org/10.1192/bjp.bp.113.143081

Peyrot, W. J., Van der Auwera, S., Milaneschi, Y., Dolan, C. V., Madden, P. A., Sullivan, P. F., Strohmaier, J., Ripke, S., Rietschel, M., & Nivard, M. G. (2018). Does childhood trauma moderate polygenic risk for depression? A meta-analysis of 5765 subjects from the psychiatric genomics consortium. *Biological Psychiatry*, *84*(2), 138–147. https://doi.org/10.1016/j.biopsych.2017.09.009

Poulin, C., Hand, D., & Boudreau, B. (2005). Validity of a 12-item version of the CES-D [Centre for epidemiological studies depression scale] used in the national longitudinal study of children and youth. *Chronic Diseases in Canada*, *26*(2-3), 65–72.

Puetz, V. B., Viding, E., Gerin, M. I., Pingault, J.-B., Sethi, A., Knodt, A. R., Radtke, S. R., Brigidi, B. D., Hariri, A. R., & McCrory, E. (2020). Investigating patterns of neural response associated with childhood abuse v. childhood neglect. *Psychological Medicine*, *50*(8), 1398–1407.

Putnam, K. T., Harris, W. W., & Putnam, F. W. (2013). Synergistic childhood adversities and complex adult psychopathology. *Journal of Traumatic Stress*, *26*(4), 435–442. https://doi.org/10.1002/jts 1833.

Quinn, P. D., & D'Onofrio, B. M. (2020). Nature versus nurture. In J. B. Benson (Ed.), *Encyclopedia of infant and early childhood development* (2nd ed. pp. 373–384). Elsevier. https://doi.org/10.1016/B978-0-12-809324-5

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385–401. https://doi.org/10.1177/014662167700100306

Reuben, A., Moffitt, T. E., Caspi, A., Belsky, D. W., Harrington, H., Schroeder, F., Hogan, S., Ramrakha, S., Poulton, R., & Danese, A. (2016). Lest we forget: Comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry*, *57*(10), 1103–1112. https://doi.org/10.1111/jcpp

Ripke, S., Wray, N. R., Lewis, C. M., Hamilton, S. P., Weissman, M. M., Breen, G., Byrne, E. M., Blackwood, D. H. R., Boomsma, D. I., Cichon, S.,

Heath, A. C., Holsboer, F., Lucae, S., Madden, P. A. F., Martin, N. G., McGuffin, P., Muglia, P., Noethen, M. M., Penninx, B. P., Pergadia, M. L., Potash, J. B., Rietschel, M., Lin, D., Müller-Myhsok, B., Shi, J., Steinberg, S., Grabe, H. J., Lichtenstein, P., Magnusson, P., Perlis, R. H., Preisig, M., Smoller, J. W., Stefansson, K., Uher, R., Kutalik, Z., Tansey, K. E., Teumer, A., Viktorin, A., Barnes, M. R., Bettecken, T., Binder, E. B., Breuer, Ré, Castro, V. M., Churchill, S. E., Coryell, W. H., Craddock, N., Craig, I. W., Czamara, D., De Geus, E. J., Degenhardt, F., Farmer, A. E., Fava, M., Frank, J., Gainer, V. S., Gallagher, P. J., Gordon, S. D., Goryachev, S., Gross, M., Guipponi, M., Henders, A. K., Herms, S., Hickie, I. B., Hoefels, S., Hoogendijk, W., Hottenga, J. J., Iosifescu, D. V., Ising, M., Jones, I., Jones, L., Jung-Ying, T., Knowles, J. A., Kohane, I. S., Kohli, M. A., Korszun, A., Landen, M., Lawson, W. B., Lewis, G., MacIntyre, D., Maier, W., Mattheisen, M., McGrath, P. J., McIntosh, A., McLean, A., Middeldorp, C. M., Middleton, L., Montgomery, G. M., Murphy, S. N., Nauck, M., Nolen, W. A., Nyholt, D. R., O'Donovan, M., Oskarsson, Högni, Pedersen, N., Scheftner, W. A., Schulz, A., Schulze, T. G., Shyn, S. I., Sigurdsson, E., Slager, S. L., Smit, J. H., Stefansson, H., Steffens, M., Thorgeirsson, T., Tozzi, F., Treutlein, J., Uhr, M., van den Oord, E. J. C. G., Van Grootheest, G., Völzke, H., Weilburg, J. B., Willemsen, G., Zitman, F. G., Neale, B., Daly, M., Levinson, D. F., Sullivan, P. F., & **Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium** (2013). A mega-analysis of genome-wide association studies for major depressive disorder. *Molecular Psychiatry*, *18*(4), 497–511. https://doi.org/10.1038/mp.2012.21

Sarro, E. C., Sullivan, R. M., & Barr, G. (2014). Unpredictable neonatal stress enhances adult anxiety and alters amygdala gene expression related to serotonin and GABA. *Neuroscience*, *258*, 147–161. https://doi.org/10.1016/j.neuroscience.2013.10.064

Scardera, S., Langevin, R., Collin-Vézina, D., Cabana, M. C., Pinto Pereira, S. M., Côté, S., Ouellet-Morin, I., & Geoffroy, M.-C. (2023). Derivation of probable child maltreatment indicators using prospectively recorded information between 5 months and 17 years in a longitudinal cohort of Canadian children. *Child Abuse & Neglect*, *143*, 106247. https://doi.org/10.1016/j.chiabu.2023.106247

Schäfer, J. L., McLaughlin, K. A., Manfro, G. G., Pan, P., Rohde, L. A., Miguel, E. C., Simioni, A., Hoffmann, M. S., & Salum, G. A. (2023). Threat and deprivation are associated with distinct aspects of cognition, emotional processing, and psychopathology in children and adolescents. *Developmental Science*, *26*(1), e13267. https://doi.org/10.1111/desc.13267

Sheridan, M. A., & McLaughlin, K. A. (2014). Dimensions of early experience and neural development: Deprivation and threat. *Trends in Cognitive Sciences*, *18*(11), 580–585. https://doi.org/10.1016/j.tics.2014.09.001

Smederevac, S., Sadikovic, S., Colovic, P., Vucinic, N., Milutinovic, A., Riemann, R., Corr, P. J., Prinz, M., & Budimlija, Z. (2022). Quantitative behavioral genetic and molecular genetic foundations of the approach and avoidance strategies. *Current Psychology*, *42*(17), 1–15. https://doi.org/10.1007/s12144-022-02724-9

Spatz Widom, C., DuMont, K., & Czaja, S. J. (2007). A prospective investigation of major depressive disorder and comorbidity in abused and neglected children grown up. *Archives of General Psychiatry*, *64*(1), 49–56. https://doi.org/10.1001/archpsyc.64.1.49

Strathearn, L., Giannotti, M., Mills, R., Kisely, S., Najman, J., & Abajobir, A. (2020). Long-term cognitive, psychological, and health outcomes associated with child abuse and neglect. *Pediatrics*, *146*(4), 389–403. https://doi.org/10.1542/peds.2020-0438

Sumner, J. A., Colich, N. L., Uddin, M., Armstrong, D., & McLaughlin, K. A. (2019). Early experiences of threat, but not deprivation, are associated with accelerated biological aging in children and adolescents. *Biological Psychiatry*, *85*(3), 268–278. https://doi.org/10.1016/j.biopsych.2018.09.008

Tarquinio Camille, L., Christine, R., Elise, E., Charles, M.-K., Marion, T., & Cyril, T. (2023). Psychometric validation of the French version of the adverse childhood experiences international questionnaire (ACE-IQ). *Children and Youth Services Review*, *150*, 107007. https://doi.org/10.1016/j.childyouth.2023.107007

Thapar, A., Eyre, O., Patel, V., & Brent, D. (2022). Depression in young people. *The Lancet*, *400*(10352), 617–631. https://doi.org/10.1016/S0140-6736(22)01012-1

Thorp, J. G., Gerring, Z. F., Colodro-Conde, L., Byrne, E. M., Medland, S. E., Middeldorp, C. M., & Derks, E. M. (2023). The association between trauma exposure, polygenic risk and individual depression symptoms. *Psychiatry Research*, *321*, 115101. https://doi.org/10.1016/j.psychres.2023

Van Dam, D. S., van Nierop, M., Viechtbauer, W., Velthorst, E., van Winkel, R., Bruggeman, R., Cahn, W., de Haan, L., Kahn, R. S., Meijer, C. J., Myin-Germeys, I., van Os, J., & Wiersma, D. (2015). Childhood abuse and neglect in relation to the presence and persistence of psychotic and depressive symptomatology. *Psychological Medicine*, *45*(7), 1363–1377. https://doi.org/10.1017/S0033291714001561

Villarroel, M. A., & Terlizzi, E. P. (2020). *Symptoms of depression among adults: United States*. Centers for Disease Control and Prevention. https://www.cdc.gov/nchs/data/databriefs/db379-H.pdf.

Wang, X., Lu, J., Liu, Q., Yu, Q., Fan, J., Gao, F., Han, Y., Liu, X., Yao, R., & Zhu, X. (2022). Childhood experiences of threat and deprivation predict distinct depressive symptoms: A parallel latent growth curve model. *Journal of Affective Disorders*, *319*, 244–251. https://doi.org/10.1016/j.jad.2022.09.061

WHO (2022). *Child maltreatment*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/child-maltreatment.

WHO (2023). *Depression*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/depression.

Willms, J., & Shields, M. (1996). *A measure of socioeconomic status for the national longitudinal study of children*. Report prepared for Statistics Canada.

Wray, N. R., Ripke, S., Mattheisen, M., Trzaskowski, M., Byrne, E. M., Abdellaoui, A., Adams, M. J., Agerbo, E., Air, T. M., & Andlauer, T. M. (2018). Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. *Nature Genetics*, *50*(5), 668–681. https://doi.org/10.1038/s41588-018-0090-3

Youth Protection Act (2021). *Chapter P-34.1*. Québec Official Publisher. http://legisquebec.gouv.qc.ca/en/pdf/cs/P-34.1.pdf