Polygenic risk score and peer victimization independently predict depressive symptoms in adolescence : Results from the Quebec Longitudinal Study of Children Development

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Abstract

Background: Peer victimization has been associated with depressive symptoms during adolescence, however not all peer victimized adolescents will exhibit such symptoms. This study tested whether having a genetic predisposition to developing depression increased the risk of experiencing depressive symptoms in peer victimized youth. To date, no study has explored such gene-environment interaction using a polygenic risk score for depression (PRS-depression) in the context of peer victimization and depressive symptoms in adolescence.

Methods: The sample included 748 participants born in 1997/98 from the Quebec Longitudinal Study of Child Development with genotype data and prospectively collected information on peer victimization (12-13 years) obtained from both self- and teacher-reports, as well as self-reported depressive symptoms (15-17 years). The PRS-depression was based on the genome-wide association meta-analysis of broad depression by Howard et al. (2019).

Results: Self- and teacher-reported peer victimization in early adolescence were both associated with depressive symptoms in adolescence (β=0.34, $p<.001$; β=0.14, $p=.001$, respectively), and this association remained significant when accounting for PRS-depression (β=0.33, $p<.001$; β=0.13, $p=.002$, respectively). PRS-depression was independently associated with depressive symptoms, but there was no significant PRS-depression by peer victimization interaction (self-reported and teacher-reported). PRS-depression was correlated with self-reported, but not teacher-reported, peer victimization.

Conclusion: Our findings suggested that a partial measure of an individual's genetic predisposition to depression, as measured by PRS-depression, and being exposed to peer

victimization (self- and teacher-reported) were independently associated with depressive symptoms in adolescence. Furthermore, PRS-depression did not exacerbate the risk of depressive symptoms among adolescents who had been peer victimized. Lastly, we found evidence of a gene-environment correlation between PRS-depression and self-reported peer victimization. Future studies are needed to replicate this finding, and to further understand the role of genetic predispositions in experiencing depressive symptoms following peer victimization.

Keywords: peer victimization, depression, polygenic risk score, adolescence, longitudinal

Introduction

Peer victimization, a common experience among children and adolescents (Craig et al., 2009), is defined as physical, verbal, or psychological harm caused by peers acting outside the norms of appropriate conduct (Finkelhor, Turner, & Hamby, 2012). It has been associated with a range of mental health problems over the life course (see reviews : Arseneault (2018) and Moore et al. (2017)), including clinical depression (Arseneault, 2018), and depressive symptoms (Geoffroy et al., 2018) after controlling for baseline mental health problems and family difficulties.

However, not all adolescents will experience depressive symptoms after being exposed to peer victimization. It has been suggested that peer victimization may be linked to a higher risk of depressive symptoms when it co-occurs with a genetic vulnerability to depression (Vaillancourt, Hymel, & McDougall, 2013). There is a strong genetic basis of depression, with heritability ranging from 30% to 50% (Kendall et al., 2021). It is therefore important to consider the contribution of genetic vulnerability to depression when studying psychosocial risk factors, such as peer victimization. For example, Benjet, Thompson, and Gotlib (2010) found evidence of an association between relational victimization (e.g., rumor spreading, social exclusion) and depressive symptoms in girls carrying the short/short allele combination of a polymorphism in the promoter region of the serotonin transporter gene (*5-HTTLPR*), but not in girls carrying the short/long or long/long allele combinations. This finding was replicated in boys and girls by Sugden et al. (2010). This points to an interaction between peer victimization and a measured candidate gene polymorphism, which together can explain a larger proportion of the association with depressive symptoms than if they were tested individually. However, these pioneer studies by Benjet et al. (2010) and Sugden et al. (2010) on the role of genetic vulnerability in depression, have focused on single genes with a candidate gene approach while depression is known to involve

multiple genes; it is polygenic (Wray et al., 2012). Thereby, a candidate gene approach would be limiting since the genetic etiology of depression is polygenic.

A polygenic approach has been made possible by the emergence of recent large genome-wide association studies (GWAS) detecting genetic variants associated with depression (Howard et al., 2019; Wray et al., 2018). Past GWAS had failed to uncover significant variants associated with a diagnosis of major depressive disorder (MDD) (Ripke et al., 2013), or had only discovered a few variants (Cai et al., 2015). More recent GWAS have considered a broader range of phenotypes in their inclusion criteria, departing from only comprising a clinical diagnosis of MDD to also including self-reported depressive symptoms. For example, Wray et al. (2018) discovered 44 variants associated with depression. Shortly after, a GWAS by Howard et al. (2019) identified 102 variants associated with a broader depression phenotype encompassing diagnosed MDD, depressive symptoms, as well as seeking help for depressive symptoms, from self-reports and medical reports.

From a methodological point of view, the inclusion of broader self-reported depression in these two GWAS has allowed the use of larger sample sizes, which are essential to detect more genetic variants with small effect sizes linked to broad depression phenotypes. Furthermore, using broader phenotyping of depression has been justified by several studies reporting a high genetic correlation between self-reported depressive symptoms and a clinical MDD diagnosis (Howard et al., 2018; Wray et al., 2018). As such, these GWAS are advantageously positioned to better understand the genetic etiology of a broader spectrum of depression phenotypes in clinical and community samples. GWAS further allow the computation of polygenic risk scores (PRS), which use GWAS statistics depicting the strength of association with depression across the genome at each single nucleotide polymorphisms (SNPs), while accounting for their individual weighted

effect sizes (Andlauer & Nöthen, 2020). The present study will use a community sample with self-reported depressive symptoms, and rely on the recent GWAS by Howard et al. (2019) to calculate a PRS for depression (PRS-depression) – in contrast to a PRS for MDD (PRS-MDD), based on GWAS solely comprising clinical and self-reported MDD cases, as in Wray et al. (2018) for example.

PRS-MDD has been used in prior studies to examine putative gene-environment interactions (G×E) in combination with adverse events such as childhood trauma (i.e., abuse and neglect) in predicting depression. A meta-analysis of nine cohorts of adults, using a retrospective measure of childhood trauma, showed that both trauma and PRS-MDD were independently associated with an increased risk of MDD (Peyrot et al., 2018), but failed to find evidence of a PRS-MDD and childhood trauma interaction. It is important to note that the studies from this meta-analysis did not use the more recent GWAS for depression by Howard et al. (2019) or PRS-MDD by Wray et al. (2018). A recent study based on the MDD GWAS by Wray et al. (2018) investigated G×E in clinical and epidemiological adolescent cohorts similarly found independent contributions of PRS-MDD and childhood abuse on depression, but no interaction (Halldorsdottir et al., 2019). In order words, childhood abuse did not influence the association between PRS-MDD and MDD. One study has investigated GxE between self-reported peer victimization in adolescence and PRS-depression using the depression GWAS by Howard et al. (2019) in predicting depressive symptoms in young adulthood, and found no interaction.

Genome-wide research on G×E is still in its infancy, and more studies are needed to examine the contribution of PRS-depression in relation to environmental stressors known to be longitudinally associated with depression. To the best of our knowledge, no study has yet examined the role of PRS-depression in the context of peer victimization and depressive symptoms

in adolescence. Importantly, the present study included peer victimization assessed through both self- and teacher-reports. Prior studies found that self- and teacher-reported measures were linked to different correlates; psychological vs behavioral difficulties, respectively (Totura, Green, Karver, & Gesten, 2009). Consequently, our study relied on both self- and teacher- reports to gain a broader and more complete overview of peer victimization. Furthermore, in light of previous and often inconsistent sex-specific G×E effects (Uher & McGuffin, 2008) we considered potential sex differences in our main analyses. The objectives of this prospective study were two-fold: (1) to test if peer victimization and PRS-depression independently predict depressive symptoms in adolescence, and (2) to investigate PRS-depression by peer victimization interaction, in other words if PRS-depression moderates the association between peer victimization and depressive symptoms.

Methods

Participants

Participants were members of the Quebec Longitudinal Study of Child Development (QLSCD; conducted by Institut de la Statistique du Québec) (Orri et al., 2020); an ongoing prospective birth cohort with biannual or annual data collection on 2,120 singletons born in the Canadian province of Quebec in 1997/98. The Ethics Committee of the Institut de la Statistique du Québec and the Research Ethics Board of the CHU Sainte-Justine Research Center approved each phase of the study, and informed consent was obtained at each time point. Further details about the cohort can be found online (https://jesuisjeserai.stat.gouv.qc.ca). At 10 years old, blood samples were collected from 992 participants and 978 were successfully genotyped, of which 816 passed quality control procedures (see **Supplement 1** for further details). The final sample size available was 748 participants, with measures of PRS-depression and depressive symptoms.

Measures

Peer Victimization (Self-reported and Teacher-reported)

Self and teacher-reported peer victimization were assessed twice at ages 12 and 13 years during the second half of the school year (February to June).

Self-reported peer victimization was assessed using a modified version of the Self-Report Victimization Scale (Ladd & Kochenderfer-Ladd, 2002). The six items reflect various types of victimization (physical, verbal, and relational): since the beginning of the school year, how many times has another student in school; 1) called you names/said mean things; 2) did not let you play in his/her group; 3) pushed/hit/kicked you; 4) said bad things behind your back; 5) teased you in a mean way; 6) made you pay them or give them something so they would leave you alone. These items were rated on a Likert scale "never", "few times" and "more often" at 12 years, and "never", "rarely", "often", and "very often" at 13 years.

Teacher-reported peer victimization was assessed using 3 items from the Behavior Questionnaire (Tremblay, Desmarais-Gervais, Gagnon, & Charlebois, 1987) reflecting physical, verbal, and relational victimization in the last 6 months: this child was 1) made fun of by other children, 2) hit or pushed by other children, 3) called names by other children. These items were all rated on a Likert scale; "never", "few times" and "more often" at 12 and 13 years.

The Cronbach alpha (α) was 0.82 at 12 years, and 0.81 at 13 years for self-reported peer victimization, and 0.77 at 12 years, and 0.85 at 13 years for teacher-reported peer victimization, indicating satisfactory internal consistency for all measures.

As self- and teacher- reported peer victimization measures had different ranges, we converted all scores to a 0-10 scale. The Pearson correlation of self-reported peer victimization at ages 12 and 13 years was .50, and for teacher-reported peer victimization it was .42 (*p*s<.001).

Depressive Symptoms

Depressive symptoms were self-reported at 15 and 17 years using the Mental Health and Social Inadaptation Assessment (MIA) (Côté et al., 2017; Geoffroy et al., 2018). The MIA assessed eight DSM-V depression/dysthymia symptoms (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) (e.g., "I felt sad and unhappy") and their reported frequencies ("never", "sometimes", "often") in the past 12 months. Depression scores at 15 years (Cronbach α =0.85) and 17 years (Cronbach α =0.85) were averaged into a single score. The Pearson correlation of depressive symptoms at ages 15 and 17 years was .61 (p<.001).

PRS-depression

PRS-depression were created for 816 participants after quality control and imputation of genotyping data. Conceptually, PRS is a proxy of an individual's genetic propensity to a given disorder based on common genetic variation. Practically, PRS represent a count function of alleles at hundreds or thousands of SNPs across the genome, with each allele weighted by an associated effect size derived from an independent large scale GWAS of a phenotype of interest (Andlauer & Nöthen, 2020). To this end, the effect sizes from a GWAS are used as weights. In the present study, PRS were computed using PRSice v.2.2.11 (Euesden, Lewis, & O'Reilly, 2015) and based on the recent GWAS meta-analysis for depression (Howard et al., 2019). Autosomal SNPs were clumped for linkage disequilibrium (LD) with the following parameters to obtain independent SNPs LD: r^2 < 0.1 within 250 kb windows. Multiple PRS were computed, each based on a different number of SNPs (GWAS p-value thresholds were: 0.01; 0.10; 0.50; 1.00). To account for population stratification (described in **Supplement 1**), PRS were regressed on ten multidimensional scaling components calculated from the pairwise genetic relationship matrix. Standardized residuals (PRS-depression) were used in all analyses. PRS-depression used in the main analyses included

the most SNPs with a *p*-value threshold significance of p=1. Other PRS thresholds (p =0.01; p=0.10; p=0.50) were included in additional analyses.

Potential confounding factors

A set of known confounding factors (described in **Supplement 2**) in the association between peer victimization and depressive symptoms (Geoffroy et al., 2018) were used in this study, including family factors at 10 years (socioeconomic status, family structure, family functioning, hostile-reactive parenting, maternal depressive symptoms, cognitive abilities), prior mental health symptoms in childhood at 8 years (oppositional/defiance symptoms, inattention/hyperactivity symptoms, depressive and anxiety symptoms).

Statistical Analyses

In **Table S1**, we described sociodemographic characteristics for the included vs excluded participant subsamples, and tested potential differences using t-tests and chi-squared tests. **Table 1** reports descriptive statistics of our variables of interest; peer victimization at 12-13 years (self- and teacher-reported), depressive symptoms at 15-17 years, and PRS-depression.

We then estimated associations between variables of interest **(Table 2)**. More specifically, sex-adjusted hierarchical linear regressions were conducted with depressive symptoms as the outcome by subsequently including peer victimization (step 1), PRS-depression (step 2), and the interaction term between peer victimization and PRS-depression (step 3) (**Table 2**). Analyses were performed separately for self- and teacher-reported measures. All variables were converted into standardized z-scores (mean=0, standard deviation=1) to facilitate interpretation.

We tested two-way interactions; sex by peer victimization (self- and teacher-reported), and sex by PRS-depression, as well as the three-way interaction; sex by peer victimization (self- and teacher-reported) by PRS-depression, in unadjusted models predicting depressive symptoms.

Unique variances (R^2) of peer victimization (self- and teacher-reported) and PRS-depression on depressive symptoms were also estimated independently (Harel, 2009).

In sensitivity analyses, we reported correlations between peer victimization, depressive symptoms, and potential confounders in **Table S2**. To further test the robustness of our findings, we then accounted for all these potential confounders in additional models testing the additional predictive value of the peer victimization and PRS on depressive symptoms and their interaction (**Table S3**). Similar patterns of findings suggest the robustness of the reported association between peer victimization, PRS-depression and depressive symptoms, and that these findings could not be accounted for by these potential confounders. Second, the main analyses included PRS-depression calculated on SNPs up to the significance threshold of p=1, but we re-estimated our main models using alternative PRS-depression thresholds; p<.01, p<.1, p<.5 (**Table 3**). These alternative PRS-depression thresholds were more conservative, hence included fewer SNPs when calculating the PRS-depression. These sensitivity analyses allowed us to confirm that our results were consistent across the different p-value thresholds used to calculate the PRS-depression.

Missing data were imputed using multiple imputation by chained equation (Azur, Stuart, Frangakis, & Leaf, 2011) to avoid losing participants due to missing data on peer victimization (2.5% for self-report and 14.2%, for teacher report) and confounders (from 2.4% for socioeconomic status to 14.8% for maternal depressive symptoms).

Results

The descriptive statistics for the study participants versus participants who were not included are presented in **Table S1**. Participants included in the study subsample (vs non-included) were more likely to 1) be female, 2) have parents who graduated from high school, 3) have a sufficient income, above the low-income cut-off, and 4) have a mother with less depressive

symptoms when they were infants. **Table 1** presents descriptive statistics on the variables of interest; self-reported peer victimization, teacher-reported peer victimization, and depressive symptoms. Additional analyses showed that self-reported and teacher-reported peer victimization were moderately correlated with each other (Pearson r=0.39, p<.001). Furthermore, additional analyses showed that PRS-depression correlated with self-reported peer victimization (Pearson r=0.11; p=.002), but not with teacher-reported peer victimization.

Associations of peer victimization at 12-13 years and PRS-depression with depressive symptoms at 15-17 years are shown in **Table 2**. In sex-adjusted analyses, peer victimization (self- and teacher-reported) significantly predicted depressive symptoms (β=0.34, p<.001; and β=0.14, p=.001, respectively) (Step 1, **Table 2**). This association remained significant when PRS-depression was entered in the model (β=0.33, p=<.001; β=0.13, p=.002, respectively) (Step 2, **Table 2**). PRS-depression was associated with depressive symptoms in these models when accounting for peer victimization (β=0.07, p=.025; β=0.10, p=.002, respectively) (Step 2, **Table 2**). Furthermore, these associations remained significant after controlling for sex, childhood mental health symptoms at 8 years (oppositional/defiance symptoms, inattention/hyperactivity symptoms, depressive and anxiety symptoms) and family factors at 10 years (socioeconomic status, family structure, family functioning, hostile-reactive parenting, maternal depressive symptoms, cognitive abilities); see **Table S3**. However, the interaction term of PRS-depression and peer victimization (self- and teacher-reported) was not significant (β=0.04, p=.238; and β=-0.001, p=.986, respectively; Step 3, **Table 2**). In two separate regression models on either self-reported or teacher-reported peer victimization, the unique variance (based on R^2) of peer victimization in the prediction of depressive symptoms was 7.4% and less than 1%, respectively. A third model showed that the PRS-depression uniquely predicted 1.2% of depressive symptoms' variance (based on R^2).

Finally, sex did not interact with either peer victimization (p=.788 for self-report, and p=.094 for teacher report), or PRS-depression (p=.190) to predict depressive symptoms. There was also no three-way interaction between peer victimization, PRS-depression, and sex (p=.600 for self-reported peer victimization; and p=.321 for teacher-reported peer victimization).

We additionally explored the possibility that the findings of the sex-adjusted analyses could be in part specific to the PRS p-value threshold we selected (p=1). The general pattern of findings for the main and interaction effects between peer victimization and depressive symptoms remained consistent across all analyzed PRS-depression thresholds (p<0.5; p<0.1; p<0.01; **Table 3**). The only exception was that PRS-depression did not predict depressive symptoms when more conservative PRS-depression thresholds were used (p<0.01 and p<0.1) in models with self-reported peer victimization.

Discussion

Previous studies showed that peer victimization is associated with depressive symptoms, but the role of genome-wide cumulative genetic vulnerability to depression as a moderator had not yet been examined. Using a longitudinal design, our findings indicate that adolescents who were victimized by their peers were more likely to experience higher levels of depressive symptoms up to five years later. This is in line with another study which found that teacher-, mother-, and self-reported peer victimization at 7-10 years were associated with depressive symptoms at 11-14 years (Zwierzynska, Wolke, & Lereya, 2013). Similar to our study, teacher and self-reported peer victimization were moderately correlated with each other (Ladd & Kochenderfer-Ladd, 2002). Together, these findings suggest that teacher- and adolescent self-reports capture different perspectives of peer victimization, but they both predict depressive symptoms.

Furthermore, we showed that the association of peer victimization with depressive symptoms remained even after the genetic vulnerability to depression was taken into account, and the strength of this association did not vary as a function of PRS-depression. Our study is the first to show that peer victimization contributes to later depressive symptoms for all adolescents, regardless of their genetic vulnerabilities to depression partially captured by a recent PRS-depression. Similarly to our finding, one study in adolescents (Halldorsdottir et al., 2019) and a meta-analysis in adults (Peyrot et al., 2018) reported that the association between childhood trauma and depression was not affected by the genetic vulnerability to depression, as measured by PRS-MDD. Additionally, a more recent study using the same GWAS by Howard et al. (2019) as the present study, showed a lack of interaction between self-reported peer victimization and PRS-depression in predicting depressive symptoms in young adulthood (Armitage, Wang, Davis, & Haworth, 2022).

Our study showed that, as early as in adolescence, the PRS-depression was associated with depressive symptoms. This is consistent with one study previously reported an association between PRS-MDD and MDD, as well as depressive symptoms in adolescents (Halldorsdottir et al., 2019). Nonetheless, the effect size of the PRS-depression was rather small in magnitude, which points to the multifactorial nature of depressive symptoms' etiology, and calls for sustained effort in delineating the genetic underpinnings of depression. PRS-depression alone accounted for 1.2% of the variance in depressive symptoms in this study, which is similar to the 1.6% variance reported by Armitage et al. (2022) between PRS-depression and depressive symptoms in young adulthood. Additionally, Halldorsdottir et al. (2019) reported that PRS-MDD predicted a unique variance of around 1% for depressive symptoms severity in a clinical sample and less than 1% in the epidemiological sample. These magnitudes are also consistent with a prior GWAS showing that

PRS-MDD accounted for about 2% of the variance in MDD in adults (Wray et al., 2018). PRS-depression predicted depressive symptoms at the PRS thresholds p=1 and p=0.5. However, associations with depressive symptoms using more conservative PRS thresholds p=0.1 and p=0.01 were not significant, which may be the result of the more limited coverage of SNPs associated with depression at lower thresholds. Indeed, the advantage of using a higher (less conservative) p-value threshold is that we include a broader range of SNPs which each contribute in a small way to a genome-wide genetic vulnerability to depression. In addition, we found that associations of PRS-depression and peer victimization (self- and teacher-report) with depressive symptoms were similar in boys and in girls, and there was no sex difference in the PRS-depression by peer victimization (self- and teacher-report) interaction. Potential sex differences in terms of PRS-depression in relation to peer victimization and depressive symptoms had not been investigated prior to this study. More studies with larger samples are needed to investigate potential sex differences in more detail.

In addition, we found that PRS-depression was weakly correlated with self-reported but not with teacher-reported peer victimization. This is in line with findings from Schoeler et al. (2019) and Armitage et al. (2022) who found that self-reported peer victimization was associated with PRS-MDD and PRS-depression, respectively. One possible interpretation could be the presence of an evocative gene-environment correlation (*r*GE) between a genetic vulnerability to depression and self-reported peer victimization. In other words, having a genetic vulnerability to depression would increase the risk of experiencing depressive symptoms, which would in turn increase the risk of experiencing peer victimization. This *r*GE hypothesis is partly supported by a meta-analysis showing that depressive symptoms are associated with later peer victimization in childhood (Christina, Magson, Kakar, & Rapee, 2021). We could further hypothesize that having

a genetic vulnerability to depression is linked to certain social and interpersonal behaviors, such as social withdrawal and sadness, which increase one's risk of being peer victimized, as previously suggested (Luchetti & Rapee, 2014; Schlag et al., 2022). However, more studies are needed to replicate this *r*GE and to further investigate potential mechanisms behind it.

Lastly, one possible explanation for the inconsistent pattern of association between self-reported vs teacher-reported peer victimization and PRS-depression may be that self-reports of peer victimization may more readily capture a perception bias towards social relationships, which may co-occur with a genetic vulnerability to depression. In other words, individuals with a genetic vulnerability to depression may perceive more acutely or be more inclined to interpret behaviors by peers as victimization (Kellij, Lodder, van den Bedem, Güroğlu, & Veenstra, 2022; Lopez & DuBois, 2005; Orth, Robins, & Roberts, 2008). Alternatively, teacher-reports could be more limited in scope compared to self-reports of peer victimization as it included only 3 items. However, to strengthen their validity, these ratings were averaged over two years and included ratings of 2 different teachers across the 2 timepoints. Furthermore, the significant year-to-year stability of self-reported and teacher-reported peer victimization (r=.50, r=.42, respectively) in this study is comparable to a meta-analysis of 77 longitudinal studies reporting similar magnitudes (r=.49, r=.57, respectively) (Pouwels, Souren, Lansu, & Cillessen, 2016). Finally, to conclude on the *r*GE finding, as stressed by Christina et al. (2021), such reverse causality hypotheses should be handled with caution to avoid blaming to the victim, but rather to identify individual characteristics that may inform intervention research. Furthermore, more studies are needed to replicate this finding before further hypotheses can be made.

The study's strengths included the use a contemporary sample of adolescents from the general population followed from birth to age 17 years, with data on peer victimization assessed

in early adolescence (12-13 years) from both the primary teachers and the adolescents themselves. This allowed us to compare associations of self-reported and non-self-reported measures with depressive symptoms, which is lacking in the literature. Our study also tested the contribution of PRS-depression in the association between peer victimization and depressive symptoms using PRS-depression derived from a recent GWAS meta-analysis on broad depression with one of the largest sample to date (Howard et al., 2019). Several more conservative PRS thresholds ($p<0.01$, $p<0.1$, $p<0.5$) were also included our analyses to confirm our results with PRS $p<1$.

However, our conclusions need to be interpreted in light of a number of limitations. First, teacher-reported peer victimization was measured using three items, while self-reported peer victimization had six items. Nevertheless, both scales assessed physical, verbal, and relational peer victimization and were associated with depressive symptoms. Second, no clinical measure of depression was available in the present study. Still, PRS-depression was associated with self-reported depressive symptoms in adolescence. Third, our results cannot be generalized to the initial QLSCD cohort as this study sample was limited to participants who provided DNA samples through blood collection at 10 years. The study participants were found to be more advantaged than non-included participants in terms of early-life factors such as socioeconomic (income) and family factors (maternal depression, parents' education).

Conclusion

In conclusion, being exposed to peer victimization in early adolescence was associated with higher depressive symptoms in middle to late adolescence. This association was not accounted for by a partial measure of genetic liability to depression (PRS-depression) nor by known confounding factors (e.g., prior mental health symptoms) (Geoffroy et al., 2018). PRS-depression weakly predicted depressive symptoms but did not influence the association between

peer victimization and depressive symptoms. In other words, peer victimization predicted depressive symptoms for all levels of genetic vulnerability to depression. In light of a fast-evolving field, future studies are needed to replicate these findings. Particularly as different methods to calculate PRS are emerging and new GWAS are being published.

Keypoints

- This study confirmed that both self-reported and teacher-reported peer victimization (aged 12-13 years) was associated with more depressive symptoms (15-17 years)
- Genetic vulnerability to depression measured by a polygenic risk score for depression (PRS-depression) also predicted depressive symptoms at 15-17 years
- PRS-depression did not moderate the association between peer victimization (self-reported and teacher-reported) and depressive symptoms (15-17 years)
- Evidence for a gene-environment correlation between PRS-depression and self-reported peer victimization was uncovered

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Table 1: Descriptive statistics for peer victimization at 12-13 years, and depressive symptoms at 15-17 years in the study sample

	Self-reported peer victimization	**Teacher-reported peer victimization**	**Depressive symptoms**
N	729	642	748
Mean(±SD)	2.05(1.71)	1.06(1.72)	3.65(2.09)
Range	0-8.75	0-9.17	0-10

Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2015),

Table 2: Hierarchical linear regression predicting depressive symptoms (15-17 years) with peer victimization (12-13 years) and PRS-depression

	Hierarchical regression on depressive symptoms using either self-reported or teacher-reported peer victimization in independent models				
		Self-reported peer victimization		Teacher-reported peer victimization	
		Beta (SE)	**p-value**	**Beta (SE)**	**p-value**
Step 1	Peer victimization	0.339 (0.032)	<.001	0.136 (0.042)	.001
Step 2	Peer victimization	0.330 (0.032)	<.001	0.130 (0.041)	.002
	PRS-depression	0.071 (0.032)	.025	0.102 (0.034)	.002
Step 3 interaction	PRS-depression*peer victimization interaction	0.039 (0.033)	.238	-0.001 (0.038)	.986

Max N based on data available for PRS-depression and depressive symptoms, n=748.

Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2015), © Gouvernement du Québec, Institut de la Statistique du Québec

The residual score for PRS-depression calculated with p-value<1 threshold was used and included all 10 principal components.

All models were adjusted for sex.

Table 3: Hierarchical regression of depressive symptoms at 15-17 years on peer victimization at 12-13 years with different thresholds PRS-depression (p<.01, p<.1, p<.5)

	Hierarchical regression on depressive symptoms using self-reported peer victimization					
	P<0.01		**P<0.1**		**P<0.5**	
	Beta(SE)	***p*-value**	**Beta(SE)**	***p*-value**	**Beta(SE)**	***p*-value**
Step 1 : Self-reported peer victimization	0.339(0.032)	<.001	0.339(0.032)	<.001	0.339(0.032)	<.001
Step 2 : Self-reported peer victimization	0.332(0.032)	<.001	0.332(0.032)	<.001	0.331(0.032)	<.001
PRS-depression	0.052(0.032)	.102	0.058(0.032)	.067	0.072(0.032)	.024
Step 3: interaction PRS-depression*Self-reported peer victimization interaction	0.016(0.032)	.625	0.042(0.032)	.194	0.038(0.033)	.251

	Hierarchical regression on depressive symptoms using teacher-reported peer victimization					
	P<0.01		**P<0.1**		**P<0.5**	
	Beta(SE)	***p*-value**	**Beta(SE)**	***p*-value**	**Beta(SE)**	***p*-value**
Step 1 : Teacher-reported peer victimization	0.137(0.042)	.001	0.137(0.042)	.001	0.136(0.042)	.001
Step 2 : Teacher-reported peer victimization	0.129(0.042)	.002	0.129(0.042)	.002	0.130(0.041)	.002
PRS-depression	0.082(0.033)	.014	0.086(0.034)	.010	0.101(0.033)	.003
Step 3: interaction PRS-depression*Teacher-reported peer victimization interaction	0.007(0.036)	.848	0.014(0.038)	.712	-0.004(0.038)	.911

Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998–2015), © Gouvernement du Québec, Institut de la Statistique du Québec

Max N based on data available for PRS-depression and depressive symptoms, n=748

The residual score for PRS-depression, with p-value<1 threshold, was used and included all 10 principal components.

Models adjusted for sex