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Does Cortisol Moderate the Environmental Association Between Peer Victimization and Depression Symptoms?
A Genetically Informed Twin Study

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Abstract

Many youths who are victimized by peers suffer from depression symptoms. However, not all bullying victims become depressed and individuals' biological sensitivity may play an important moderating role in this regard. In line with this notion, peer victimization has been associated with increased depressive symptoms in youth with higher basal cortisol secretion. It is unclear, however, whether this moderating effect of cortisol really concerns the *environmental* effect of peer victimization on depression. Indeed, genetic factors can also influence individuals' environmental experiences, including peer victimization, and part of these genetic factors may be those associated with depression. Using a genetically informed design based on 159 monozygotic and 120 dizygotic twin pairs (52% girls) assessed at age 14 years, this study examined whether cortisol secretion moderates the environmental or the genetic association between peer victimization and depression symptoms. Salivary cortisol at awakening was obtained with buccal swabs during four school week days. Peer victimization and depression were assessed via self-reports. Cholesky modeling revealed that peer victimization was associated with depression symptoms via both genetic and environmental pathways. Moreover, the *environmental* association between peer victimization and depression symptoms steadily increased with increasing levels of morning cortisol. The *genetic* association between peer victimization and depression symptoms also varied, albeit less, as a function of individuals' cortisol secretion. These findings support the hypothesis that peer victimization increases internalizing psychopathology mainly in youth with heightened biological reactivity to environmental conditions.

Keywords: Peer Victimization, Depression Symptoms, Cortisol Secretion, Behavioral Genetics, Adolescents

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1. Introduction

Peer victimization in schools, defined as the use of power and aggression to cause distress or to control another person carries severe risks for the victims (Craig et al., 2009). Among the most immediate sequelae are internalizing problems, most notably depression symptoms (Reijntjes et al., 2010). Not all bullying victims develop depression symptoms, however. Indeed, a meta-analysis of longitudinal studies showed that predictive effect sizes from peer victimization to internalizing symptoms (including depression) ranged from .04 to .41, with an average effect size of .18 (Reijntjes et al., 2010). This modest effect size suggests that moderating factors that enhance or buffer the detrimental impact of peer victimization on internalizing symptoms are at play.

One important factor that may moderate the extent to which bullying victims develop depression symptoms may be their biological sensitivity to context. According to the Biological Sensitivity to Context (BSC) hypothesis (Ellis et al., 2011), some individuals are more sensitive to environmental influences – whether good or bad – than others. When exposed to environmental stressors such as peer victimization, individuals with heightened biological sensitivity will thus be more likely to suffer negative sequelae. This biological sensitivity is believed to be partly rooted in genetic influences that are mediated by physiological reactivity.

1.1. The Moderating Role of Cortisol in the Link Between Peer Victimization and Depression Symptoms

Hormonal pathways, notably cortisol secretion, may play a critical role in individuals' physiological reactivity to adverse environments (Fries et al., 2005). Cortisol, a glucocorticoid hormone secreted by the hypothalamus-pituitary-adrenal (HPA) axis, is involved in the regulation of many systems critical for stress response. Cortisol typically follows a time-dependent pattern of secretion, with higher levels at awakening and a gradual decrease over the remainder of the day (Stone et al., 2001). The HPA system is particularly responsive to stressors that have a socio-evaluative component, such as peer victimization (Dickerson and Kemeny, 2004). There are, however, notable inter-individual differences in diurnal cortisol secretion as well as in cortisol reactivity to acute stress (e.g., Miller et al., 2007). These differences are believed to have important implications for individuals' physical and mental health (Fries et al., 2005). Whereas lower levels of cortisol, especially of basal cortisol, have often been linked with externalizing behaviors in adolescents (Alink et al., 2008), higher levels of cortisol are typically associated with internalizing symptoms, including depression (Halligan et al., 2007). Moreover, elevated morning cortisol as well as heightened cortisol reactivity to social stress predict

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increases in adolescents' depression symptoms over time (Goodyer et al., 2000; Susman et al., 1997). Individual differences in cortisol secretion may thus explain why some bullying victims develop depression symptoms whereas others do not.

The potential moderating role of cortisol secretion in the link between peer victimization and depression symptoms has been formally tested in only one study so far (Rudolph et al., 2011). The results showed that peer victimization was associated with increased depressive symptoms in youths with high basal cortisol secretion, i.e., as measured in anticipation of a social stress task. This finding seemingly supports the notion that a high biological sensitivity can exacerbate environmental influences on depressive symptoms. It is unclear, however, whether this moderating effect of cortisol really concerns the *environmental* association peer victimization and depression, as implicitly assumed by the BSC hypothesis. This question is important, because many (positive and negative) social experiences partly arise as a function of individuals' genetic makeup (Jaffee and Price, 2007). Indeed, evidence from genetically informed research, such as twin studies, suggests that heritable factors explain over half of inter-individual differences in peer victimization among youth (e.g., Brendgen et al., 2011). Moreover, a significant part of the genetic factors that influence individuals' negative experiences with peers, including peer victimization, also influence depression symptoms (Bowes et al., 2013; Brendgen et al., 2009). Importantly, the *genetic* association between peer-related stress and depression symptoms reflects a gene-environment correlation (rGE), and rGE is considered to indicate the effect of individuals' genotype – and by extension their genetically driven characteristics – on their environmental experiences, not the other way around (Lau and Eley, 2008). A finding that cortisol moderates only the genetic - but not the environmental - association between peer victimization and depression symptoms would be inconsistent with the BSC hypothesis. Addressing this issue would not only inform conceptual models but may also help improve intervention strategies to prevent depressive symptomatology in bullying victims.

1.2. Study Objectives

The present study used a genetically informative design based on Monozygotic (MZ) and Dizygotic (DZ) twin pairs, whose peer victimization, salivary cortisol, and depression symptoms were assessed when they were 14 years old. This developmental period is of interest, as many youth show an increase in depression symptoms from late childhood through early adolescence (Dekker et al., 2007). We focused on morning salivary

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cortisol, because a) it is influenced by both environmental and genetic factors (Ouellet-Morin et al., 2016) and b) elevated morning cortisol secretion has been linked to elevated depression symptoms (Halligan et al., 2007). We expected that this association would at least partly be explained by common underlying genetic factors. Even more relevant for the present study, we expected that common genetic factors would at least partly explain the correlation between peer victimization and depression symptoms, indicating rGE. However, the association between peer victimization and depression symptoms should not only be explained by common underlying genetic factors, but also be environmentally-driven. We were particularly interested in assessing whether the environmentally-driven association between peer victimization and depression symptoms is moderated by cortisol secretion levels. These associations were examined while controlling for several potential confounders linked to peer victimization, depression symptoms or cortisol, i.e., family adversity, harsh parenting, birth weight, pubertal status, Body Mass Index (BMI), and individuals' aggressive behavior and biological sex (e.g., Cole et al., 2014; Jessop and Turner-Cobb, 2008; Kiess et al., 1995; Rudolph et al., 2010; Wüst et al., 2005). The morning cortisol measure was also corrected for potential effects of time of awakening, sampling time, sleep duration and quality, medications, menstruation for girls, and current and persistent health conditions.

2. Material and Methods

2.1. Sample

Study participants were part of a population-based sample of 448 MZ and same-sex DZ twin pairs from the greater Montreal area who were recruited at birth between November 1995 and July 1998. Twins were first seen at 5 months of age and then prospectively assessed for a variety of child and family characteristics. Ninety-five percent of parents lived together, 44% of the twins were the firstborn children, 66% of mothers and 60% of fathers were between 25 and 34 years old, 17% of mothers and 14% of fathers had not finished high school, 28% of mothers and 27% of fathers held a university degree, 83% of the parents were employed, 10% of the families received social welfare or unemployment insurance, and 30% of families had an annual income of < \$30,000. Most families were of European descent (87%), 3% were of African descent, 3% were of Asian descent, and 1% were Native North Americans. Zygosity was assessed with 8-10 highly polymorphous genetic markers. Twins were diagnosed as Monozygotic when concordant for every genetic marker. When genetic material was insufficient, zygosity was determined based on physical resemblance at ages 18 months and 9 years (Spitz et al.,

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1996). The comparison of both methods in a subsample of 237 same-sex pairs revealed a 94% correspondence rate. The present study includes data collected in grade eight (*mean* age = 14.07 years, *SD* = 0.30), when 279 twin pairs participated. Analyses for the present paper were performed on the 203 twin pairs (MZ males = 54, MZ females = 66, DZ males = 42, DZ females = 41) with valid data on cortisol, of whom 78% had collected saliva at awakening on each of the four collection days, 17% on three days, 4% on two days and 2% on one day. Participants with and those without valid cortisol data did not differ on any measure except with respect to aggression (see description of control variables below), with the former being less aggressive than the latter.

2.2. Procedure

Letters explaining the objectives of the study were sent to the families, followed by a home visit. After obtaining informed consent from the parents and assent from the participants, research assistants explained the collection protocol, which included sampling saliva at awakening on four collection days (Tuesdays and Thursdays on two consecutive weeks) as well as the one-time completion of an interview-based questionnaire by the twins. Research assistants ensured that participants (and their parents) were familiar with the material. Families were visited a second time to gather the saliva tubes and conduct the interviews with the twins. Instruments and study procedures were approved by the Institutional Review Board of the Ste-Justine Hospital.

2.3. Main Measures Collected at Age 14 Years

Peer victimization was assessed using twins' self-reports on nine items derived from the Social Experiences Questionnaire (Crick and Grotpeter, 1996) (e.g., "During this school year, how many times has another kid called you names or said mean things to you?, ...stopped you from being in his or her group although you wanted to be?, ...pushed, hit or kicked you?, ...threatened you or said mean things about you via e-mail, chat room, or cell phone?"). Responses were given on a three-point scale ranging from 0 (never), 1 (once or twice) to 2 (often). Item scores were averaged to yield a global victimization score (Cronbach's alpha = .76, *Mean* = 0.25, *SD* = 0.28, *Min* = 0.00, *Max* = 1.22).

Depression symptoms were assessed via the brief version of the Children's Depression Inventory (Kovacs, 1992). Twins rated the frequency of 7 items primarily concerned with depressive affect (e.g., "I feel like crying") during the previous 2 weeks on a scale from 0 (rarely) to 2 (often). Item scores were averaged (Cronbach's alpha = .80, *Mean* = 0.27, *SD* = 0.26, *Min* = 0.00, *Max* = 1.77).

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Saliva collection at awakening and cortisol analysis. Participants were provided with saliva tubes (Sarstedt©), diaries to report collection times and instructions for collection. Saliva samples were first placed in the participants' refrigerator during data collection days and then stored in freezers at -20°C once returned to the laboratory until cortisol determination using a high sensitivity enzyme immune assay kit (Salimetrics® State College, PA, Catalogue No. 1-3102). Frozen samples were brought to room temperature to be centrifuged at 15000xg (3000rpm) for 15 minutes and all analyzed in one batch. The range of detection for this assay is between 0.012-3ug/dL (.33-82.76 nmol/L). We identified 1% cortisol samples with a value greater than 3 *SDs* above the mean of their respective sampling time and replaced them by the last value within 3 *SDs*. Participants were considered “compliant” if the awakening collection was completed within the first 15 min following awakening and not distinct between the twins (\leq eight min). A total of 8.61% of the samples were discarded due to noncompliance. Cortisol values were converted into nmol/L (to convert ug/dL to nmol/L, multiply by 27.588) and naturally log transformed before analyses.

Creating aggregated indicators of cortisol across several days is recommended when examining individual characteristics or experiences in relation to cortisol levels (Adam and Kumari, 2009). To this end, the four cortisol estimates (one for each collection day) were included in a confirmatory factor analysis (CFA) to derive a more stable indicator free from situational-specific variation. In these analyses, we also examined whether estimates were affected by a wide range of *potential confounding variables* (sex, time of awakening, sampling time, sleep duration and quality, medications, menstruation for girls, current health conditions such as cold, fever, allergies, as well as persistent health conditions such as diabetes). Significant confounding variables were statistically controlled in the CFA. These analyses were conducted in Mplus Version 6.11 using Full Information Maximum Likelihood estimation and the COMPLEX option adjusting standard error estimates to correct for the non-independence of observations. The CFA confirmed that the respective estimates derived at each collection day could be grouped into a global cortisol factor ($\chi^2 (1) = 0.94, p = .76; RMSEA = .00; CFI = 1.00$). Factor scores were saved for further analyses as described below (*Mean* = 7.40 nmol, *SD* = 1.71 nmol, *Min* = 3.40, *Max* = 15.55).

2.4. Additional Control Variables

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Pubertal Development at age 14 years was assessed with the Pubertal Development Scale (Petersen et al., 1987). Participants rated their physical development on a 4-point scale (0“no development” to 3“development is complete”) on several characteristics, including: growth spurt in height, pubic hair, and skin change for boys and girls; facial hair growth and voice change in boys; breast development and menarche in girls. Item scores were averaged to create an overall pubertal development scale (Mean = 1.51, SD = .50, Min = .00, Max = 2.60).

Birthweight in kg was derived from birth records (Mean = 2.44, SD = .55, Min = 0.82, Max = 3.94).

Body Mass Index (BMI) at age 14 years was calculated as the participant’s self-reported weight in kilograms divided by self-reported height in meters squared (BMI=kg/m²) (Mean = 20.47, SD = 3.82, Min = 13.08, Max = 38.89).

Family adversity. A composite family stress index was created based on mother reports on: 1) family status (twins living with both biological parents or not), 2) age of the mother at the birth of the twins, 3) mother’s level of education and 4) family revenue. A score of 0 was attributed to family status if the child was living with both natural parents and a score of 1 was attributed to all other cases. A score of 0 was attributed to teen-aged mothers and a score of 1 was attributed to all other cases. A score of 1 was attributed to mother’s level of education if the mother did not have her high school diploma and a score of 0 was attributed to all other cases. A score of 1 was attributed to family revenue if the family annual revenue was below 20 000\$ more than 50% of the time since the birth of the twins and a score of 0 was attributed to all other cases. A total family stressors index was then computed by summing the individual stressors (M = 1.21, SD = 0.58, min = 0.00, max = 3.00).

Harsh parenting at age 14 years was assessed via mother ratings on five items adapted from the Parenting Practices Scale (Strayhorn and Weidman, 1988) (e.g., “I often hurt this child”, “I sometimes hit this child when I am angry”, “I often criticize this child”). Responses were given using a four-point Likert-type scale ranging from 0 (Definitely false) to 3 (Definitely true). The respective item scores were averaged to create an overall parental hostility score (Mean = 0.50, SD = 0.45, Min = 0.00, Max = 2.20, Alpha = .77).

Participant’s own aggressive behavior at age 14 years was assessed via self-ratings on six items from the MASPAQ (LeBlanc, 1996; LeBlanc and Fréchette, 1989). Participants indicated, for instance, whether they had in the previous year “threatened to hit someone in order to force them to do something they didn’t want to do?”, “taken part in fights between groups of young people (gangs)”, “gotten into a fistfight with someone else”.

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Responses were given on a four-point Likert-type scale ranging from 0 (Never) to 3 (Very often). Due to their highly skewed distribution, item responses were dichotomized into 0 (Never) and 1 (At least once) and then summed to create an overall aggression score (Mean = 0.37, SD = 0.80, Min = 0.00, Max = 4.00).

3. Results

3.1. Correlational analyses

For all three main study variables (peer victimization, cortisol, and depression symptoms, within-twin pair correlations were higher among MZ twin pairs (who are genetically identical) than among DZ twin pairs (who on average share only half of their genes): MZ $r = .28$ and DZ $r = .15$ for peer victimization, MZ $r = .43$ and DZ $r = .19$ for cortisol secretion, MZ $r = .46$ and DZ $r = .24$ for depression symptoms. This pattern suggests that all three variables are partly influenced by genetic factors (see detailed analyses below). Phenotypic correlations showed that peer victimization was uncorrelated with cortisol secretion ($r = .03, p = .55$), but positively correlated with depression symptoms ($r = .32, p = .001$). Cortisol secretion was also positively correlated with depression symptoms ($r = .13, p = .01$). In addition, cortisol secretion and depression symptoms were correlated with each of the main control variables as well as with sex (r s ranging from $-.14$ to $.22$). Cortisol secretion and depression symptoms were therefore regressed on these confounding variables and residual values of cortisol secretion and depression symptoms were used in all subsequent analyses.

3.2. Main Analyses: Univariate Models

In a first series of analyses, univariate variance decomposition models (Neale, 2009) were fitted to the data to estimate the relative contribution of genetic and environmental factors to victimization, cortisol secretion, and depression symptoms, respectively. By comparing within-pair correlations for MZ twins and DZ twins, sources of variability of a measured variable (phenotype) can be estimated in terms of latent additive genetic effects (A), latent shared environmental effects (C) that affect siblings in the same way, and latent nonshared environmental effects (E) that affect siblings differently (Neale, 2009). Within-twin pair correlations of the latent additive genetic factors (A) are fixed to 1.0 for MZ twins and to 0.5 for DZ twins. Within-twin pair correlations of the latent shared environmental factors (C) are fixed to 1.0 for both MZ and DZ twins. Within-twin pair correlations of the latent nonshared environmental factors (E) are fixed to 0.0 for both MZ and DZ twins. The squared path coefficients between these latent factors and the observed measures, i.e., parameters a^2 , c^2 , and e^2 .

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represent partitions of variance of each phenotype, with measurement error included in e^2 . All analyses were performed with the Mplus software package. There were 0.66% missing data points in the study sample stemming from variables other than cortisol. Missing data were handled using Full Information Maximum Likelihood estimation (FIML). Model fit was assessed based on the Root Mean Squared Error Approximation (RMSEA) as well as the Log-Likelihood (LL) and χ^2 statistics (see Table 1). Low and nonsignificant LL and χ^2 values and values of RMSEA below .08 indicate good model fit and parsimony. Inspection of the parameter estimates revealed that all three variables were influenced by addition genetic factors, explaining 28% of the variance of peer victimization, 42% of the variance of cortisol secretion, and 46% of the variance of depression symptoms. The remaining portions of variance of the three variables were explained by nonshared environmental factors, whereas shared environmental factors played no significant role.

3.3. Main Analyses: Multivariate Model Without Interaction Terms

Following the findings from the univariate analyses, a multivariate Cholesky model was specified where the covariance structure of peer victimization, cortisol secretion, and depression symptoms was partitioned into (1) “common” latent factors A_P and E_P that simultaneously influence peer victimization and depression symptoms, (2) “common” latent factors A_C and E_C that simultaneously influence cortisol secretion and depression symptoms, and (3) “unique” latent factors A_D and E_D that are specific to depression symptoms (see Figure 1). Because the preliminary analyses had revealed that peer victimization was uncorrelated with morning cortisol secretion, no common factors influencing these two variables were specified. Coefficients a_P , and e_P represent the factor loadings of peer victimization on the latent factors A_P and E_P . Coefficients a_{PD} and e_{PD} represent the factor loadings of depression symptoms on the latent factors A_P and E_P . Coefficients a_C and e_C represent the factor loadings of cortisol secretion on the latent factors A_C and E_C . Coefficients a_{CD} and e_{CD} represent the factor loadings of cortisol secretion on the latent factors A_C and E_C . Finally, coefficients a_D and e_D represent the factor loadings of depression symptoms on the latent factors A_D and E_D . Thus, to give an example, the total variance of depression symptoms (V_D) can be expressed as $V_D = a_{PD}^2 + a_{CD}^2 + a_D^2 + e_{PD}^2 + e_{CD}^2 + e_D^2$. The relative contribution of the “common” latent genetic factor A_P to the overall genetic variance of depression symptoms ($a_{PD}^2 / (a_{PD}^2 + a_{CD}^2 + a_D^2)$) indicates the overlap or correlation between genetic influences on peer victimization and depression symptoms (rGE). The relative contribution of the “common” latent genetic factor

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E_P to the overall environmental variance of depression symptoms (e_{PD}^2)/($e_{PD}^2 + e_{CD}^2 + e_D^2$) can be interpreted as the environmental influence linking peer victimization to depression symptoms, net of rGE.

The results from the first multivariate model (without interaction terms) are shown in the upper part of Table 2. The fit indices indicated that this first model showed acceptable fit to the data. Inspection of the parameter estimates revealed that 16% ($= .26^2 / (.21^2 + .26^2 + .57^2)$), of the genetic factors influencing depression symptoms overlapped with those influencing cortisol secretion. Moreover, these common underlying genetic factors entirely explained the association between cortisol secretion and depression symptoms, as the common environmental influences linking these two variables were estimated to be close to zero and not significant ($e_{CD} = .06, p = .304$). Another 9% ($= .21^2 / (.21^2 + .26^2 + .57^2)$), of the genetic factors influencing depression symptoms were those that also influenced peer victimization, indicating rGE. In addition, however, there was also an environmental association between peer victimization and depression symptoms ($e_{PD} = .22, p = .000$), which accounted for 10% ($= .22^2 / (.22^2 + .06^2 + .67^2)$) of environmental influences on depression symptoms.

3.4. Main Analyses: Multivariate Model With Interaction Terms

Next, the Cholesky model was expanded to include two interaction terms: 1) an interaction term predicting depression symptoms between the common genetic factor A_P and Cortisol Secretion, represented by the term $\beta_{A_PD(C)}$, and 2) an interaction term predicting depression symptoms between the common environmental factor E_P and Cortisol Secretion, represented by the term $\beta_{E_PD(C)}$. These interaction terms tested whether the additive genetic and-or the environmental effects linking peer victimization with depression symptoms varied depending on the level of morning cortisol secretion. Since χ^2 and RMSEA are not available for a multivariate model that includes interaction terms, that model was compared to a model where these interactions terms were constrained to zero using the 2LL difference test, which is equivalent to a nested χ^2 - difference test (Purcell, 2002).

The results from the second multivariate model (with interaction terms) are presented in the lower part of Table 3. The likelihood ratio test revealed that inclusion of the interaction terms in the significantly improved model fit, $2\Delta LL(2) = 6.68, p = .03$. Both interaction terms were statistically significant. This finding indicates that both the genetic and the environmental association between peer victimization and depression symptoms

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vary significantly depending on individuals' level of morning cortisol secretion. For illustrative purposes, we plotted the magnitude of the variance of depression symptoms - and of its components – that was explained by peer victimization as a function of the level of cortisol secretion (Figure 2). As can be seen, for youth with low levels (-1 SD) of morning cortisol, both the genetic association and the environmental association between peer victimization and depression symptoms were close to zero. In other words, peer victimization was unrelated to depression symptoms in youth with very low levels of morning cortisol. However, the *environmental* association between peer victimization and depression symptoms steadily increased with increasing levels of morning cortisol. Indeed, environmental effects related to peer victimization explained around two thirds of the variance shared with depression symptoms for youth with high levels (+1 SD) of morning cortisol. The *genetic* association between peer victimization and depression symptoms also increased with increasing levels of morning cortisol, albeit to a lesser extent. Specifically, whereas there was no genetic association (i.e., no rGE) linking depression symptoms with peer victimization in individuals with low (-1SD) or moderate (mean) levels of cortisol secretion, a notable rGE emerged in individuals with high (+1SD) levels of cortisol secretion.

4. Discussion

Using a genetically informative design based on twins, the main goal of this study was to examine whether the *environmental* association between peer victimization and depression symptoms would be moderated by levels of cortisol secretion. Specifically, we aimed to test whether the environmental association between peer victimization and depression symptoms would be stronger in youth with higher levels of morning cortisol than in youth with lower levels of cortisol secretion, even when controlling for common underlying genetic influences.

Replicating findings from previous research (Happonen et al., 2002; Scourfield et al., 2003), adolescents' depression symptoms were significantly influenced by genetic factors, with the remaining variance mostly explained by environmental influences unique to each individual. Importantly, however, our results also showed that 16% of the genetic effects on depression symptoms were also associated with individuals' susceptibility for increased cortisol secretion. Indeed, the correlation between cortisol secretion and depression symptoms was entirely explained by these common underlying genetic factors. These results concord with the notion that depression has at least in part a neurophysiological origin, notably HPA axis functioning (Wichers et al., 2008).

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4.1. Genetic and Environmental Associations Between Depression Symptoms and Peer Victimization

In addition to being linked with cortisol secretion, interindividual differences in depression symptoms were also associated with interindividual differences in peer victimization. A significant portion of the link between peer victimization and depression symptoms was due to common underlying genetic influences, indicating rGE. The finding that genetic factors underlying depression symptoms are also linked to peer victimization concurs with previous findings that youths with a genetic vulnerability for depression are more at risk than others to experience negative life events, including peer victimization (Bowes et al., 2013; Brendgen et al., 2009; Lau and Eley, 2008). However, there was also an environmental association between peer victimization and depression symptoms, which may reflect environmental influences from peer victimization to depression symptoms. This interpretation would be consistent with previous findings showing that peer victimization is a serious risk factor for the development of internalizing problems (Reijntjes et al., 2010).

4.2. The Role of Cortisol in the Genetic and Environmental Associations Between Depression Symptoms and Peer Victimization

Analyses revealed that both the *genetic* and the *environmental* association between peer victimization and depression symptoms varied significantly depending on individuals' levels of cortisol secretion. Specifically, whereas there was no genetic association (i.e., no rGE) linking depression symptoms with peer victimization in individuals with low or moderate levels of cortisol secretion, a notable rGE emerged in individuals with high levels of cortisol secretion. It is possible that individuals who have both a high genetic vulnerability for depression symptoms and high levels of cortisol secretion express their negative thoughts and feelings in a way that puts them at especially high risk of victimization by peers. Indeed, because cortisol helps mobilize energy stores and facilitate behavioral responses to stress (Gunnar and Quevedo, 2007), individuals with higher than normal morning cortisol levels may be more prone than others to overreact to even mild teasing. In support of this notion, elevated cortisol secretion has been linked with withdrawal and with persistent (trait) rather than temporary (state) anxious and fearful behavior in youth (Greaves- Lord et al., 2007; Pérez-Edgar et al., 2008). Elevated cortisol has also been shown in children who react with exaggerated emotional and angry outbursts to perceived provocations or threats (Lopez-Duran et al., 2009). Peers may perceive such behavior as provocative or even amusing, which may lead to further ridiculing and harassment (Gazelle and Shell, 2017, in press). These

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explanations are speculative, however, and further research is needed to understand why youth with a disposition for depression symptoms and elevated cortisol secretion may be more likely to become victimized by their peers than others.

More central to the objective of the present study, the environmental association between peer victimization and depression symptoms also increased with increasing cortisol levels. Specifically, whereas environmental effects related to peer victimization did not predict depression symptoms in youth with very low levels of morning cortisol, environmental effects related to peer victimization explained around two thirds of the variance shared with depression symptoms for youth with high levels of morning cortisol. The finding that cortisol moderates the *environmental* association between peer victimization and depression symptoms may be interpreted as concordant with the Biological Sensitivity to Context (BSC) hypothesis (Ellis et al., 2011). When exposed to environmental stressors such as peer victimization, individuals with heightened biological sensitivity may be especially vulnerable to suffering negative consequences. This finding thus corroborates that from a previous non-genetically informed study showing that peer victimization is associated with increased depressive symptoms only in youths with high basal cortisol secretion (Rudolph et al., 2011). Whereas Rudolph and colleagues examined basal cortisol in anticipation of a social stress task, our study shows that the same moderating effect of cortisol can be found when examining morning cortisol in a natural setting. The present findings thus add to the accumulating evidence that hormonal pathways, notably cortisol secretion, play a critical role in individuals' biological reactivity to environmental conditions (Fries et al., 2005).

4.3. Strengths and Limitations

Disentangling genetic and environmental pathways through a genetically informed design based on twins, the present study adds to and clarifies the scant existing literature linking peer victimization, depression symptoms, and cortisol secretion. By collecting salivary cortisol over four days, we obtained more reliable measurements than a single day assessment (Kraemer et al., 2006). Our study is not without limitations, however. While saliva samples obtained at home allowed us to measure cortisol levels in a natural environment, the sampling procedure could not be directly controlled. Mean sampling times suggested that most participants adhered well to the protocol and control of the sampling time also helped minimize potential bias. Nevertheless, compliance in collecting saliva samples at specific times at home is not always satisfactory despite detailed

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instructions (Kudielka et al., 2003). Future studies should thus ideally utilize track caps to electronically monitor sampling times (e.g., medication event monitoring: MEM caps). Another limitation concerns the use of self-reports to assess peer victimization. However, evidence suggests that subjective rather than objective stress impacts physiological stress response and health outcomes (Adler et al., 2000). Findings also rest on cross-sectional data and future studies should ideally include two time points within the same school year to more clearly discern directionality of effects. Generalization could also be limited since data were based on twins. However, twins do not differ from singletons in the level of peer victimization (Boivin et al., 2013), mood levels or cortisol reactivity to daily stressors (Jacobs et al., 2007). Moreover, although twins more often have low birth weight, they do not differ from singletons in regard to other confounders, such as BMI or pubertal status (Kaprio et al., 1995). These variables were also controlled in our study. Finally, our results cannot be generalized to clinical populations, as they show different patterns of cortisol secretion (Goodyer et al., 1996).

4.4. Conclusions

Despite these limitations, our study provides further insights about the critical role of the HPA axis in the link between adverse environmental experiences and depression symptoms. A high genetic vulnerability for depression symptoms, when coupled with heightened physiological reactivity as indicated by morning cortisol secretion, is related to an increased risk of adverse environmental experiences such as peer victimization. By the same token, individuals with heightened levels of morning cortisol are also more at risk than others to suffer from depression symptoms when exposed to negative environmental experiences such as peer victimization. Considering the important role of HPA axis functioning in the link between peer victimization and depression symptoms, interventions that optimize physiological stress regulation may be a promising avenue to test further the hypothesized role of the HPA axis in this link and, eventually, to help break this vicious cycle (Matousek et al., 2010).

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Table 1

Univariate Model Results

	A	C	E	%A ²	%C ²	%E ²	RMSEA	LL	χ^2	<i>p</i>
<i>Peer Victimization</i>	.52 (.11;.92)	.07 (-2.29; 2.43)	.82 (.73; .91)	28.1	0.6	71.3	.00	-754.8	0.50	.78
<i>Morning Cortisol</i>	.62 (.50; .74)	.00 (-1.58; 1.58)	.73 (.65; .82)	41.8	0.0	58.2	.03	-581.2	0.10	.95
<i>Depression Symptoms</i>	.66 (.37; .94)	.06 (-2.72; 2.83)	.71 (.63;.78)	46.3	0.4	53.3	.00	-728.4	0.09	.96

Note. Confidence Intervals are in parentheses. All models have 4 parameters (including means) and 2 degrees of freedom.

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Table 2

Cholesky Model Results

Model	Parameter	Estimate	LL	Number of parameters	AIC	BIC	RMSEA	χ^2 (df)	<i>p</i>
Without interaction			-2031.5	13	4089.0	4136.3	.00	4.95 (17)	.99
	a _P	.52 (.39; .66)							
	a _{PD}	.21 (.03; .39)							
	a _C	.63 (.51; .75)							
	a _{CD}	.26 (.09; .43)							
	a _D	.57 (.45; .69)							
	e _P	.82 (.74; .90)							
	e _{PD}	.22 (.12; .32)							
	e _C	.73 (.65; .81)							
	e _{CD}	-.06 (-.18; .06)							
	e _D	.67 (.60; .74)							
With interaction			-1572.4	15	3174.9	3224.6			
	a _P	-.40 (-.65; -.15)							
	a _{PD}	.09 (-.20; .37)							
	$\beta_{A_PD(C)}$.22 (.04; .39)							
	a _C	.64 (.51; .76)							

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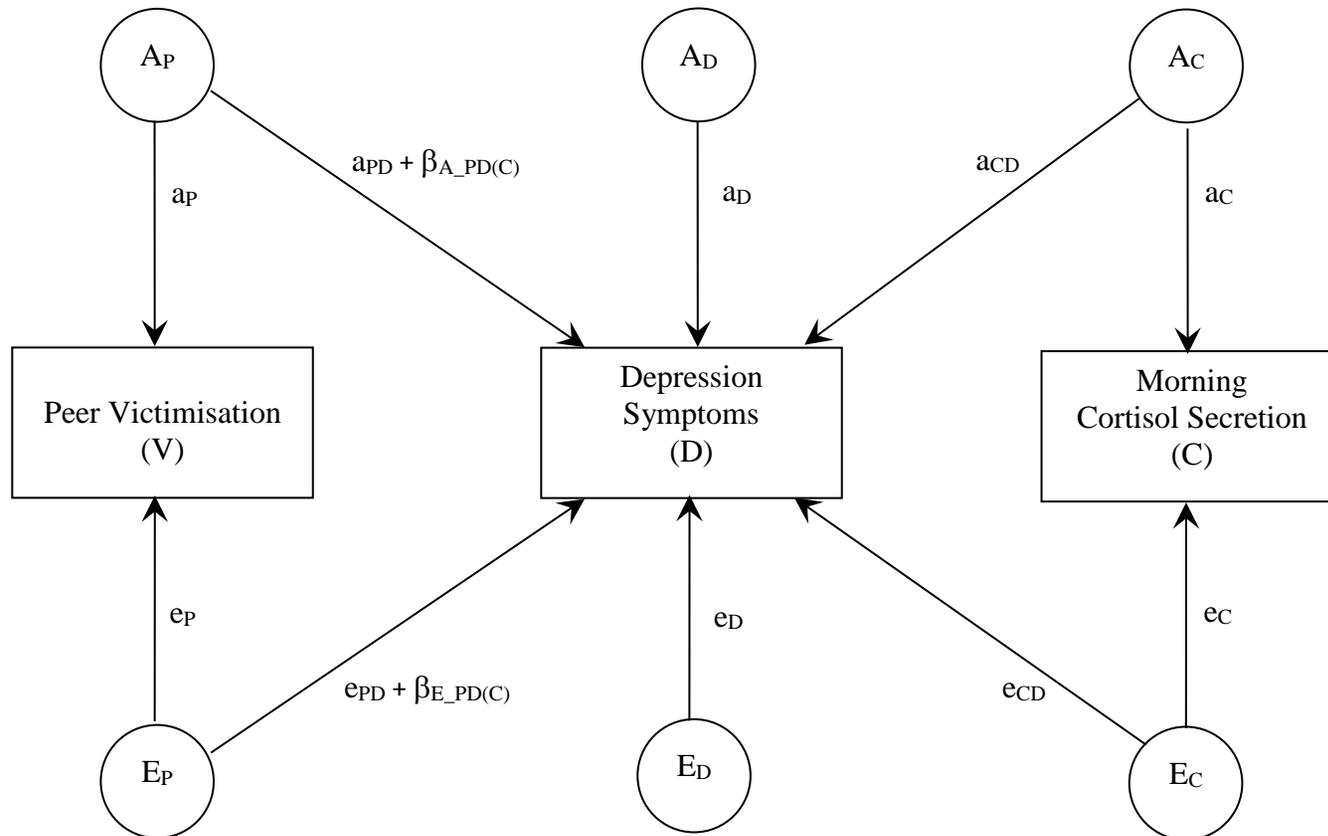
a _{CD}	.21 (.05; .36)
a _D	-.47 (-.67; -.27)
e _P	.83 (.68; .97)
e _{PD}	.32 (.20; .43)
β _{E_PD(C)}	.13 (.04; .39)
e _C	-.74 (-.82; -.65)
e _{CD}	.04 (-.06; .15)
e _D	.61 (.50; .73)

Note. Confidence intervals are in parentheses. No fit statistics are available in Mplus for models that include interaction terms.

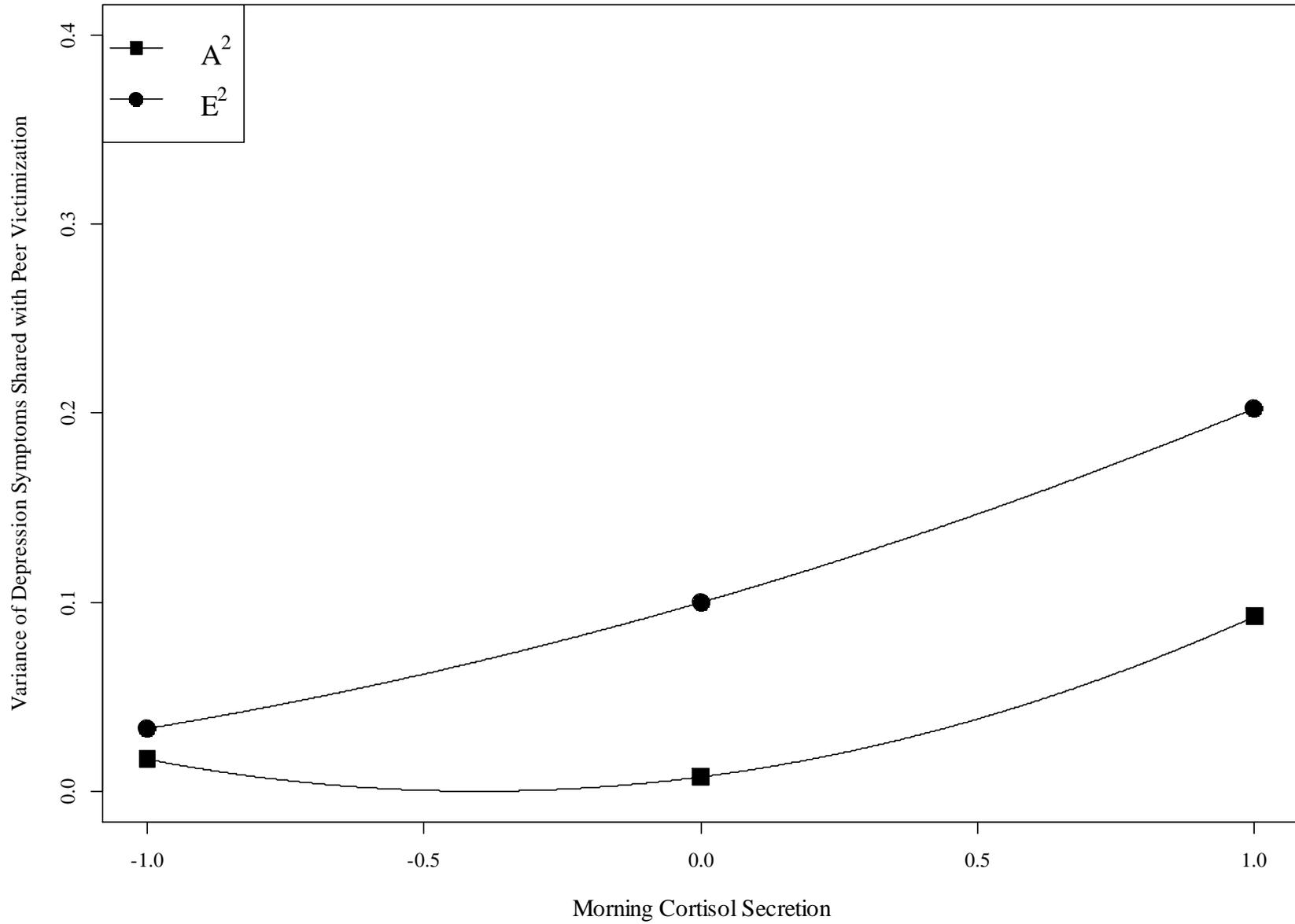
Figure Captions

Figure 1. Multivariate model (for one member of a twin pair) of peer victimization, cortisol secretion, and depression symptoms including interaction terms.

Figure 2. Plot of the genetic and environmental variance of depression symptoms shared with peer victimization (in % of total variance of depression symptoms) as a function of morning cortisol secretion. Values for cortisol are indicated as -1 SD, the mean (0) and +1 SD.



Variance components



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