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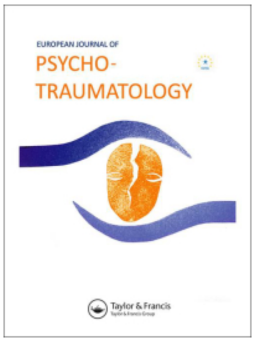

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CLINICAL RESEARCH ARTICLE

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A sex-specific pathway linking early life maltreatment, vagal activity, and depressive symptoms

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ABSTRACT

Background: Experiences of early life maltreatment (ELM) are alarmingly common and represent a risk factor for the development of psychopathology, particularly depression. Research has focused on alterations in autonomic nervous system (ANS) functioning as a mediator of negative mental health outcomes associated with ELM. Early alterations in autonomic vagal activity (vmHRV) may moderate the relationship between ELM and depression, particularly when considering forms of emotional maltreatment. Recent evidence suggests that the relationships of both ELM and vmHRV with depression may be non-linear, particularly considering females.
Objective: Building on and extending theoretical considerations and previous work, the present work aims to further the current understanding of the complex relationships between ELM exposure, vmHRV, and depression.
Methods: This study uses an adaptive modelling approach, combining exploratory network-based analyses with linear and quadratic moderation analyses, drawing on a large sample of males and females across adolescence (total $N = 213$; outpatient at-risk sample and healthy controls) and adulthood (total $N = 85$; community-based convenience sample).
Results: Exploratory network-based analyses reveal that exposure to emotional abuse is particularly central within a network of ELM subtypes, depressive symptoms, and concurrent vmHRV in both adolescents and adults. In adults, emotional neglect shows strong associations with both emotional abuse and vmHRV and is highly central as a network node, which is not observed in adolescents. Moderator analyses reveal significant interactions between emotional maltreatment and vmHRV predicting depressive symptoms in adult females. Significant quadratic relationships of emotional maltreatment and vmHRV with depression are observed in both adolescent and adult females.
Conclusions: The present findings contribute to the understanding of the psychological and physiological mechanisms by which ELM acts as a risk factor for the development of depression. Ultimately, this will contribute to the development of targeted and effective intervention strategies to mitigate the detrimental effects of early adversity.

Una vía específica por sexo que vincula el maltrato en los primeros años de vida, la actividad vagal y los síntomas depresivos

Antecedentes: Las experiencias de maltrato en los primeros años de vida (ELM, por sus siglas en inglés) son alarmantemente comunes y representan un factor de riesgo para el desarrollo de psicopatología, particularmente depresión. La investigación se ha centrado en las alteraciones del sistema nervioso autónomo (SNA) que funcionan como mediador de los resultados negativos de salud mental asociados con ELM. Las alteraciones tempranas en la actividad vagal autónoma (vmHRV, por sus siglas en inglés) pueden moderar la relación entre ELM y la depresión, particularmente cuando se consideran formas de maltrato emocional. La evidencia reciente sugiere que las relaciones, tanto de las ELM como de vmHRV con la depresión pueden ser no lineales, particularmente considerando a las mujeres.
Objetivo: Basándose en y ampliando consideraciones teóricas y trabajos previos, el presente trabajo tiene como objetivo mejorar la comprensión actual de las complejas relaciones entre la exposición a ELM, vmHRV y la depresión.
Métodos: Este estudio utiliza un enfoque de modelado adaptativo, que combina análisis exploratorios basados en redes con análisis de moderación lineal y cuadrática, basándose en

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Early life maltreatment; depression; sex-specific pathway; autonomic vagal activity; network analysis; nonlinear quadratic relationships

PALABRAS CLAVE
Maltrato en los primeros años de vida; depresión; vía específica por sexo; actividad vagal autónoma; análisis de red; relaciones cuadráticas no lineales

HIGHLIGHTS

- Early exposure to chronic and severe adversity, which includes experiences of maltreatment, defined by the World Health Organization as physical, sexual, emotional abuse and/or neglect of children under the age of 18, is highly prevalent in the general population (estimated at 40–50 percent), and is a well-documented risk factor for depression.
- The present work combines network-based analyses with tests of different functions (i.e. linear, nonlinear quadratic) in moderator analyses to further explore the complex relationships among ELM exposure, vmHRV, and depression.
- The present findings contribute to the understanding of the psychological and

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una muestra grande de hombres y mujeres durante la adolescencia (total $N = 213$; muestra de pacientes ambulatorios en riesgo y controles sanos) y la edad adulta (total $N = 85$; muestra por conveniencia basada en la comunidad).
Resultados: Los análisis exploratorios basados en redes revelan que la exposición al abuso emocional es particularmente central dentro de una red de subtipos de ELM, síntomas depresivos y vmHRV concurrente tanto en adolescentes como en adultos. En los adultos, la negligencia emocional muestra fuertes asociaciones tanto con el abuso emocional como con la vmHRV y es muy central como nodo de red, lo que no se observa en los adolescentes. Los análisis de moderadores revelan interacciones significativas entre el maltrato emocional y la vmHRV que predicen los síntomas depresivos en mujeres adultas. Se observan relaciones cuadráticas significativas de maltrato emocional y vmHRV con depresión tanto en mujeres adolescentes como adultas.
Conclusiones: Los presentes hallazgos contribuyen a la comprensión de los mecanismos psicológicos y fisiológicos por los cuales ELM actúa como factor de riesgo para el desarrollo de depresión. En última instancia, esto contribuirá al desarrollo de estrategias de intervención específicas y eficaces para mitigar los efectos perjudiciales de la adversidad temprana.

physiological mechanisms by which early exposure to chronic and severe maltreatment acts as a risk factor for the development of depression.
- Ultimately, this will contribute to the development of targeted and effective intervention strategies to mitigate the detrimental effects of early adversity.

1. Introduction

Exposure to adversity early in life is a highly prevalent and global phenomenon (Kessler et al., 2010) and a leading transdiagnostic risk factor for a wide range of physical and mental health problems, observed even in mid- to late-life (Dong et al., 2004; Felitti et al., 1998; Grummitt et al., 2021; Rich-Edwards et al., 2012). A particularly severe form of early adversity is exposure to early life maltreatment (ELM), which is commonly defined as chronic or severe exposure to various forms of abuse and/or neglect (i.e. emotional and/or physical abuse and/or neglect by primary caregivers, as well as sexual abuse by any adult), experienced before the age of 18 years (Leeb et al., 2008). Exposure to ELM is also alarmingly common and represents a well-documented risk factor for depression in adulthood (Infurna et al., 2016; Kessler et al., 2010; Li et al., 2016; Mandelli et al., 2015). This association is assumed to manifest in childhood or adolescence (LeMoult et al., 2020). The prevalence of depression increases in adolescence compared to pre-adolescence, and adolescent depression is a strong predictor of recurrent depression in adulthood; (Thapar et al., 2022) thus, the risks associated with ELM may be particularly consequential during the adolescent years (Mash & Wolfe, 2015; Merikangas et al., 2010). ELM is associated with an earlier onset and more persistent course of depression, and may even be linked with a lack of response to psychotherapy and pharmacological treatments (McLaughlin et al., 2012; Nanni et al., 2012; Teicher & Samson, 2013). Critically, as depression is a major global health problem, particularly among adolescents and young adults, (Klaufus et al., 2022, World Health Organization (WHO) 2021) it is essential to better understand the mechanisms by which well-documented risk factors such as ELM influence depressive symptomatology.

Neuroscientific research has focused on potential mediators of the adverse outcomes that are associated with ELM. Many neurodevelopmental studies and theoretical models agree that the many mechanisms by which ELM affects long-term mental and physical health reflect biological embedding during periods of developmental plasticity (Belsky & de Haan, 2011; Evans et al., 2013; Humphreys & Zeanah, 2015; McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). ELM exposure can alter the structure and functioning of the developing nervous system, (Hertzman & Boyce, 2010) and a growing literature documents developmental time windows during which ELM exposure is particularly detrimental to mental health (Danese et al., 2007; Gabard-Durnam & McLaughlin, 2020; Jenness et al., 2021; Miller et al., 2018; Miller et al., 2021; Nelson & Gabard-Durnam, 2020; Sheridan et al., 2020). In addition to sensitive periods in early development, (Zeanah et al., 2011) the onset of adolescence, and a variety of social and biological changes that occur during adolescence may also affect mental health (Andersen & Teicher, 2008; Fuhrmann et al., 2015; Kolb, 2009). Consistent with increased rates of depression, adolescence likely presents another sensitive window when environmental experience can have considerable impact across major mental and physical health domains. Increased plasticity can be observed not only at the level of brain circuitry, but also at the level of other physiological systems (e.g. the hypothalamic–pituitary–adrenal axis has been found to recalibrate to the current environment during adolescence [Sisk & Gee, 2022]) – supporting increased vulnerability to depression.

Among potential mediators of adverse outcomes associated with ELM, psychophysiological research has focused on the relationship between ELM exposure and changes in the functioning of the autonomic nervous system (ANS). The ANS is an extensive network of efferent and afferent nerves that work in conjunction with the central nervous, endocrine, and circadian systems to respond adaptively to changes in the environment, and maintain the body in dynamic, context-appropriate homeostasis (Riganello et al., 2019; Thayer & Lane, 2000; Ulrich-Lai &

Herman, 2009). Inter-individual differences in autonomic vagal activity, indexed by vagally-mediated heart rate variability (vmHRV), are of interest in the context of emotional regulation or dysregulation, respectively, and higher resting-state vmHRV is considered an indicator of better self-regulation and adaptability (Thayer & Lane, 2009). In the context of adverse physical and mental health outcomes, and particularly in adolescent depression, the vagus nerve has been implicated as a key player in mediating neurodevelopmental risk (Koenig 2020). Changes in vmHRV have been investigated as one of the mechanisms involved in the pathways by which ELM increases the risk of psychopathology, as documented by systematic reviews and meta-analyses on the topic (Koss & Gunnar, 2018; Sigrist et al., 2021; Wesarg et al., 2022; Young-Southward et al., 2020). While these have shown that direct linear associations between ELM and vmHRV are difficult to establish, vmHRV has been shown to be potentially reduced in ELM-exposed individuals compared to nonexposed individuals in the presence of psychopathology (Sigrist et al., 2021).

Evidence has also accumulated on the association between vmHRV and depression, and meta-analyses suggest an association between major depressive disorder and reductions in vmHRV, in both adolescent (Baumeister-Lingens et al., 2023; Koenig et al., 2016) and adult samples (Kemp et al., 2010). The association between vmHRV and depressive symptoms has been examined in longitudinal studies, and both population-based (Jandackova et al., 2016) and twin studies (Huang et al., 2018) suggest that reductions in vmHRV may precede the onset of depressive symptoms. Another line of research examining the dynamic changes in vmHRV during and after psychotherapeutic (Blanck et al., 2019; Chambers & Allen, 2002) or pharmacological (Balogh et al., 1993; Khaykin et al., 1998; Koenig et al., 2018) treatment for depression suggests that improvement in depressive symptoms is associated with a re-increase in vmHRV.

Of note, previous studies have highlighted two critical aspects of the association between vmHRV and depression. Firstly, the association between vmHRV and depressive symptoms is likely to differ between females and males. Studies of clinical samples have shown that women with depressive symptoms have increased vmHRV during rest, in contrast to men with depressive symptoms (Chambers & Allen, 2007; Chen et al., 2010; Dietrich et al., 2011; Koenig et al., 2017; Kuang et al., 2019; Thayer et al., 1998; Tobaldini et al., 2020). It has been suggested that evolutionarily-based gender differences in mechanisms of vmHRV might explain such differences (i.e. positive associations between vmHRV and depressive symptoms in females in contrast to consistently negative associations in males) (Jandackova et al., 2016; Jarczok et al., 2018; Jarczok et al., 2018; Thayer et al., 1998; Verkuil et al., 2015). Secondly, and relatedly, while most research on this topic has characterized the relationships between vmHRV and emotion as strictly linear ([Thayer & Lane, 2009] for a review), more recent work supports a non-linear association between vmHRV and emotional outcomes, particularly depression (Spangler et al., 2021). A non-linear, i.e. U-shaped, quadratic relationship between vmHRV and depressive symptoms implies a positive and negative association between depression and vmHRV within the same non-linear function, such that at low levels of depression, the association with vmHRV is negative, whereas at higher levels of depression this association may become positive. Indeed, a U-shaped quadratic relationship between vmHRV and depression has been found specifically in women (Spangler & Friedman, 2017). The parental investment theory (Trivers, 1996) and the tend-and-befriend theory (Taylor et al., 2000) have been used to explain these findings, suggesting that high vmHRV in women may represent an effortful, compensatory emotion regulation response to cope with greater depression (i.e. a 'tend-and-befriend' response) that is not found in men (Thayer et al., 2003). Furthermore, the quadratic association between vmHRV and emotion in women may be considered in the context of the vagal tank theory (Laborde et al., 2018) as more recently proposed. This theory suggests relatively higher levels of vmHRV to be indicative of greater psychophysiological resources (e.g. integration of neural, metabolic, and cognitive resources) that may be used for self-regulation and thus adaptive emotional responses. Low vmHRV in women would then represent fewer self-regulatory resources resulting in deficient emotion regulation and, in turn, higher levels of depression, moderate vmHRV in women may represent greater self-regulatory resources allowing for context-appropriate emotion regulation and thus lower levels of depression, and high vmHRV in women may represent very high self-regulatory resources and reserves that have been built up to cope with increased depressive symptoms. According to this theory, a strictly linear association between vmHRV and emotional outcomes such as depression in men may be due to vmHRV similarly indexing the degree of self-regulatory resources, without the presence of a compensatory response to high vmHRV (Spangler et al., 2021).

While the association between ELM and depression may be generally assumed to be linear (i.e. greater ELM exposure may result in a greater risk of depression), this assumption may also be challenged in light of recent evidence. One meta-analytic study found that ELM exposure may be a non-linear predictor of depression by characterizing the shape of the respective dose–response relationship (Tan & Mao, 2023). In addition, a recent primary study that used a machine learning approach to examine the association between ELM exposure and depressive affect in adulthood found that reported levels of exposure to specific forms of ELM (including emotional neglect) predicted depression risk in a non-linear relationship (Betz et al., 2022). The results of these studies suggest that ELM exposure may be a non-linear predictor of depression.

Given the initial evidence for a temporal association between vmHRV and depression, such that reduced vmHRV would precede the development of depressive symptoms, (Huang et al., 2018; Jandackova et al., 2016) studies have examined whether vmHRV levels would partially mediate or moderate the association between ELM and depression. Indeed, vmHRV has shown to moderate the association between ELM and concurrent internalizing symptoms, as well as depressive symptom severity, in adolescents (Duprey et al., 2021; McLaughlin et al., 2015; Vaughn-Coaxum et al., 2020). Notably, these studies have shown that exposure to emotional maltreatment (both emotional abuse and neglect) appears to be a particularly important risk factor of reduced vmHRV in the context of depression, in line with previous evidence and underlying theories suggesting that different forms of ELM pose unique mechanisms of risk. Specifically, to the extent that different forms of ELM represent vastly different exposures with distinct influences on development, they have been found to be differentially relevant in shaping pathways to depressive symptoms in clinical and non-clinical samples (Betz et al., 2021; Cecil et al., 2017; de Oliveira et al., 2018; Humphreys et al., 2020; LoPilato et al., 2020; Salokangas et al., 2019; Sheridan & McLaughlin, 2014; Sheridan & McLaughlin, 2014). Specifically, a growing body of literature suggests that childhood emotional maltreatment is an important contributor to the development of depression (Humphreys et al., 2020). Thus, distinguishing among ELM subtypes is a critical task in clarifying the role of vmHRV in the association between ELM exposure and depression. Given the above findings of non-linear relationships between vmHRV and depression and corresponding sex differences, as well as potential non-linear relationships between ELM exposure and depression risk, it may be important to consider testing for non-linear relationships when examining vmHRV as a moderator or mediator of the adverse outcomes associated with ELM.

Recent work has suggested that a complex systems approach may be more appropriate than previous methods for modelling the complex dynamics associated with ELM and its subtypes (Spangler et al., 2021; Spangler & Friedman, 2017; Trivers, 1996). Indeed, a complex systems approach has been postulated to outperform commonly used statistical methods for capturing and modelling ELM, as these, from this perspective, are unable to adequately approximate its true complexity. Broadly speaking, a complex system refers to a system that is greater than the sum of its parts (Meadows, 2009) and that can be dynamic, as different components can interact with each other. When referring to ELM and the co-occurrence of its different subtypes, from a complex systems perspective, it may be important to consider direct and indirect effects of different forms of ELM exposure, and to consider them simultaneously. As a complex systems approach, network analysis, which is increasingly applied especially in psychological sciences to address issues of complexity in psychological research, (Epskamp et al., 2018) is a statistical method that allows unique direct and indirect relationships between many variables of interest to be estimated and examined simultaneously in a single model (Borsboom & Cramer, 2013). As a recent example of its usefulness, one study used network analysis to identify distinct clusters of adversity across childhood and adolescence, with emotional abuse in the family environment being particularly central and predictive of mental health outcomes in early adulthood (Pollmann et al., 2023). These findings are also consistent with previous studies that have considered specific subtypes based on more traditional modelling techniques, as noted above (Duprey et al., 2021; McLaughlin et al., 2015; Vaughn-Coaxum et al., 2020).

In summary, there is evidence of a strong positive association between ELM exposure (and especially emotional maltreatment) and depression (for a recent meta-analysis on the topic, see [Humphreys et al., 2020]), while a clear association between vmHRV and depression has also been established. Both relationships have shown to potentially be more complex (i.e. nonlinear), while respective sex differences have been found specifically in the relationship between depression and vmHRV. In addition, reductions in vmHRV associated with ELM may be present in clinical samples with psychopathology, (Sigrist et al., 2021; Wesarg et al., 2022) and low levels of vmHRV may drive depression in individuals who have experienced emotional maltreatment early in life. The following questions may arise of this: Is the association between ELM exposure, and particularly emotional maltreatment, and depression of similar shape (i.e. non-linear quadratic) as assumed for the relationship of depression with vmHRV, at least considering females? Furthermore, if so, is there a link between non-linear quadratic relationships of ELM exposure with depression and levels of vmHRV in predicting depression risk? Conversely, how does the putative non-linear quadratic relationship between vmHRV and depression in females change as a function of emotional maltreatment?

The present study was conducted with three major objectives. First, using descriptive analyses, it aimed to replicate findings from previous studies of group differences in individuals exposed and not exposed to different forms of ELM, respectively, taking into account levels of vmHRV, depressive symptoms, and more general dimensions of psychopathology. Significantly higher levels of depression and higher general dimensions of psychopathology, but no significant differences in vmHRV, were expected in adolescents and adults who reported ELM exposure as compared with adolescents and adults who reported no exposure. Second, this study aimed to extend findings from previous studies examining different forms of ELM and their association with depression using exploratory network-based analyses, taking into account inter-individual differences in concurrent vmHRV. Based on previous research (Brown et al., 2016; Cecil et al., 2017; de Oliveira et al., 2018; Humphreys et al., 2020; Salokangas et al., 2019; Spertus et al., 2003), it was hypothesized that forms of emotional maltreatment would emerge as highly central nodes (i.e. variables) in exploratory network analyses considering all five ELM subtypes, vmHRV, and depression, in adolescents and adults. Furthermore, besides direct relationships between forms of emotional maltreatment and depressive symptoms, indirect links between emotional maltreatment and depression over the variable vmHRV were expected. As a third objective, this study aimed to explore and contrast linear and quadratic functions when considering the relationship between ELM exposure (i.e. emotional maltreatment), vmHRV and depression, and to examine interactions between emotional maltreatment and vmHRV in predicting depressive symptoms. In addition to non-linear quadratic relationships between vmHRV and depression, potential non-linear quadratic associations between exposure to emotional maltreatment and depression were explored. The study aims were addressed by considering two large samples from different age groups, i.e. adolescents and adults, and by taking into account the influences of sex in some of the relationships of interest.

2. Materials and methods

2.1. Study samples

Adolescent sample

The adolescent sample was drawn from an ongoing study conducted at the outpatient clinic for risk-taking and self-harm behaviour at the Department of Child and Adolescent Psychiatry, University of Heidelberg. Following an initial diagnostic assessment, adolescents presenting to the clinic had the possibility to participate in the nested AtR!Sk-Bio cohort, which is an ongoing study aiming to identify biological correlates of risk-taking and self-harming behaviour in adolescence. Recruitment for the study takes place within six weeks after a diagnostic assessment conducted in the outpatient clinic, and is based on the following inclusion criteria: age 12–17 years, completed diagnostic assessment, and informed and written consent of adolescents and their caregivers. Patients showing acute psychotic symptoms or lacking speech comprehension are excluded. Besides a patient sample, healthy controls for the study are recruited via public advertisements, and they undergo an adapted form of the diagnostic assessment. Eligibility criteria for healthy control participants comprise: age 12–17 years, no history of NSSI, no endorsement of any psychiatric disorder, and no treatment for any psychiatric disorder prior to participation in the study. All healthy control participants and their caregivers provided informed and written consent to participate in the study.

In the present analyses, all patients and healthy controls in the AtR!sk cohort with available and physiologically plausible ECG data, as well as complete data on the relevant psychometric instruments (as detailed below), were included, resulting in a total sample of $N = 213$ participants (89.67% female). Of the $N = 213$ included participants, 167 were patients (and of these, 87.43% were female) and 46 were healthy controls (97.83% female). Female participants and patients were thus overrepresented in the present sample of adolescents.

The Ethics Committee of the Faculty of Medicine, University of Heidelberg, approved the scientific evaluation of AtR!Sk (IRB approval number S-449/2013) and the add-on neurobiological assessments (IRB approval number S-514/2015). Studies on the sample have previously been published (Flach et al., 2021; Koenig et al., 2022; van der Venne et al., 2021).

Adult sample

An adult sample was recruited through word of mouth in the general population and among university students at the Department of Dynamic, Clinical and Health Psychology (Sapienza University of Rome) during the period 2019–2021. Inclusion criteria were age 18 years or older, completed diagnostic assessment, and Italian mother tongue. Patients with major central nervous system disorders (e.g. epilepsy, dementia, Parkinson's disease) were excluded, as were patients with any condition that might affect their ability to participate, including refusal to give informed consent. All participants with available and physiologically plausible ECG data were included in the present analyses, resulting in a total sample of $N = 85$ (85.53% female) participants. Female participants were overrepresented in the present sample of adults.

The study was approved by the Ethical Committee of the Department of Dynamic and Clinical Psychology, Sapienza, University of Rome (Prot. no. 0000453 and Prot. no. 0000112).

2.2. General procedures

Adolescent sample

In short, the study comprised two separate appointments, of which the first comprised a diagnostic assessment, with relevant instruments described below. The neurobiological assessment, marking the second appointment, started at 8 AM. To account for potential interferences with biological measures, participants were asked whether they had been fasting as instructed. The subsequent biological assessments were preceded by a resting-state measurement, where ECG was recorded. All participants received 40€ upon completion of the neurobiological assessment.

Adult sample

After giving written informed consent to participation, participants were asked to fill out a battery of questionnaires to assess the presence of early life maltreatment and psychopathological symptoms. Then, a second morning appointment was scheduled in which ECG was recorded. Participants were informed of the following restrictions: no caffeine, alcohol, nicotine, or strenuous exercise for 2 h prior to the appointment.

2.3. Clinical interviews and self-report measures

Individuals from the adolescent sample were screened by means of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID), (Sheehan et al., 2010) a short semi-structured interview designed to assess common axis I psychiatric disorders in children and adolescents aged 6–19 years. In the adult sample, the presence of psychiatric diagnoses was self-reported.

2.3.1. Depressive symptomatology

To assess the severity of depressive symptoms in the adolescent sample, the German Version of the Children's Depression Inventory (CDI) (Kovacs, 2015) was used ('Depressionsinventar für Kinder und Jugendliche', DIKJ) (Stiensmeier-Pelster et al., 1989). The DIKJ is a 26-item self-rating instrument with high internal consistency ($\alpha = .82–.88$), and has been used widely to assess depressive symptoms in children and adolescents from eight to 17 years of age (Frühe et al., 2012). Items are summed to create a total score, with higher scores indicating higher levels of depression. In the present sample, Cronbach's α was .94.

In the adult sample, the Beck Depression Inventory-II (BDI-II), (Beck & Steer, 1996) one of the most widely used measures to assess depressive symptoms and their severity in adults, has been deployed. The BDI-II is a 21-item self-report measure to assess symptoms of major depression according to diagnostic criteria listed in the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV). A number of studies have examined the validity and reliability of BDI-II across different populations and countries (Wang & Gorenstein, 2013). Results have consistently shown good internal consistency and test-retest reliability of the BDI-II in community samples, (Gomes-Oliveira et al., 2012; Kojima et al., 2002; Segal et al., 2008) clinical outpatients (Grothe et al., 2005) and in clinical inpatients (Subica et al., 2014). Items are summed to create a total score, with higher scores indicating higher levels of depression. In the present sample, Cronbach's α was .91.

2.3.2. General dimensions of psychopathology

General dimensions of psychopathology were assessed in either sample using the Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1994). The instrument encompasses nine symptom subscales (comprising a total of 83 items) as well as seven additional items. The mean score on all 90 items (including the seven additional items) is referred to as the global severity index (GSI), which was used in the present analyses. Cronbach's α in this study was .98 in the adolescent sample and .98 in the adult sample, respectively.

2.3.3. Early life maltreatment

Participants in the adolescent sample completed the German version of the Childhood Experiences of Care and Abuse Questionnaire (CECA.Q), which has provided good psychometric properties (Bifulco et al., 2005; Kaess et al., 2011). In the present sample, Cronbach's α was .74 for the total score. The CECA.Q covers negative dimensions of parental care (that is, antipathy and neglect) physical abuse and sexual abuse. To dichotomize ELM exposure (i.e. no ELM exposure vs. exposed), subscales were computed and cut-off scores selected for optimal association with depression outcomes were applied according to Bifulco et al (Bifulco et al., 2005). (i.e. antipathy mother ≥ 28; antipathy father ≥ 30; neglect mother ≥ 25; neglect father ≥ 26; physical abuse mother ≥ 3; physical abuse father ≥ 3; sexual abuse ≥ 1). Next, to make ELM scales comparable across samples, items from the original subscales (antipathy mother; antipathy father; neglect mother; neglect father; physical abuse mother; physical abuse father; sexual abuse) were aggregated to form severity scores for each of the five ELM subtypes of interest in the present study (i.e. emotional abuse: 8 items for mother and father, respectively; emotional neglect: 6 items for mother and father, respectively; physical abuse: 7 items for mother and father, respectively; physical neglect: 2 items for mother and father, respectively; sexual abuse: 7 items).

Participants in the adult sample completed a brief version of the Childhood Trauma Questionnaire (CTQ), (Bernstein, et al., 1994, 2003), a retrospective measure of child abuse and neglect that has demonstrated high internal consistency and good test-retest reliability (Bernstein & Fink, 1998; Bernstein et al., 1994). In the present sample, Cronbach's α was .75 for the total score. In accordance with the instrument's scoring guidelines, items were combined, and severity scores calculated for each of the five ELM subtypes of interest (emotional abuse: 5 items; emotional neglect: 5 items; physical abuse: 5 items, physical neglect: 5 items, sexual abuse: 5 items). For dichotomization, cut-off scores according to Bernstein and Fink (Bernstein & Fink, 1998) were used (physical abuse $\geq$ 8; sexual abuse $\geq$ 6; emotional abuse $\geq$ 9; physical neglect $\geq$ 8; emotional neglect $\geq$ 10).

2.4. Assessment and processing of cardiac autonomic data

Adolescent Sample

vmHRV was assessed using an electrocardiographic device (ECG Move3 Sensor, Movisens, Karlsruhe, Germany). The device was attached to the participant's chest at the lower end of the sternum with a belt. ECG signals were recorded at a sampling rate of 1024 Hz during a 5-min baseline period while participants performed a low-demanding colour detection task (CDT) (Jennings et al., 1992). Data were visually inspected after each recording using UnisensViewer software (version: 2.0) and saved in CSV format. ECG data were further processed in Kubios HRV 3.0 Premium (Tarvainen et al., 2014). Automated R-peak detection was manually corrected and artifacts were removed. Smoothing priors were selected as the detrending method (λ 500) for IBI data. Kubios output was saved in TXT format for later automated reading of corrected inter-beat intervals (IBIs) and HRV analysis. The root mean square difference (RMSSD) of successive IBIs, measured in ms, was calculated for each participant as a measure of resting vmHRV.

Adult Sample

Participants were fitted with the Firstbeat Bodyguard 2 device (Firstbeat Technologies) and R-R intervals were recorded at rest for 5 min. HR and vmHRV were then analyzed using Kubios HRV software, Premium version (Tarvainen et al., 2014). An automatic beat correction algorithm was used for correcting artifactual inter-beat intervals (Lipponen & Tarvainen, 2019). The mean correction percentage was 0.51%. HRV was assessed by computing the root mean square of successive beat-to-beat interval differences (rMSSD, ms), which reflects vagal regulation of HR and is less susceptible to respiratory influences compared to the alternative frequency-domain high frequency (HF-HRV) activity (Penttilä et al., 2001).

2.5. Statistical procedure

Data were analyzed in R version 4.2.0 (R Core Team, 2022) with R studio version 2022.07.1 (R Core Team, 2022). The R code used in the present analyses and supporting the findings of this study are available online (https://osf.io/vd7rh/?view_only = d547aa842a92457b9eaa5381941f91a8).

2.5.1. Descriptive statistics and group comparisons

Data were inspected visually to explore potential outliers and general distributions of the data. Of note, and as anticipated, subsequent normality tests suggested cardiac data were non-normal, and in line with established procedures (Shaffer & Ginsberg, 2017; Task Force, 1996) natural logarithms (ln) of these variables were calculated to reduce their skew; subsequent statistical analyses were based on ln-transformed values. Descriptive summary statistics were computed, and ELM-exposed and not exposed subgroups were contrasted considering the variables of interest (age, vmHRV, depressive symptoms, and general dimensions of psychopathology) using frequentist statistics (i.e. independent samples t-test if data approximated Gaussian distribution, and Mann–Whitney U test as non-parametric equivalent). Bivariate correlations (Spearman's rho, ρ) were further explored between variables of interest within the adolescent and adult sample, respectively.

2.5.2. Exploratory network analysis

Following established reporting standards (Burger et al., 2023) for psychological network analyses of cross-sectional data, separate network models were computed within each sample. These models comprehensively captured five forms of ELM exposure – physical neglect, emotional neglect, emotional abuse, physical abuse, and sexual abuse – alongside depressive symptom severity and vmHRV, all represented on a continuous scale.

To prepare the data for network analysis, a standard scaling technique (studentization) was applied, ensuring consistency by aligning values to a mean of zero and a standard deviation of one. Using the R package *bootnet* (Epskamp et al., 2018), networks were estimated employing Gaussian graphical models (GGMs) (Epskamp & Fried, 2018). These models represent associations between variables in the network, where each link signifies a partial correlation coefficient conditioned on all other variables, with coefficients ranging from −1 to 1.

To focus on significant associations and avoid spurious connections, we applied the regularization method Least Absolute Shrinkage and Selection Operator (LASSO) (Costantini et al., 2015) along with the Extended Bayesian Information Criterion (EBIC) (Chen & Chen, 2008). This approach aims to simplify the network structure by emphasizing essential connections and minimizing unnecessary links. Specifically, by setting γ to 0.5 (Foygel & Drton, 2010) (Barber & Drton, 2015; Foygel & Drton, 2010; van Borkulo et al., 2014), our objective was to retain only genuine partial correlations in the model, prioritizing accuracy while ensuring a streamlined network representation.

The results of estimating the networks were plotted using the *qgraph* package (Epskamp et al., 2012). The Fruchterman-Reingold algorithm, an iterative, force-embedded algorithm, was used for visualization.

Computed network indices and tests

We calculated node strength, bridge centrality, and performed a Network Comparison Test (NCT) between adolescent and adult samples, assessing global structure, edge strength, and network strength (Anyigbo et al., 2021; Bussemakers et al., 2019; Kogan et al., 2013; Sheridan & McLaughlin, 2014; Spinazzola et al., 2014; Vachon et al., 2015).

Assessment of network accuracy and stability

Using bootnet (Epskamp & Fried, 2018), we evaluated edge-weight accuracy via 2000 bootstrap samples, determining confidence intervals (Christou-Champi et al., 2015; Costantini et al., 2015). Node strength stability assessed correlations after dropping participants (Costantini et al., 2015).

2.5.3. Moderator analyses

To examine interactions between emotional maltreatment and vmHRV in the prediction of depressive symptoms, a set of moderator analyses was conducted. Of note, these analyses were restricted to inclusion of only female participants to account for potential sex differences in the relationship between, e.g. vmHRV and depression. The female adolescent sample included in moderator analyses included $n = 191$ participants, and the female adult sample included $n = 71$ participants. Scatter plots were used to visualize bivariate relationships between variables of interest, and to examine likely functions in these relationships (i.e. linear, quadratic, else), before running the regression models.

Multiple linear regression models

To examine whether vmHRV acted as a moderator of the relationships of the ELM subtypes emotional abuse or emotional neglect with depressive symptoms, while assuming linear relationships, we conducted multiple linear regression. Two multiple linear regression models were computed for each sample, with final models including emotional abuse or emotional neglect, vmHRV, and the interaction term between emotional abuse or emotional neglect and vmHRV, respectively, as predictors, and severity of depressive symptoms as outcome variable, while also controlling for age. All predictors were mean-centered. To further examine significant moderation effects, interactions were plotted graphically using interaction plots. Finally, we examined whether linear assumptions were satisfied or had been violated by conducting visual linearity checks.

Polynomial regression

In a second step, as the assumption of quadratic effects of vmHRV (i.e. self-interaction) in association with depressive symptoms might be justified based on the current literature, and to further examine a potential quadratic function in the relationship between emotional maltreatment and depression, we extended the linear regression models to account for nonlinear specifications of emotional abuse and neglect, respectively, as well as vmHRV (full quadratic models). Concretely, assuming that the relationship between vmHRV and depression might follow a U-shaped quadratic function, and to examine whether the relationship between emotional maltreatment and depressive symptoms might follow an inverted U-shaped quadratic function, quadratic terms were added in the specification of predictor variables in the respective regression models (please refer to the R-script made available online for further technical details). Prediction errors (i.e. root mean-squared error; RMSE) were calculated for each model, and linear and quadratic models were compared using the F-test. Significant interactions were plotted using interaction plots.

3. Results

3.1. Sample characteristics and group comparisons

Table 1 shows summary statistics for the adolescent and adult samples, respectively, and group

Table 1. Summary characteristics of key demographics and clinical data for the adolescent and adult sample, respectively, considering exposure to ELM as grouping variable.

	1: ELM exposure reported						2: No ELM exposure reported						Group comparison (1 vs. 2)			
	Adolescent Sample ($N = 113$)			Adult Sample ($N = 39$)			Adolescent Sample ($N = 100$)			Adult Sample ($N = 46$)			Adolescents		Adults	
Demo-graphics	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	*W* / χ2	*p*	*W* / χ2	*p*
Age (y)	14.97	1.39	12–18	24.76	3.70	19–40	14.75	1.49	12–19	24.22	3.12	19–31	5139.5	.247	836.5	.738
Sex: *N* (%) females	103 (90.27)	–	–	32 (82.05)	–	–	89 (46.35)	–	–	39 (54.93)	–	–	0.09	.762	0.11	.735
Psycho-pathology	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	*W*	*p*	*W*	*p*
SCL-90-R score	139.55	64.85	8.00–297.00	55.44	12.42	33.00–75.00	73.39	67.59	0.00–281.00	44.20	9.69	33.00–74.00	1634	<.001	414.5	<.001
Depressive Symptoms																
DIKJ	29.51	9.64	4.00–47.00	–	–	–	17.23	12.04	0.00–41.00	–	–	–	2408	<.001	–	–
BDI-II	–	–	–	18.26	10.60	3.00–37.00	–	–	–	10.61	8.00	0.00–31.00	–	–	514	<.001
ELM Subtypes																
Physical Neglect	2.28	0.81	1.00–4.00	9.00	3.09	5.00–17.00	1.41	0.55	1.00–3.00	5.52	0.96	5.00–9.00	2060.5	<.001	199.5	<.001
Emotional Neglect	2.29	0.70	1.00–3.83	14.21	5.36	5.00–24.00	1.66	0.58	1.00–3.00	7.52	2.25	5.00–13.00	2440.5	<.001	267.5	<.001
Emotional Abuse	3.53	0.81	1.25–5.00	13.62	4.77	5.00–23.00	1.66	0.62	1.00–3.00	6.59	1.76	5.00–12.00	463	<.001	159.5	<.001
Physical Abuse	0.15	0.28	0.00–1.00	7.67	3.44	5.00–19.00	0	0	–	5.15	0.47	5.00–7.00	4200	<.001	383	<.001
Sexual Abuse	0.15	0.24	0.00–1.00	7.97	4.95	5.00–22.00	0	0	–	5.15	0.47	5.00–7.00	3600	<.001	614	<.001
Cardiac autono-mic data	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	*W*	*p*	*W*	*p*
HR	75.81	10.21	58.40–107.06	80.66	9.68	50.40–100.31	75.96	11.56	51.08–105.14	84.29	17.51	58.57–126.47	5407	.789	907	.933
rMSSD	55.06	27.17	15.15 –142.04	48.33	41.71	11.82–247.15	57.31	34.38	16.73–239.51	45.92	23.30	9.48–90.02	5269	.958	975	.494

Note. BDI-II = Beck Depression Inventory-II; DIKJ = Depressionsinventar für Kinder und Jugendliche; ELM = Early Life Maltreatment; HR = Heart Rate; rMSSD = root Mean Square of Standardized Differences; SCL-90-R = Symptom Checklist-90-Revised; SD = Standard Deviation.

comparisons considering subgroups differentiated by ELM exposure.

Considering both samples (adolescents and adults), statistically significant differences emerged between ELM-exposed and non-exposed individuals regarding the severity of depressive symptoms and general psychopathology, but not regarding vmHRV. Based on bivariate correlation analyses (Supplementary Figure 1), a significant correlation was observed in the adolescent sample between depression severity and all five ELM subtypes, i.e. emotional abuse ($\rho = .55$, $p < .001$), emotional neglect ($\rho = .40$, $p < .001$), physical abuse ($\rho = .24$, $p < .001$), physical neglect ($\rho = .29$, $p < .001$), and sexual abuse ($\rho = .14$, $p < .050$). In the adult sample, depression severity was significantly correlated with the ELM subtypes emotional abuse ($r = .40$, $p < .001$), emotional neglect ($\rho = .24$, $p < .050$), physical abuse ($\rho = .29$, $p < .010$), and physical neglect ($\rho = .39$, $p < .001$), but not with sexual abuse. In the adolescent sample, depressive symptoms were also significantly negatively correlated with vmHRV ($\rho = -.15$, $p < .050$), whereas none of the ELM subtypes, nor age, were significantly associated with vmHRV. In the adult sample, depressive symptoms were not significantly correlated with vmHRV; vmHRV showed a significant negative correlation with emotional neglect ($\rho = -.31$, $p < .010$) but not with any other ELM subtype, nor with age.

3.2. Exploratory network-based analyses

Network visualization and key connections of interest

We computed and visualized networks of ELM exposure, depressive symptoms, and concurrent vmHRV in adolescence and adulthood. The resulting networks are shown in Figure 1. Overall, non-zero partial correlations emerged between different forms of ELM exposure, between forms of ELM exposure and depressive symptoms, and between ELM exposure and depression and vmHRV. Emotional abuse emerged as a highly central node in both the adolescent and adult network and showed relatively strong partial correlations with several other nodes. Emotional neglect also appeared as a highly central node in the adult network and showed a relatively strong partial correlation with emotional abuse in this sample. In the adolescent network, the vmHRV node was only connected to the node representing depressive symptoms ($r = -.02$), while the depression node was further connected to the emotional abuse ($r = .32$), physical abuse ($r = .03$), and emotional neglect ($r = .12$) nodes. In the adult network, vmHRV was connected to two other nodes, that is, the node representing depressive symptoms ($r = -.04$) and the emotional neglect node ($r = -.19$). The

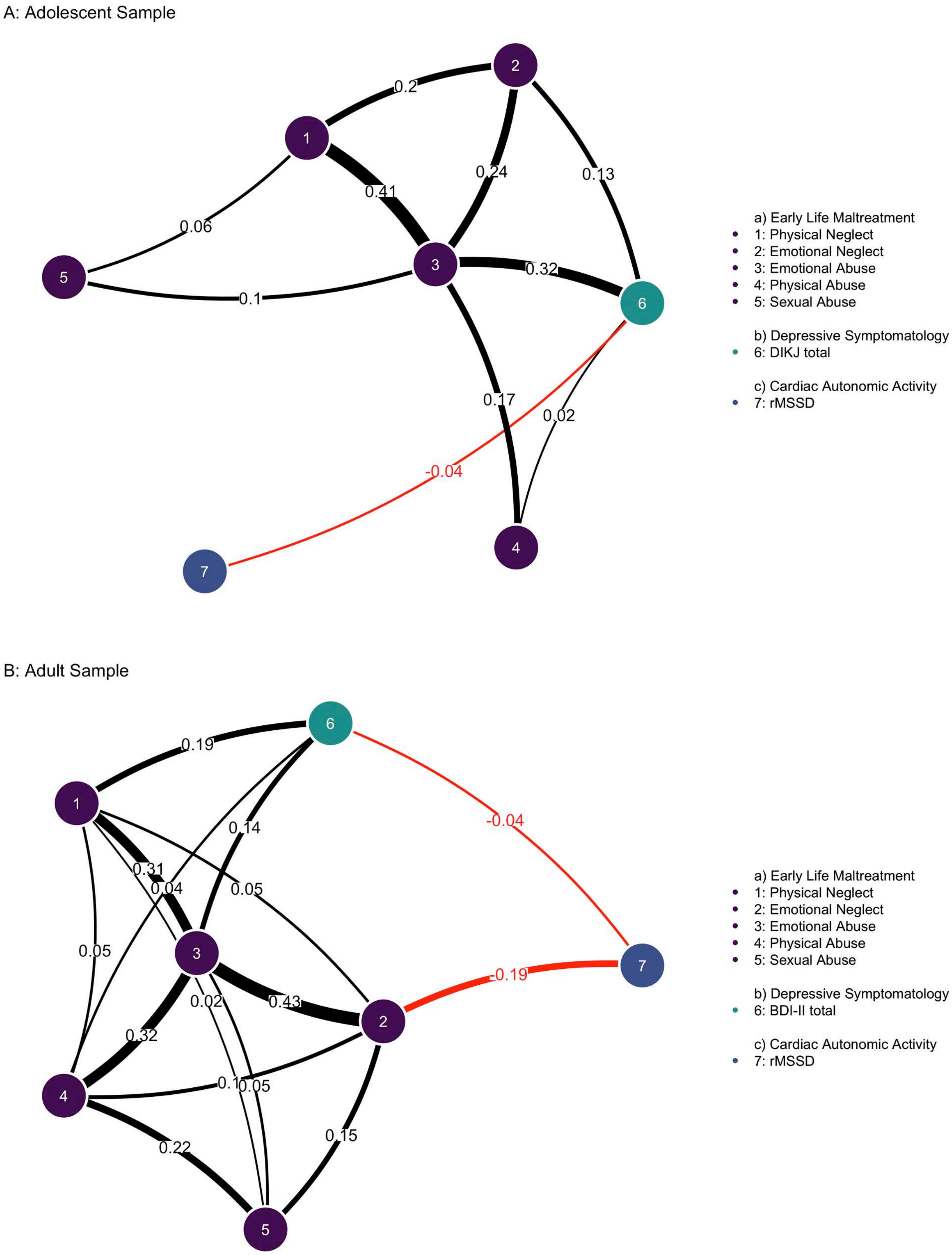

Figure 1. Visualization of the network models, including nodes representing ELM exposure, depressive symptoms, and vmHRV. Network layout is adjusted on the Fruchterman-Reingold algorithm (Fruchterman & Reingold, 1991), resulting in edges with stronger connections being grouped together. Red lines indicate negative partial correlations, while black lines indicate positive partial correlations. The more saturated the edge, the stronger the partial correlation.

node representing depressive symptoms in the adult network was also connected to emotional abuse ($r = .14$), physical abuse ($r = .04$), and physical neglect ($r = .19$).

Node strength centrality and bridge strength

We estimated the node strength centrality and bridge strength of each node (Supplementary Figure 2). For both networks (adolescent and adult), as expected based on the visual representation (Figure 1), emotional abuse showed the highest node strength centrality (Supplementary Figure 2, left panels), and can therefore be considered particularly central within the modelled networks. In the adult network, emotional neglect also showed relatively high node strength centrality. In both networks, vmHRV showed the lowest node strength centrality and was therefore modelled more in the periphery of each network (Figure 1). In both samples, depressive symptoms had the highest bridge strength. Notably, bridge nodes have the highest number of connections with opposite node clusters, i.e. they act as 'bridges' connecting different nodes. While vmHRV had the lowest bridge strength in the adolescent sample, vmHRV had relatively high bridge strength in the adult sample.

Direct path analysis

We analyzed the direct and indirect connections between nodes in the networks using path diagrams, taking the most central node (which was emotional abuse) as the starting point. In both networks, emotional abuse was directly related to depressive symptoms, with a much stronger association in the adolescent sample. In both networks, emotional abuse was indirectly related to (reduced) vmHRV via the node representing depressive symptoms, but this association was very weak in the adolescent sample. In the adult sample, emotional abuse was indirectly related to (reduced) vmHRV through relatively strong connections via the emotional neglect node. See Supplementary Figure 3.

Network Comparison Test

The network invariance test showed that the difference between network structures was not significant ($M = .259$, $p = .183$). Because there were no significant differences in network structure, we did not test for specific edge differences in the networks. The global strength invariance test was also not significant ($S = 0.773$, $p = .086$). Overall, therefore, we found no evidence of a difference between the two networks, suggesting that the networks in both age groups are statistically similar. See Supplementary Figure 4.

Network stability and accuracy

We estimated the reliability of our exploratory inferences by calculating the edge-weight accuracy and node strength stability of both networks using *bootnet* (the results of these analyses are provided in Supplementary Figures 5 and 6). The nonparametric bootstrap produced relatively wide confidence bands in both the adolescent and adult networks; therefore, the reported edge-weights (estimates of partial correlation coefficients in the networks) must be interpreted with relative caution. The case-dropping bootstrap suggested that node centrality coefficients were relatively stable in both networks, based on centrality stability coefficients; thus, the presented centrality indices (i.e. node strength, bridge strength centrality) can be interpreted with relative confidence.

3.3. Moderator analyses

Visualization of bivariate relationships between variables of interest

First, scatterplots visualizing the relationships between the predictors of interest (i.e. emotional abuse, emotional neglect, and vmHRV) and the outcome variable (i.e. depressive symptoms) were examined (Figure 2). As can be seen in Figure 2, in adolescents, the relationship of vmHRV, but not of emotional neglect and abuse (more of a quadratic function) with the outcome appeared to be relatively linear, whereas in adults, the relationships of both vmHRV and emotional abuse with depression fit a more quadratic function – although, as must be noted, confidence bands suggested broad distributions especially toward higher values on the x-axes in both samples.

Multiple linear regression results

Considering the present subsample of adolescent females, the final multiple linear regression model including emotional abuse as a predictor variable was statistically significant ($F_{4,\ 171} = 27.28$, $p < .001$; RMSE = 10.04). The variables emotional abuse ($b = 6.46$, $SE = 0.66$, $t = 9.$, $p < .001$), vmHRV ($b = -4.00$, $SE = 1.51$, $t = -2.64$, $p = .009$), and age ($b = -1.11$, $SE = 0.55$, $t = -2.01$, $p = .046$) were significant linear predictors of depressive symptom severity in this model. The interaction between emotional abuse and vmHRV in predicting depressive symptoms ($b = 2.42$, $SE = 1.30$, $t = 1.85$, $p = .066$) was marginally statistically significant. When considering emotional neglect instead of emotional abuse as a predictor variable in an otherwise identical model for adolescents, the resulting model was also statistically significant ($F_{4,\ 166} = 11.53$, $p < .001$; RMSE = 11.37). In this model, the variables emotional neglect ($b = 7.50$, $SE = 1.25$, $t = 6.01$, $p < .001$), and vmHRV ($b = -3.88$, $SE = 1.76$, $t = -2.50$, $p = .029$) were significant linear predictors of depressive symptom severity. The interaction between emotional neglect and vmHRV in predicting depressive symptoms was not statistically significant in this model.

Considering the present subsample of female adults, the final multiple linear regression model including emotional abuse as a predictor variable was also statistically significant ($F_{4,65} = 6.99$,

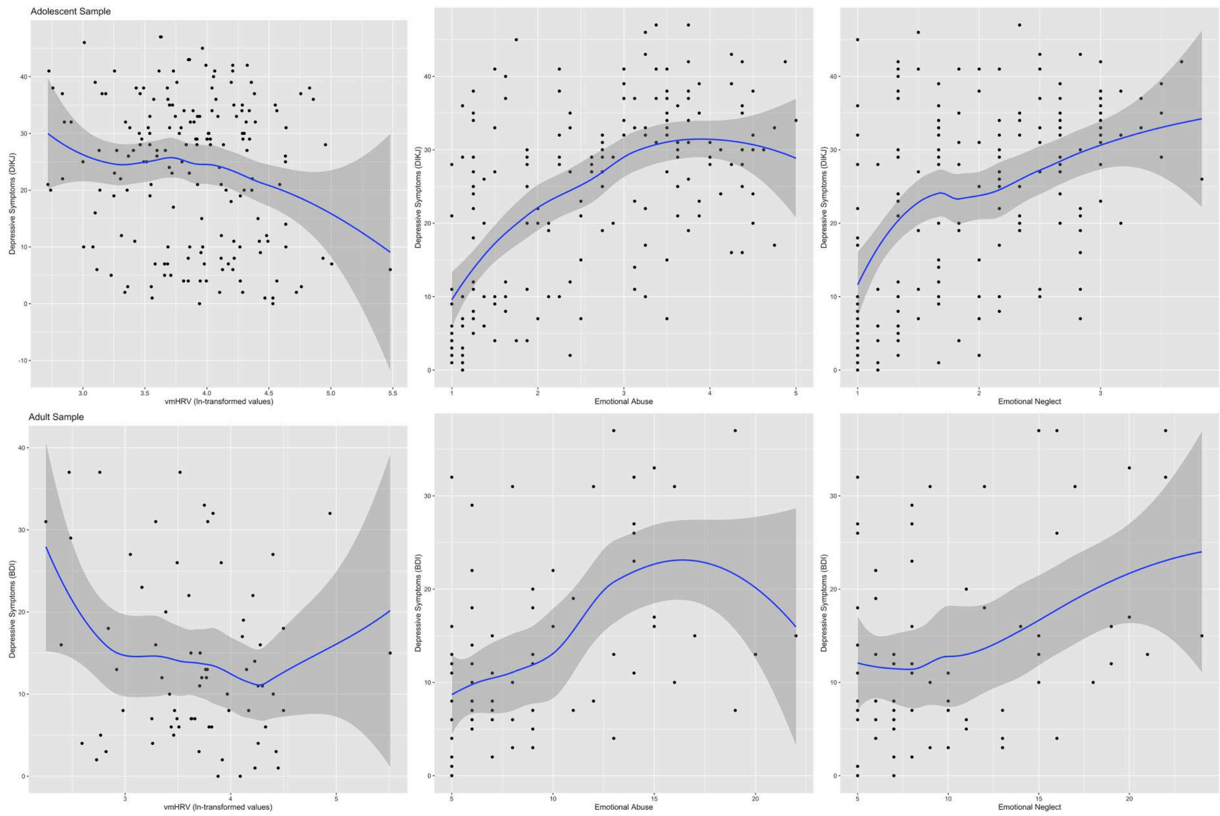

Figure 2. Scatter plots visualizing the relationships of (ln-transformed) vmHRV values, emotional abuse, and emotional neglect with depressive symptoms in adolescent (upper panes) and adult females (lower panes), respectively. In adolescents, the relationships of vmHRV and emotional neglect with depression appeared likely to be linear, in contrast to emotional abuse, which adapted a rather nonlinear function; in adults, the relationships of both vmHRV and emotional abuse with depression adapted a rather quadratic function, while considering emotional neglect, the respective relationship appeared to be linear.

$p < .001$; RMSE = 8.48). The variable emotional abuse ($b = 1.07$, SE = 0.24, $t = 4.50$, $p < .001$) was the only statistically significant predictor of depressive symptoms in this model. The interaction between emotional abuse and vmHRV ($b = -0.62$, SE = 0.34, $t = -1.80$, $p = .076$) was not statistically significant. The alternative linear model including emotional neglect as a predictor variable was statistically significant ($F_{4,\ 65} = 4.15$, $p = .005$; RMSE = 9.05). The variable emotional neglect ($b = 1.07$, SE = 0.24, $t = 4.50$, $p < .001$) as well as the interaction between emotional neglect and vmHRV ($b = -0.89$, SE = 0.41, $t = -2.18$, $p = .033$) were statistically significant in predicting depressive symptoms in this model. The significant interaction terms identified in linear regression models between emotional abuse and vmHRV in adolescents and emotional neglect and vmHRV in adults were visualized in interaction plots (see Supplementary Figure 7A and 7B). Interestingly, visual linearity check of all interactions suggested the likely presence of nonlinear relationships at several instances within the adolescent (see Supplementary Figure 7) and the adult (see Supplementary Figure 8) samples.

Polynomial regression results

Considering female adolescents, the full quadratic regression model with emotional abuse as a predictor proved significant ($F_{6,169} = 21.13$, $p < .001$), reducing prediction error (RMSE = 9.72) compared to the linear model. Significant predictors of depressive symptom severity were emotional abuse ($b = 6.72$, SE = 0.65, $t = 10.33$, $p < .001$), vmHRV ($b = -3.72$, SE = 1.48, $t = -2.50$, $p = .013$), and age ($b = -1.25$, SE = 0.54, $t = -2.29$, $p = .023$). However, neither the nonlinear specification of vmHRV nor the emotional abuse × vmHRV interaction significantly predicted depressive symptoms. Nonetheless, the nonlinear specification of emotional abuse (quadratic effect: $b = -2.12$, SE = 0.66, $t = -3.18$, $p = .001$) significantly influenced depressive symptoms. The addition of quadratic specifications for emotional abuse and vmHRV significantly improved model fit ($F_{171,\ 169} = 5.79$, $p = .004$). Substituting emotional neglect as a predictor in an otherwise identical model yielded a statistically significant model ($F_{6,\ 165} = 8.38$, $p < .001$), albeit with a marginal decrease in prediction error (RMSE = 11.25). In this model, the linear predictors emotional neglect ($b = 8.47$, SE = 1.37, $t = 6.20$, $p < .001$) and vmHRV ($b = -3.68$, SE = 1.76, $t = -2.09$, $p = .038$) significantly predicted depressive symptoms. However, neither the nonlinear specifications of emotional neglect or vmHRV nor the emotional neglect × vmHRV interaction significantly predicted depressive symptoms. Furthermore, adding quadratic specifications for emotional neglect and vmHRV did not significantly improve the model fit, as indicated by an F-test comparing the full linear model with the full quadratic model.

For female adults, the full quadratic regression model with emotional abuse as a predictor was significant ($F_{6,\ 63} = 6.98$, $p < .001$), reducing prediction error (RMSE = 7.86) compared to the linear model. Emotional abuse ($b = 1.46$, SE = 0.29, $t = 5.02$, $p < .001$) was the sole statistically significant linear predictor of depressive symptoms. Additionally, both the quadratic specification of emotional abuse ($b = -.12$, SE = 0.05, $t = -2.36$, $p = .021$) and vmHRV ($b = 4.91$, SE = 1.88, $t = 2.62$, $p = .011$) significantly predicted depressive symptoms, along with a significant emotional abuse × vmHRV interaction ($b = -0.93$, SE = 0.34, $t = -2.76$, $p = .008$). The inclusion of emotional neglect instead of emotional abuse did not yield statistically significant results. Figures 3C and D illustrate these nonlinear relationships between emotional abuse, vmHRV, and depressive symptoms for both female adolescents and adults.

4. Discussion

4.1. Main findings

In this study, we aimed to clarify the complex relationships among ELM, depressive symptoms, and vmHRV to contribute to a better understanding of how different levels of autonomic vagal activity in the context of ELM exposure may affect mental health outcomes, specifically depression, during both adolescence and adulthood.

Our results mirrored previous research, demonstrating group differences in adolescents and adults reporting and not reporting exposure to ELM. Moreover, emotional abuse emerged as the most significant type of ELM, i.e. node, in a network of ELM exposure, depression, and vmHRV. Differences between the two age groups were furthermore observed, such as a stronger association of vmHRV reductions with emotional neglect compared to emotional abuse, and a nonlinear rather than a linear relationship between depression and vmHRV, in adult but not adolescent females. As an interesting and somewhat novel finding, in the present study, we found a significant

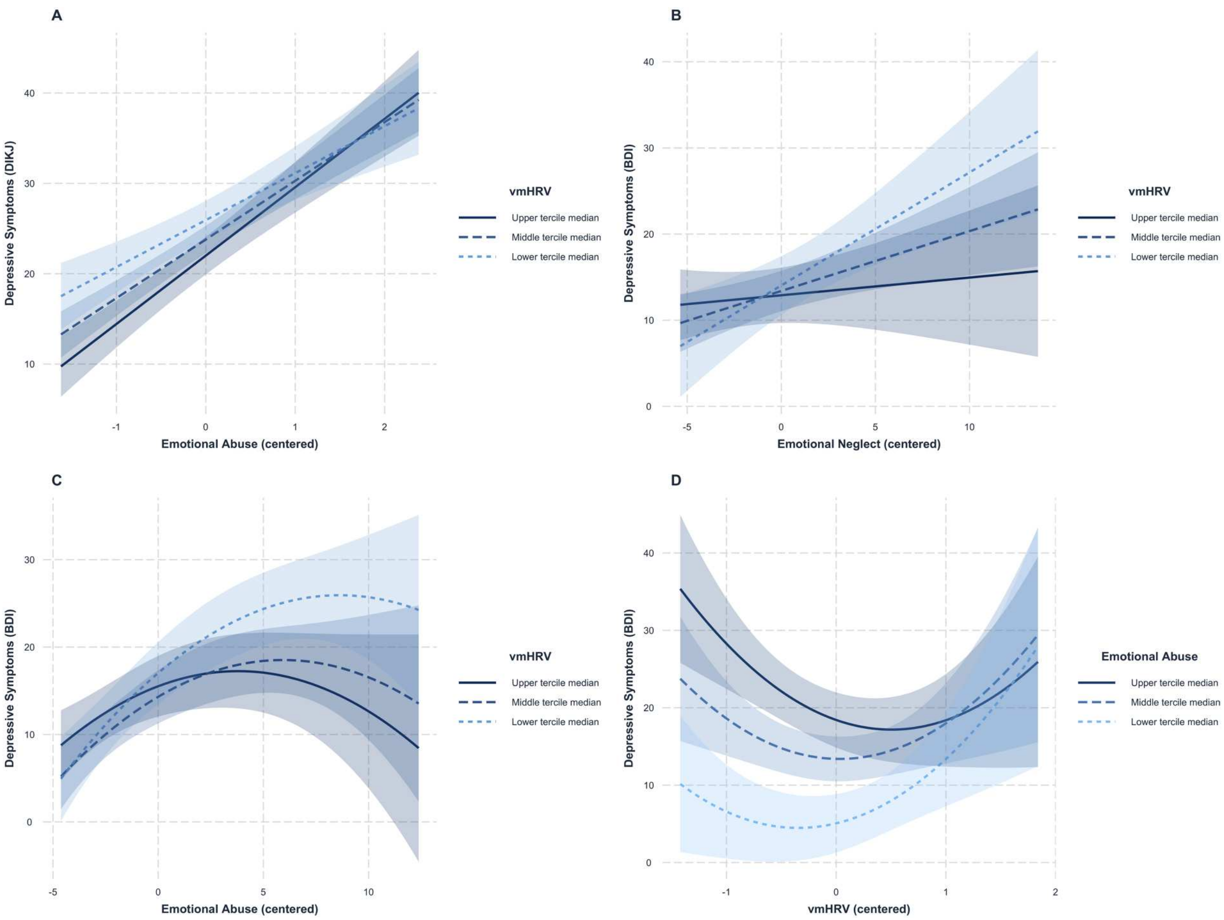

Figure 3. Visualization of interactions between resting-state vmHRV and emotional maltreatment in the prediction of depressive symptoms. In linear models, a marginally statistically significant interaction was observed between emotional abuse and vmHRV in female adolescents (A), and a significant interaction was found between emotional neglect and vmHRV in female adults (B). In a quadratic model, in female adults, the interaction between emotional abuse and vmHRV was found to be statistically significant (C; D)

non-linear (i.e. inverted U-shaped) relationship between exposure to emotional abuse and depressive symptoms, which was observed in both adolescent and adult females – whereas this relationship varied significantly as a function of vmHRV in adults.

Through examining the co-occurrence of ELM subtypes and the relationship of these exposures with depression severity and concurrent vmHRV both in an adolescent and an adult sample, emotional abuse emerged as a central node in the network analysis. A small negative relationship between vmHRV and depression was noted in both groups ($r = -.04$, both samples). However, emotional neglect displayed a stronger partial correlation with reduced vmHRV in adults ($r = -.19$), linking emotional abuse to reduced vmHRV, subsequently linked to depression. Pathway diagrams illustrated these patterns, revealing direct and indirect connections between nodes in the networks. Specifically, emotional abuse directly correlated with depressive symptoms, with a notably stronger link in the adolescent sample. Furthermore, in both age groups, emotional abuse indirectly affected (reduced) vmHRV through the node representing depressive symptoms. Notably, in adults, emotional abuse also indirectly impacted (reduced) vmHRV via relatively strong connections with the emotional neglect node.

The present findings may indicate a changing impact of specific ELM subtypes on mental and physical health over time, with effects and interrelationships growing more complex, including increased indirect links, with older age (Grasso et al., 2016). Adverse experiences show a more intricate pattern with age, wherein the co-occurrence of exposures becomes more diverse, and there is greater variance in experienced types and patterns of exposures (Thayer et al., 2012). Individuals experiencing one early adversity are more prone to encountering other forms of adversity across their lifespan, resulting in broader or more intricate associations between different types of ELM (and other exposures) and specific mental and physical health outcomes. Specific combinations of adverse exposures have been associated with distinct outcomes in adulthood (Anyigbo et al., 2021; Bussemakers et al., 2019). Early life emotional maltreatment, encompassing emotional abuse and neglect, may thereby present as a risk factor for depressive symptoms in adulthood through indirect links to vmHRV.

Notably, emotional abuse emerges as a highly central node in both adolescent and adult networks, as seen in Figure 1. Traditionally, certain forms of ELM, like physical and sexual abuse, were believed to exert more significant effects on mental and physical health compared to others, such as emotional abuse and neglect (Vachon et al., 2015). However, the present exploratory network analyses, consistent with prior studies, underscore emotional maltreatment as a central and impactful form linked to depression development (Spinazzola et al., 2014). Notably, network-based analyses also reveal emotional abuse as a prevalent type of maltreatment experienced across different ages by the same individual (Pollmann et al., 2023). Despite its prevalence and potential lifelong negative effects, emotional maltreatment remains largely overlooked in interventions for young people. These findings may pave the way for tailored intervention strategies aiming to address emotional maltreatment and its enduring consequences.

The present study replicated and extended prior findings by exploring the interplay between emotional maltreatment, vmHRV, and depression, accounting for potential sex-specific effects, in moderator analyses. Significant interactions between emotional abuse, emotional neglect, vmHRV, and depression were revealed in both samples (Figure 3A; 3B). More specifically, we found significant relationships associations between nonlinear specifications of emotional abuse and depression, which presents an interesting and novel finding; and further underlines the importance of considering the complexity of relations in the context of ELM exposure. In adult females, a full quadratic model including nonlinear specifications of vmHRV showed a significantly better model fit than a linear model. In the nonlinear model, both the nonlinear (i.e. quadratic) relationship between vmHRV and depression and the interaction between emotional abuse and vmHRV in predicting depressive symptoms, were statistically significant (Figure 3D). Thus, in line with previous studies, (Kogan et al., 2013; Spangler et al., 2021) we found that in female adults, vmHRV had a U-shaped, quadratic relationship with depressive symptoms, where moderate levels of vmHRV were associated with the lowest levels of depression; on the left side of the function, lower vmHRV was linked with higher depression severity, while at the right end of the function, higher vmHRV was linked with higher depression. This nonlinear relationship further varied as a function of severity of emotional abuse, such that at the lowest levels of vmHRV, higher levels of emotional abuse seemed to have the greatest impact on depression (see Figure 3D) – consistent with a putative buffering effect of vmHRV. Recent models like the Dimensional Model of Adversity and Psychopathology (DMAP) categorize ELM into deprivation (neglect) and threat (abuse) axes, proposing distinct neurobiological mechanisms for their impact (McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). While both types heighten psychopathology risk, they operate through different mechanisms. The study's findings of distinct interactions between abuse and neglect with vmHRV suggest potential differential neurobiological pathways. Future research should longitudinally explore how emotional neglect and abuse, in interaction with vmHRV, represent distinct mechanistic pathways for depression risk across different ages. In addition, further examining nonlinear patterns across different ELM subtypes and age groups is crucial for understanding consistent phenomena across samples. Machine learning methods could offer insights into these intricate associations and improve predictions, especially given the limitations of linear associations within samples.

Biobehavioral theories like the Neurovisceral Integration Model (NIM) propose an inverse relationship between vmHRV and depression, indicating higher vmHRV as a reflection of better emotion regulation (mediated by prefrontal activity) and greater self-regulatory capacity (Christou-Champi et al., 2015; Thayer et al., 2012). These associations have been observed in adult males (Anyigbo et al., 2021; Carney et al., 1995; Thayer et al., 1998; Wang et al., 2013). In adult females, this relationship may differ. Individuals with lower vmHRV might show linear associations, while those with higher levels might exhibit a reversal, linking higher vmHRV with increased depression (Spangler et al., 2021; Tobaldini et al., 2020). This nonlinear interaction, particularly prominent in women, reveals a quadratic pattern where low to moderate vmHRV inversely relates to depression. However, at higher levels, it could signify a compensatory response to severe depression, resulting in a positive association. Sex appears to moderate these effects, primarily observed in women (Spangler et al., 2021). Supporting the NIM assumptions, females with lower vmHRV seem more prone to higher depression levels, especially with increased exposure to emotional abuse, indicating lower emotion regulation capacities. Notably, nonlinear associations emerge in adult females but not in adolescents, possibly due to ongoing brain circuit maturation affecting socioemotional processes (Koenig 2020). Considering the divergent pathways between adolescent and adult females regarding ELM exposure, depression, and vmHRV associations as presently found, a two-peak depletion model might explain these differences. In adolescence, higher ELM exposure may create an alert yet vulnerable system, potentially adaptive but susceptible to subsequent adversity. Over time, higher vmHRV, as a compensatory mechanism in maturing systems, might strain resources, linking elevated vmHRV with increased depression in adulthood.

Overall, this study focused on gaining a deeper understanding of how complex relationships between different forms of ELM exposure might affect depressive symptoms in the context of concurrent vmHRV levels, with the goal of helping to refine the ways in which we investigate etiological pathways and, ultimately, identify and intervene with those at risk. Interestingly, a recent systematic review and meta-analysis ($k = 103$ studies, $N = 13{,}044$ participants) concluded that the development of more flexible autonomic functioning (i.e. higher autonomic vagal activity) may be associated with positive parenting, and that this effect may be even stronger in children at increased developmental risk (Alen et al., 2022). In this sense, early intervention should continue to receive increasing attention in the field of psychiatry, and strategies to promote positive development of autonomic vagal activity early in life may be one way to mitigate some of the risk associated with exposure to adversity early in life.

4.2. Limitations

The findings of this study should be understood in light of several limitations, shaping directions for future research. Firstly, the study's cross-sectional design restricts understanding temporal links between ELM exposure, vmHRV, and depressive symptoms. Secondly, differences in sample recruitment settings between adolescents (clinical setting in Germany) and adults (community sample in Italy) might contribute to divergent findings beyond age distinctions. Thus, caution is needed when drawing conclusions due to these sample characteristic variations. Moreover, our study's specific recruitment settings limit the generalizability of findings to adolescents from the broader population. A larger, more diverse sample including adults, multiple measurement time points, and extended follow-up periods would enhance replicability and sensitivity in future investigations. Additionally, the study's focus on ELM exposure rather than lifetime adversity might limit a comprehensive understanding, although prior evidence suggests stronger links from more recent adversity exposure to psychopathology (Dunn et al., 2018). The use of different measures to assess ELM exposure and depressive symptoms in adolescents and adults respectively might contribute to observed differences between samples, potentially hindering direct comparisons. Furthermore, the broad variability in conceptualizing and measuring ELM across studies hampers progress and effective preventive measures in the field. Neglecting the timing of ELM experiences is another notable limitation, and considering differences in etiology, clinical presentations, and developmental aspects between adolescent and adult depression is crucial. Lastly, and importantly, the exploratory approach of the study involved multiple statistical tests in different analyses, increasing the risk of Type I error due to the problem of multiple comparisons. While correction methods such as Bonferroni or false discovery rate control for this, they may produce overly conservative results, compromising the study's ability to accurately detect meaningful effects. Implementing such corrections in our exploratory network analysis and regressions across different samples could have compromised the interpretability and exploratory nature of our findings, which is why we refrained from such corrections. Instead, our aim was to uncover potential associations and patterns within the data and to generate hypotheses for further investigation, rather than to draw definitive conclusions. Applying strict corrections could miss meaningful trends, particularly in the case of subtle effects or complex data structures. While recognizing the importance of controlling for multiple testing in confirmatory analyses, appropriate correction methods will need to be applied in subsequent studies or confirmatory analyses to validate and confirm the associations identified in this work.

5. Conclusion

This study further highlights the utility of more adaptive modelling techniques, such as exploratory network-based analysis, as well as the importance of considering relationships that are more complex and nonlinear in nature in the context of research focused on ELM exposure and its physical and mental health outcomes. Not only may direct and indirect links between adversities be an important factor to consider, but the relationships between individual forms of ELM exposure and their links to other outcomes of interest may be more complex than traditionally assumed. Importantly, our analyses showed that different forms of ELM may have different consequences in terms of negative mental health outcomes and underlying physiology also depending on the age at which ELM exposure and subsequent outcomes are examined. This study will hopefully contribute to much-needed knowledge and inspire the conduct of future studies that examine the mechanisms by which well-documented risk factors influence depressive symptoms, and drive the development of effective, targeted intervention strategies to mitigate ELM exposure and its consequences.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data Availability Statement

The data that support the findings of this study are available on reasonable request from the responsible authors (VC, MK). The data are not publicly available due to ethical restrictions. Code used in the analyses is made publicly available by the corresponding author and can be accessed online (https://osf.io/vd7rh/?view_only = d547aa842a92457b9eaa5381941f91a8).

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