



Co-occurring childhood maltreatment exposure and depressive symptoms in adulthood: Testing differential effects of stress dysregulation and perceived stress

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ABSTRACT

Objectives: Objectives were to explore: 1) the association between sub-groups with different multi-type childhood maltreatment exposures and depressive symptoms in late adulthood, and 2) the mediating effects of dysregulated physiological stress system function and perceived stress in midlife on the aforementioned associations.

Methods: Data come from the Biomarker project ($n = 1,053$) of the Midlife Development in the United States study. Latent profile analysis was used to identify sub-groups with differing childhood maltreatment type and chronicity. We then test our mediation hypothesis using a product of coefficients method procedure.

Results: Two vulnerable sub-groups were identified (Class 2: Emotional and physical maltreatment class, $n = 52$, and Class 3: Sexual abuse class, $n = 79$) along with a normative sub-group (Class 1: Normative class, $n = 922$) comprising of a majority of adults. Both vulnerable sub-groups had higher levels of perceived stress in late adulthood. Perceived stress mediated the association between both vulnerable sub-groups and depressive symptoms. Physiological stress dysregulation mediated the association only between the emotional and physical maltreatment class and depressive symptoms in late adulthood.

Conclusion: Therapeutic approaches targeted at prevention of perceived stress for both vulnerable sub-groups identified in this study and those targeting physiological dysregulation in addition for the emotional and physical maltreatment class could be critical for depressive symptom recovery.

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Children who are victims of maltreatment by their caregivers not only have impaired functioning as children but also suffer from higher levels of psychological problems as adults (Cicchetti & Toth, 2005). One such critical psychological problem during adulthood that is often associated with childhood maltreatment exposure is the presence of depressive symptoms (Li, D'Arcy, & Meng, 2016; Nelson, Klumparendt, Doebler, & Ehring, 2017). The purpose of this study is to clarify links between co-occurring childhood maltreatment types and chronicity (i.e. frequency of maltreatment) and depressive symptoms in late adulthood by examining the relative contribution of two key mechanisms in midlife: perceived or psychological stress, and dysregulated stress system function.

Co-occurring maltreatment exposure

Research suggests that maltreatment types can co-occur (Finkelhor, Turner, & Hamby, 2011) and therefore it is critical to assess these co-occurring maltreatment types together in order to truly capture maltreatment exposure in childhood and understand its subsequent negative effects (Debowska, Willmott, Boduszek, & Jones, 2017). Maltreatment exposures are multidimensional and vary by exposure type and frequency (Finkelhor et al., 2011). However, a recent meta-analysis revealed that a limited

number of studies evaluate profiles of maltreatment based on both types and chronicity of maltreatment, even though such an approach is critical for understanding the heterogeneity in maltreatment exposure that can lead to differences in biological functioning and health throughout life (Debowska et al., 2017). Preliminary studies on co-occurring maltreatment types demonstrate that physical abuse, emotional abuse and neglect types of maltreatment tend to co-occur more frequently with one another compared to their co-occurrence with sexual abuse (Higgins & McCabe, 2001). The current study uses a latent profile approach to evaluate sub-groups of individuals with exposure to multiple childhood maltreatment types and chronicity and subsequent depressive symptoms in late adulthood.

Childhood maltreatment and depressive symptoms

The association of childhood maltreatment with depressive symptoms and depression in adulthood has been previously demonstrated by numerous studies (Li et al., 2016; Nelson et al., 2017). For example, a meta-analysis showed that childhood neglect, emotional abuse, and physical abuse were all linked to higher likelihood of depressive symptoms among adults (Norman et al., 2012). Similar findings were reported by another study that found increased risk for depression in adulthood following physical abuse,

physical neglect, and sexual abuse (Li et al., 2016). Whereas one meta-analysis revealed that emotional maltreatment and neglect were more strongly associated with later life depression than sexual abuse (Infurna et al., 2016), others have revealed that sexual abuse (Li et al., 2016) and emotional abuse were the strongest predictors of adult depression (Nelson et al., 2017). Based on these findings, it seems clear that all maltreatment types carry risk for adult depression. It is likely that the discrepancies in findings regarding the most impactful maltreatment type for depressive symptoms in adulthood is due to high covariance (Higgins & McCabe, 2001) between maltreatment types that can result in only the most severe form of maltreatment type emerging as the most significant (due to partialling out of variance between correlated maltreatment types). However, as noted above, less is known about the association between co-occurring maltreatment types based on chronicity and type of maltreatment and depressive symptoms in adulthood, even though empirical evidence suggests that exposure to multiple maltreatment increases the risk for depressive symptoms and major depressive disorder in adulthood (Spatz Widom, DuMont, & Czaja, 2007).

Hypothalamic-pituitary-adrenal (HPA) axis dysregulation, and perceived stress

Several mechanisms are proposed for how maltreatment exposure may lead to later depressive symptoms. According to the allostatic load model, the body regulates its functions in the presence of acute stressors as a means of coping resulting in dysregulation of several biological systems (e.g. immune, cardio-metabolic, endocrine, etc.; McEwen & Wingfield, 2010). Prolonged regulation of the body's functions due to chronic stressors can, however, lead to detrimental outcomes over-time, including depressive symptoms (Li et al., 2016; McEwen & Wingfield, 2010). Central to the allostatic load model is the hypothalamic-pituitary-adrenal (HPA) axis, which is one of the major systems that gets activated as a response to stressors (Teicher, Andersen, Polcari, Anderson, & Navalta, 2002) and produces the stress hormone cortisol that serves as a potential biological mechanism between environmental stressors, and health outcomes (Doom, Cicchetti, & Rogosch, 2014).

Studies have identified dysregulated basal stress levels, specifically a blunting of the cortisol stress response, as a key mechanism linking childhood maltreatment to internalizing problems in childhood (Cicchetti, Rogosch, Gunnar, & Toth, 2010). Similar findings are reported by studies evaluating functioning during adulthood, demonstrating that the association between childhood trauma and depression during adulthood is at least partially mediated by dysregulation of physiological stress response (Heim, Newport, Mletzko, Miller, & Nemeroff, 2008). According to the allostatic load theory, exposure to chronic stressors such as childhood maltreatment is associated with altered basal levels of cortisol; the cortisol stress response follows a pattern of initially high levels and reactivity of cortisol in childhood when dealing with the acute stressor, but becomes blunted and results in lower cortisol production in adulthood due to the chronicity of the stressor (Miller, Chen, & Zhou, 2007; Tarullo & Gunnar, 2006). Indeed, maltreated children tend to have elevated basal levels of cortisol

immediately following the trauma (De Bellis & Putnam, 1994; Gunnar & Vazquez, 2015). However, after the maltreatment exposure and associated stress becomes chronic, maltreated individuals likely undergo an allostatic shift down-regulating the HPA axis and producing lower levels of cortisol (Morris, Compas, & Garber, 2012; Power, Thomas, Li, & Hertzman, 2012), to protect the body against the neurotoxic effects of chronically high cortisol (McEwen & Wingfield, 2010). This down-regulated HPA axis function, as indicated by low cortisol, is then associated with increased risk of depression in adults (Heim et al., 2008; Keller et al., 2006). However, physiological stress system function may not be the only stress-related mechanism at play.

Maltreatment exposure is also associated with negative appraisals of stressful situations (Cicchetti & Toth, 2005). Negative appraisal of stressful situations translates into higher levels of perceived stress, which can lead to a feeling of helplessness and mental health problems such as depression (Hyman, Paliwal, & Sinha, 2007). At least one study has demonstrated that higher self-reported or perceived stress was a mechanism promoting higher levels of depressive symptoms among adults with a history of childhood maltreatment (Vranceanu, Hobfoll, & Johnson, 2007). However, this study used cross-sectional data, thereby making it difficult to ascertain the direction of associations found (i.e. perceived stress and depression may be highly correlated at any given time point). Thus, because both physiological indicators of stress and perceived stress have been identified as potential mechanisms of the association of childhood maltreatment exposure and adult depressive symptoms, it is important to clarify the extent to which these mechanisms overlap, or if one better explains the association than the other for specific combinations of maltreatment exposure (based on type and chronicity). Additionally, no previous study has examined these mediating mechanisms simultaneously in midlife to understand their influence on the association between childhood maltreatment exposure and depressive symptoms in late adulthood. Midlife is an important developmental period for health outcomes later in adulthood (Lachman, Teshale, & Agrigoroaei, 2015) and it is likely that early experiences influence health in midlife (Kuh, Ben-Shlomo, Lynch, Hallqvist, & Power, 2003).

Perception of stress and relative impact to physiological stress dysregulation

Recent studies have demonstrated mixed findings regarding the association of self-reported or perceived stress and physiological stress assessed by basal cortisol with well-being outcomes across the lifespan. To illustrate, both perceived stress and cortisol levels played a role for diverse outcomes, including worse academic performance in college students (Ng, Koh, & Chia, 2003), slower wound healing in adults (Ebrecht et al., 2004), and delayed cognitive development among babies (Davis & Sandman, 2010). However, both mechanisms have not always been supported. In studies of psychopathology in adulthood, greater perception of stress was associated with higher levels of ADHD compared to cortisol (Hirvikoski, Lindholm, Nordenström, Nordström, & Lajic, 2009; Lackschewitz, Hüther, & Kröner-Herwig, 2008).

Even though both perceived stress and physiological dysregulation have been evaluated distinctly for depressive symptoms among adults with a history of childhood maltreatment (Heim et al., 2008; Vranceanu et al., 2007), the relative impact of both perceived stress and physiological stress dysregulation has not been explored for the associations between sub-groups with differing childhood maltreatment types and chronicity in adulthood. This evaluation of mechanisms will inform future intervention endeavors targeted at preventing negative consequences of childhood maltreatment exposure. For example, if perceived stress carries more weight in the association, interventions targeting stress reduction in adults who experienced childhood maltreatment might reduce the risk for depression in adulthood (Kimbrough, Magyari, Langenberg, Chesney, & Berman, 2009; Wilson, Vidal, Wilson, & Salyer, 2012). Conversely, if physiological dysregulation mediates the association, then interventions earlier in development that emphasize consistent and responsive caregiving in order to reduce the effect of maltreatment on cortisol dysregulation (Fisher, Van Ryzin, & Gunnar, 2011) may be more effective. If both mechanisms prove to be equally important factors for symptoms of depression, then findings will point to multiple points of intervention.

Present study

The present study builds on and extends previous research by evaluating the following research questions: Q1: What is the association between sub-groups with differential multi-type maltreatment exposures and depressive symptoms longitudinally in late adulthood (around age 65)? Q2: Are the mechanistic effects of dysregulated stress system function and perceived stress in midlife (around age 55) similar or different?

Methods

Data for this study come from the longitudinal survey of Midlife Development in the United States (MIDUS; Brim, Ryff, & Kessler, 2004). The main MIDUS study consists of three waves of data collection starting in 1995–96 and includes a national probability sample that was selected via random digit dialing ($n=3,487$), a sample of siblings ($n=950$), and a nationally representative sample of twins ($n=998$). The follow-up data collection took place between 2004 and 2006 (wave 2) and 2013 and 2014 (wave 3).

Relevant to this study, at wave 2, a sub-sample of the MIDUS participants took part in the Biomarker project (Dienberg Love, Seeman, Weinstein, & Ryff, 2010). The Biomarker project was a clinical sub-study used to assess physiological functioning and health-related biomarkers. The biomarker project included participants who had completed both the phone interviews and self-administered questionnaires and were willing to travel to the clinic and stay overnight. This sample differed from the main MIDUS sample on their level of education – the biomarker sample was slightly better educated (Dienberg Love et al., 2010). The analytic sample ($n=1,053$) included participants from the longitudinal study who participated in the biomarker study at wave 2 and had completed the childhood maltreatment questionnaire.

Measures

Retrospective childhood maltreatment at wave 2

Exposure to childhood maltreatment was assessed during the biomarker study at wave 2 by the frequently used retrospective measure: Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998). Respondents reported on exposure to five types of maltreatment during childhood: Emotional Abuse, Physical Abuse, Sexual Abuse, Physical Neglect and Emotional Neglect. Each maltreatment type consisted of five items and items were scored on a 1 (Never true) to 5 (Very Often True) scale, with higher scores indicating greater maltreatment chronicity assessed by duration of maltreatment exposure. To illustrate, if respondents reported 1, then they never experienced that specific item for that maltreatment type during childhood. Reports of 5 on an item indicated chronic and frequent exposure/experiences of that item during childhood. The five scores (created by summing all the items) for each maltreatment type were used to estimate latent profiles of maltreatment exposure (range 5–25): Emotional Abuse ($\alpha = .88$), Physical Abuse ($\alpha = .79$), Sexual Abuse ($\alpha = .94$), Physical Neglect ($\alpha = .70$) and Emotional Neglect ($\alpha = .89$).

Perceived stress at wave 2

Perceived Stress was assessed during the biomarker study visit at wave 2 using 10-items from the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983). The response pattern for the scale ranges from 1 “never” to 5 “very often”. Positive items were reverse coded so that higher values were indicative of more perceived stress. Scale score was computed by computing the sum of all items and ranged from 1 to 50 ($\alpha = .86$).

Urinary free cortisol at wave 2

The measure of HPA axis dysregulation was basal levels of cortisol production as measured by urinary free cortisol over a 12-hour period, starting at Day 1 and ending on Day 2 of the biomarker study visit at wave 2 and was adjusted for creatinine. At 7 pm, individuals were asked to start collecting urine sample in urinal (men) or hat (women). Urine collected between 7 pm and 7 am was poured into two collection containers (half in each) and refrigerated. Time of final urine collection was recorded. Individuals with urine samples collected over a period of less than 11 hours or greater than 13 hours were excluded from the analytic sample ($n=10$). Any urine sample collected before 6 pm/am and after 8 pm/am was also excluded from our analysis ($n=16$). Individuals with Cushing’s disorder were also excluded from the analytic sample ($n=2$). Further individuals with voids or incomplete cortisol data were also excluded from the sample ($n=43$). Further, outliers ($n=32$) were winsorized to +3 SD and to a minimum value of 0.08 ug/dL (the assay detection limit), and the measure was log-transformed to correct skewness and kurtosis.

Depressive symptoms at wave 3

Depressive symptoms were also assessed through telephone interviews at wave 3 using the Recent Care of Common Mental Disorder in the United States: Prevalence and

Conformance with Evidence-Based Recommendations (Wang, Berglund, & Kessler, 2000) questionnaire. Participants were asked whether they had experienced each of seven symptoms for two weeks over the last 12 months. “Yes” responses were coded 1, “No” responses were coded as 0, and scores were summed into a count variable ($\alpha = .83$).

Depression diagnostic criteria at wave 3

At wave 3, the Recent Care of Common Mental Disorder in the United States: Prevalence and Conformance with Evidence-Based Recommendations (Wang et al., 2000) scale was used to create a dichotomous variable indicating if the participant met American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders III-R (Spitzer, First, Gibbon, & Williams, 1990) criteria for a major depression diagnosis by MIDUS data collectors. “Yes” was coded as 1 and “No” as 0.

Covariates

The following demographic covariates were included in the model: gender (1 = “male”; 0 = “female”), race (1 = “white”; 0 = “other”), education was also coded as a categorical variable (1 = “some college or bachelor’s degree”; 0 = “less than college”). Marital status was coded as a categorical variable (1 = “currently married”; 0 = “single/divorced/widowed”), and age of the participant was included as a continuous covariate. Cortisol-influencing covariates included use of corticosteroids and use of hormones or hormone pills or birth controls. We also included a count of other childhood adversities as a covariate - 1. parents had disability, 2. parents used alcohol or drugs, 3. parental death before age 16, 4. parents had mental health problems, and 5. parents divorced - that could potentially confound the outcome.

Analytic strategy

All model analyses were conducted using Mplus 7.4 statistical software (Muthén & Muthén, 2005). Latent profile analysis was used to identify sub-groups distinguished by the chronicity of different types of maltreatment exposures wherein individuals with similar levels of exposure to different types of maltreatment were grouped together. Latent profile analysis takes into account heterogeneity of exposure and groups people into sub-groups using posterior probabilities. Final models were selected based on four statistical fit indicators: lower, model fit values on *AIC*, *BIC* and *adjusted-BIC* and higher *entropy* were considered better statistical fit indices. Model fit indices, and model convergence were used to decide on final class solution. Once an optimal solution was determined, substantive class labels were applied using posterior probabilities (*threshold* = 0.99) and sub-group descriptive statistics were obtained. Descriptive statistics for each subgroup included *mean* statistics, standard deviations (*std. dev.*) and sample size (*n*). Dummy variables were created for the vulnerable classes and the normative class (class with low levels of maltreatment exposure) was used as the reference.

Direct effects between latent profiles of childhood maltreatment exposures and depressive symptoms and risk for depression diagnosis at wave 3 were estimated using path

models (i.e. full mediation models) to answer research Q1. Significance test for the indirect effects were obtained to answer research Q2 using product of coefficients method procedure (MacKinnon, Fairchild, & Fritz, 2007). The approach tests all paths simultaneously, has greater statistical power to detect mediation effects, and allows the identification of five key patterns of association: 1) direct and indirect effects in the same direction (complementary mediation), 2) direct and indirect effects in opposite direction (competitive mediation), 3) mediated effects without direct effects (indirect only mediation), 4) direct associations with no mediation and 5) no direct or indirect association (Zhao, Lynch, & Chen, 2010). The mediation model included the latent profiles of childhood maltreatment exposures as independent variables, two stress measures (perceived stress and urinary cortisol) at wave 2 (midlife) as the mediators and depressive symptoms and risk for depression diagnosis at wave 3 (late adulthood; longitudinal) as the outcomes. All covariates were regressed onto the outcomes (depressive symptoms or diagnosis) and both mediators (perceived stress and urinary cortisol). Full information maximum likelihood (*FIML*) was used to accommodate missing data (Arbuckle, 1996). Family-level nesting (i.e. twins and siblings) was also corrected to improve precision of estimates.

Results

Latent profile analysis yielded a 3-class solution (See Figure 1). The model fit (Table 1) for the 3-class solution was better than the 2-class solution. Although the 4-class solution was better on certain model fit indices, the 4-class solution did not converge and did not replicate when the number of random starts were increased.

Therefore, the 3-class solution was considered the optimal solution for profiles of maltreatment exposure in MIDUS, and the following sub-group labels were assigned: Class 1: Low exposures to all maltreatment types (*normative class*), Class 2: High emotional and physical maltreatment and low sexual abuse (*physical and emotional maltreatment class*) and Class 3: High sexual abuse (*sexual abuse class*). Two dummy variables were created: one for each risk group, with the normative group as the reference, and included in the subsequent path models.

Table 2 summarizes the descriptive statistics for each sub-group. Supplemental Table 1 includes mean difference test of each maltreatment exposure type between the three groups. Specifically, both sub-groups had higher frequency of all maltreatment exposures compared to the normative class ($t = 5.76-63.06$, $df = 972-999$, $p < .001$). The emotional and physical maltreatment class had higher frequency of emotional and physical abuse as well as emotional and physical neglect compared to the sexual abuse class ($t = 4.07-7.46$, $df = 129$, $p < .001$). Similarly, the sexual abuse class had higher levels of sexual abuse compared to the emotional and physical maltreatment class ($t = 19.53$, $df = 129$, $p < .001$).

Supplemental Table 2 includes zero-order correlation between the study variables. Membership in both maltreatment groups was positively correlated with higher depressive symptoms in late adulthood ($r = 0.09, 0.17$) and with more perceived stress in midlife ($r = 0.14, 0.11$).

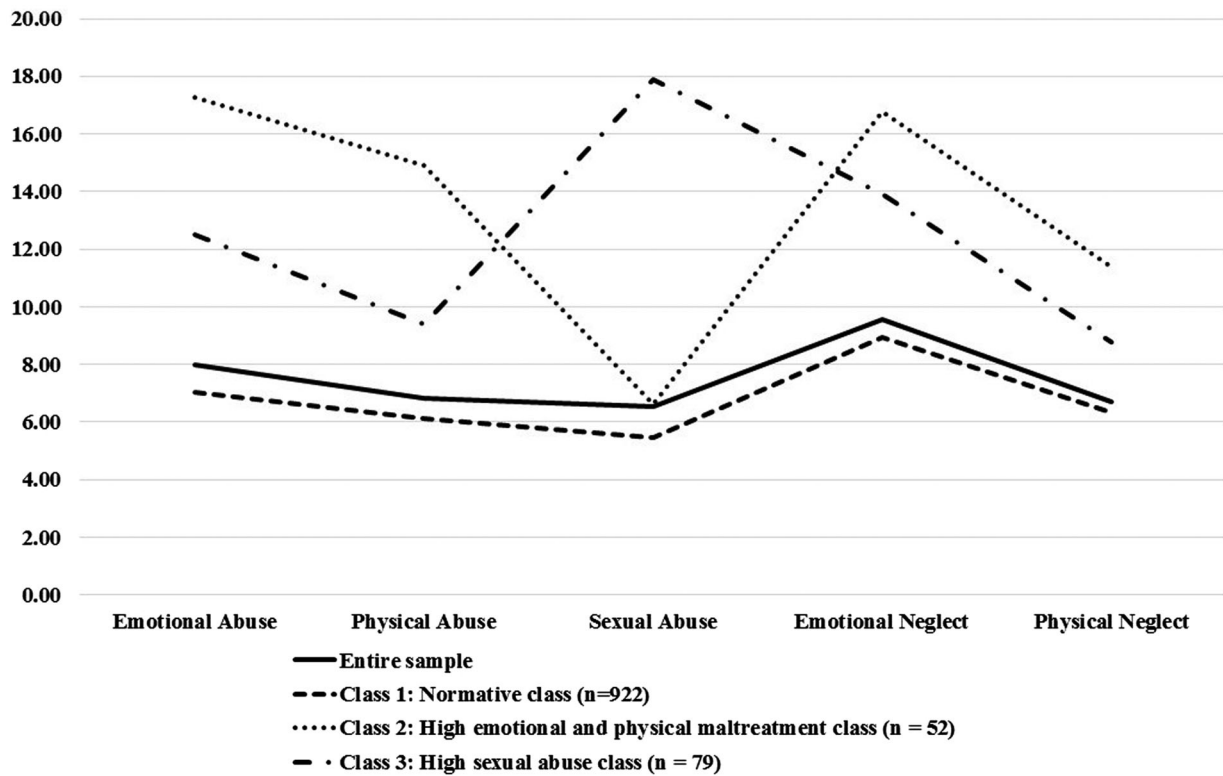


Figure 1. Class solution and entire sample average for maltreatment exposure. x-axis: maltreatment types and y-axis: frequency of exposure (range: 0–25).

Table 1. Fit indices for latent profile analysis of disability trajectories.

	AIC	BIC	Adj-BIC	Entropy
Two class solution	29668.05	29832.27	29730.62	0.98
Three class solution	30004.97	30138.39	30055.81	0.99
Four class solution	28754.18	28949.18	28828.48	0.99

Note. Adj-BIC refers to adjusted BIC.

Table 2. Descriptive statistics.

	Class 1: Normative class (n = 922)			Class 2: Emotional and physical maltreatment class (n = 52)			Class 3: Sexual abuse class (n = 79)		
	n	mean	std. dev	n	mean	std. dev	n	mean	std. dev
Key Variables									
Emotional abuse	922	7.04	2.86	52	17.27	4.30	79	12.48	5.41
Physical abuse	922	6.14	1.53	52	14.90	3.44	79	9.39	4.53
Sexual abuse	920	5.46	1.29	52	6.62	2.69	78	17.88	4.01
Emotional neglect	922	8.92	3.77	52	16.79	3.74	79	13.92	5.53
Physical neglect	922	6.32	2.11	52	11.37	3.54	79	8.76	3.61
Depressive symptoms in late adulthood	828	0.47	1.50	45	1.31	2.52	71	1.68	2.79
Depression diagnosis in late adulthood	828	8%	0.27	45	22%	0.42	71	27%	0.45
Urinary cortisol	878	2.50	0.77	51	2.17	0.79	75	2.41	0.85
Perceived stress	876	21.25	5.95	51	25.29	6.96	75	24.15	6.89
Covariates Continuous									
Other childhood adversities	922	4.69	1.54	52	5.65	1.60	79	5.33	1.83
Age	922	55.79	11.86	52	49.04	8.69	79	53.27	11.41
Covariates Proportions									
Sex hormone medication	878	12%	0.33	51	4%	0.20	75	15%	0.36
Corticosteroid medication	878	4%	0.20	51	4%	0.20	75	7%	0.25
Race: White	892	94%	0.24	50	96%	0.20	74	95%	0.23
Gender: Male	922	48%	0.50	52	40%	0.50	79	15%	0.36
Marital Status: Married	920	73%	0.44	52	75%	0.44	79	58%	0.50
Education: Some college/ bachelor's degree	922	52%	0.50	52	54%	0.50	79	52%	0.50

Note: 1. Categorical variables are presented as proportion of the sample. To illustrate, for the demographic variable gender, in our sub-sample, 45% were male and the remaining were women.

Membership in the emotional and physical maltreatment class was negatively correlated with urinary cortisol level (i.e. blunted; $r = -0.09$).

Direct effects from the mediation model are summarized in Table 3. Being a member of the sexual abuse class ($\beta =$

0.13; $OR = 2.75$) and having higher perceived stress scores ($\beta = 0.26$; $OR = 1.1.3$) were associated with more depressive symptoms and a greater likelihood of meeting criteria for a depression diagnosis in late adulthood. Lower urinary cortisol concentration in midlife ($\beta = -0.11$; $OR = 0.63$) was also

Table 3. Estimating Direct Effects for Model with Depressive Symptoms Outcome.

Predictors	Direct effects on depressive symptoms in late adulthood				Predictors	Direct effects on depression diagnosis in late adulthood					
	<i>b</i>	<i>p</i>	<i>s.e.</i>	β		<i>b</i>	<i>p</i>	<i>s.e.</i>	OR	95% CI [LL,UL]	
Class 2: High emotional and physical maltreatment	0.43	.257	0.38	0.05	Class 2: High emotional and physical maltreatment	0.56	.199	0.43	1.75	0.97	1.15
Class 3: High sexual abuse	0.87	.005	0.31	0.13	Class 3: High sexual abuse	1.01	.002	0.33	2.75	1.05	3.41
Urinary cortisol	-0.23	.003	0.08	-0.11	Urinary cortisol	-0.47	.002	0.15	0.63	0.76	0.94
Perceived stress	0.07	<.001	0.01	0.26	Perceived stress	0.12	<.001	0.02	1.13	1.28	1.56
Direct effects on urinary cortisol						Direct effects on urinary cortisol					
Predictors	<i>b</i>	<i>p</i>	<i>s.e.</i>	β	Predictors	<i>b</i>	<i>p</i>	<i>s.e.</i>	β		
Class 2: High emotional and physical maltreatment	-0.37	.001	0.11	-0.10	Class 2: High emotional and physical maltreatment	-0.37	0.001	0.11	-0.10		
Class 3: High sexual abuse	-0.17	.104	0.11	-0.06	Class 3: High sexual abuse	-0.17	0.100	0.11	-0.06		
Direct effects on perceived stress						Direct effects on perceived stress					
Predictors	<i>b</i>	<i>p</i>	<i>s.e.</i>	β	Predictors	<i>b</i>	<i>p</i>	<i>s.e.</i>	β		
Class 2: High emotional and physical maltreatment	3.39	.001	1.00	0.12	Class 2: High emotional and physical maltreatment	3.40	.001	1.00	0.12		
Class 3: High sexual abuse	2.43	.004	0.84	0.10	Class 3: High sexual abuse	2.47	.004	0.85	0.10		

Note: 1. Normative class was the reference group; 2. CI = Confidence Interval, LL = lower limit; UL = upper limit; 3. CI is for the Odds ratio.

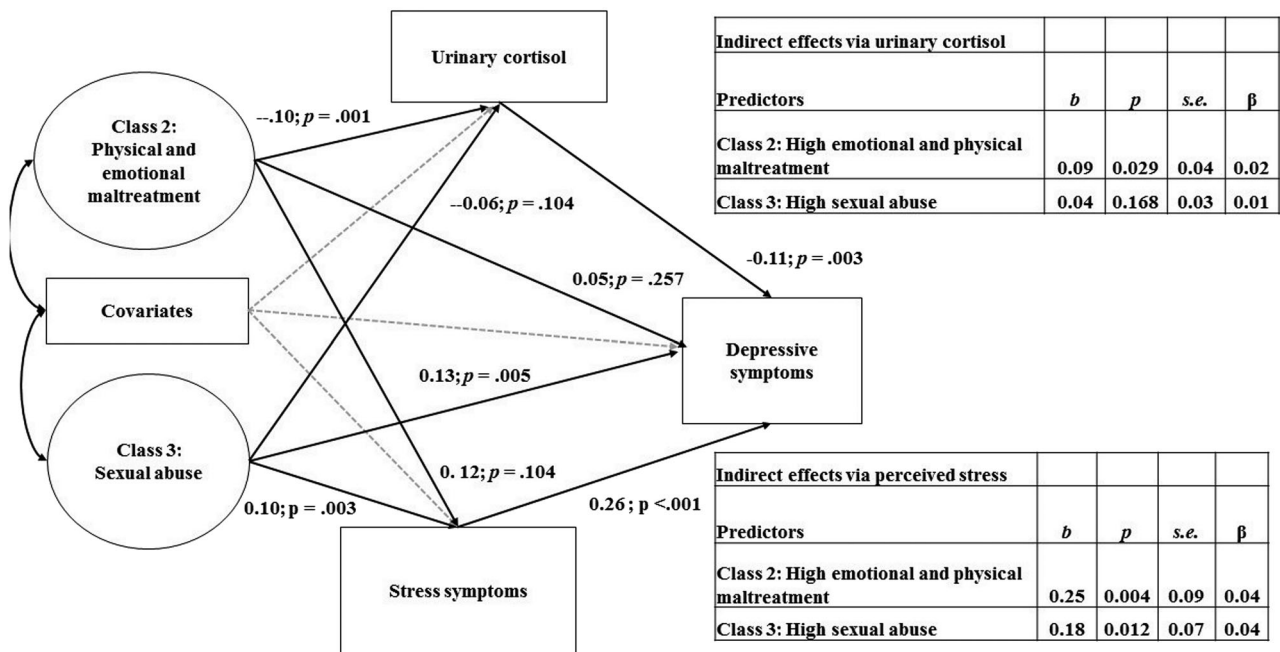


Figure 2. Mediation model for depressive symptoms conditioned on all covariates.

Note. 1. Both urinary cortisol and perceived stress were tested as mediators in the same model for each outcome; 2. OR = Odds ratio CI = Confidence interval, LL = Lower limit; UL = Upper limit; 3. CI is for the Odds ratio; 4. Normative class was the reference group.

associated with higher depressive symptoms and greater likelihood of meeting the criteria for a depression diagnosis in late adulthood. Finally, membership in physical and emotional maltreatment class was associated with higher levels of perceived stress ($\beta = 0.12$) and blunted cortisol response in midlife ($\beta = -0.10$). Membership in the sexual abuse class was associated only with higher levels of perceived stress ($\beta = 0.10$).

Figures 2 and 3 summarize the indirect effects. Association between membership in the sexual abuse class and depressive symptoms and meeting the criteria for a depression diagnosis in late adulthood, were in part explained for by perceived stress levels in midlife. There were indirect associations between physical and emotional maltreatment class membership and depressive symptoms and meeting the criteria for a depression diagnosis in late adulthood through perceived stress and urinary cortisol in

midlife. The association between physical and emotional maltreatment class membership and depressive symptoms and meeting the criteria for a depression diagnosis in late adulthood was fully mediated by the combination of perceived stress and urinary cortisol in midlife.

Post-Hoc Analysis. We tested for gender differences in post-hoc analyses. Associations did not differ by gender of the respondent ($\chi^2 = 3.63, df = 8, p = 0.887$) and the mediation effects also did not differ by gender ($\chi^2 = 1.37, df = 4, p = 0.849$).

Discussion

The present study identified three distinct sub-groups based on their types and chronicity of maltreatment exposures and found that the two sub-groups with higher

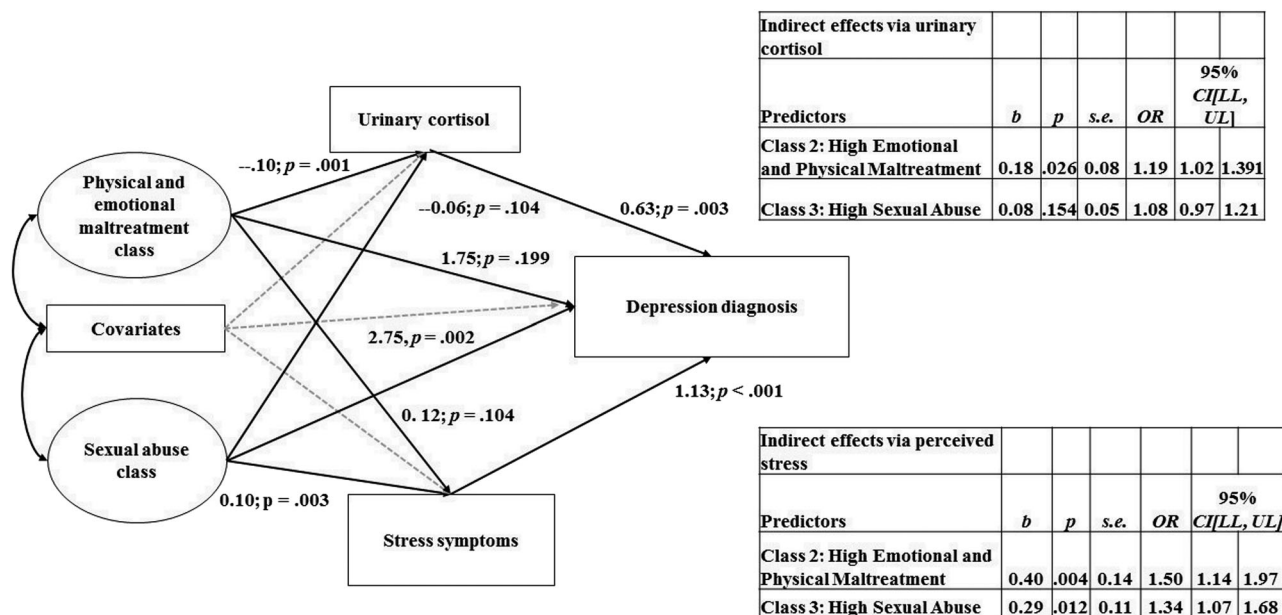


Figure 3. Mediation model for depression diagnosis conditioned on all covariates.

Note. 1. Both urinary cortisol and perceived stress were tested as mediators in the same model for each outcome; 2. OR = Odds ratio CI = Confidence interval, LL = Lower limit; UL = Upper limit; 3. CI is for the Odds ratio; 4. Normative class was the reference group.

maltreatment chronicity had higher depressive symptoms in late adulthood (Q1). Further, we found that dysregulated stress system function was a mechanistic link in this association for individuals in the sub-group marked by particularly high levels of emotional and physical maltreatment relative to sexual abuse, whereas perceived stress in midlife was a mechanistic link for both maltreatment sub-groups and depressive symptoms (Q2). These findings suggest that targeting prevention of perceived stress for both vulnerable sub-populations identified in this study, and both perceived stress and physiological dysregulation for the emotional and physical maltreatment class may help to prevent depression symptoms and/or promote recovery.

In addition to contrasting the importance of the mediating effects of perceived stress versus physiological stress, our study adds to the literature by using latent profile analysis to capture different patterns of co-occurring childhood maltreatment exposures based on both type and chronicity of exposure. This approach helps identify heterogeneity in response pattern in a variety of constructs that can co-occur in order to create mutually exclusive groups that are representative of sub-groups (Lanza & Cooper, 2016), as well as multi-dimensionality of constructs and mental health outcomes (Decuyper et al., 2013; Kuramoto, Bohnert, & Latkin, 2011). Thus, findings may be useful in identifying most vulnerable sub-groups that could benefit from certain prevention efforts to reduce adulthood depression (Lanza & Cooper, 2016).

Co-occurring maltreatment exposure

We identified three distinct sub-groups based on their types and chronicity of maltreatment exposures. Our findings for the maltreatment sub-groups mostly align with previous research evaluating childhood maltreatment exposure in adult samples. The physical and emotional maltreatment class comprised of individuals who had higher than average chronicity of exposure to physical and emotional neglect, and physical and emotional abuse,

similar to prior findings (Higgins & McCabe, 2001). However, the higher than average prevalence of other maltreatment type chronicity in the sexual abuse group is a novel finding that suggests that in this sample of adults, sexual abuse more often co-occurs with other types of maltreatment exposure than as a single-type. Specifically, individuals in the sexual abuse class on average reported greater chronicity of sexual abuse exposure throughout childhood compared to both other sub-groups. The emotional and physical maltreatment class had higher chronic exposure to all childhood maltreatment types except sexual abuse.

This pattern of effects contrasts with previous findings with adult samples that sexual abuse might be the most frequently occurring single-type maltreatment exposure (Higgins & McCabe, 2001), but is supported by recent sub-group analysis with maltreated children wherein chronic and regular sexual abuse exposure is present with relatively modest levels of other types of maltreatment exposures (Petrenko, Friend, Garrido, Taussig, & Culhane, 2012). The sexual abuse class was therefore the group characterized by the most severe and widespread chronic maltreatment exposure in this study, and this finding may extend to adult samples with childhood maltreatment exposure more generally.

Mechanisms of childhood maltreatment and depressive symptoms

Results for our first research question further corroborates the idea that the sexual abuse class marked the most severe maltreatment, as only sexual abuse sub-group membership was directly associated with more depressive symptoms in late adulthood even after accounting for the two mediating mechanisms. However, in our analysis of mechanisms (second research question), both sub-groups exhibited higher levels of perceived stress, which was subsequently associated with longitudinal depressive symptoms as well as higher odds of meeting the diagnostic

criteria for depression in late adulthood. These findings corroborate previous research findings wherein perceived or self-reported stress was an important mechanism through which childhood maltreatment exposure transmitted its effects on concurrent depressive symptoms in adulthood (Vranceanu et al., 2007). Our findings provide a longitudinal extension, demonstrating that perceived stress is a mechanism between maltreatment exposure and depressive symptoms assessed 10 years later (following the measure of perceived stress) in late adulthood. Thus, there is strong evidence that perceived stress plays an important role for how individuals develop and maintain depressive symptoms following maltreatment exposure. Perceived stress is related to depressive episodes particularly when individuals view stressors as uncontrollable and unpredictable, and exceeding their ability to cope (Hammen, 2005). Any maltreatment exposure may therefore increase the likelihood that individuals perceive seemingly innocuous events as uncontrollable, unpredictable, and stressful and the increased psychological burden creates an additional vulnerability to depression.

Much like previous research (Carpenter et al., 2009; Heim et al., 2008), we also found an association between emotional and physical maltreatment class membership and physiological cortisol dysregulation, and physiological stress (assessed by urinary cortisol) was a significant mediator of the association between maltreatment exposure and depressive symptoms among members of this class. However, unlike previous research (Shenk, Noll, Putnam, & Trickett, 2010), we did not find an association between sexual abuse exposure and cortisol production, or that cortisol was a significant mediator between sexual abuse exposure in childhood and longitudinal depressive symptoms in late adulthood.

We chose to examine urinary free cortisol for three primary reasons. First, urinary cortisol is an adequate measure of cumulative basal cortisol levels and provides a single index of cortisol production over a sampling period as demonstrated by previous research (Short et al., 2016). Second, one of the objectives of this study is to understand how cortisol production and dysregulation of the HPA axis compare to self-reported (or perceived) stress and then understand the differential effect of the two measures on the association between profiles of childhood maltreatment and depression in late adulthood. Importantly, we are interested in understanding HPA axis dysregulation as assessed by the allostatic load model and urinary cortisol is one of the central measures of allostatic load in the overarching study from which these data were drawn (Seeman, Singer, Rowe, Horwitz, & McEwen, 1997). Therefore, this measure of cortisol should be more closely aligned to the global (or overall) stress assessed by perceived stress scale used in this study, because urinary cortisol is often considered a measure of more cumulative levels of stress (Fibiger, Singer, Miller, Armstrong, & Datar, 1984) and shows an association with perceived stress measures in some studies (Ursache, Noble, & Blair, 2015). Last, the urinary cortisol measure is considered an appropriate stable measure of overall cortisol production and endocrine dysregulation (Remer, Maser-Gluth, & Wudy, 2008) compared to salivary cortisol which is more suited to assess fluctuations in cortisol production (Doane, Chen, Sladek, Van Lenten, & Granger, 2015).

Previous research demonstrates that even though understudied for its long-term effects, high levels of emotional maltreatment may be ubiquitous for health problems compared to other types of maltreatment exposure. This may be because victims of emotional maltreatment have a higher chronicity of exposure that may impair attachment bonds between the caregiver and child due to unresponsive parenting that is characteristic of emotional maltreatment (Taillieu, Brownridge, Sareen, & Afifi, 2016). Moreover, certain chronic stressors can lead to dysregulation of the HPA axis and are detrimental outcomes over-time, including depressive symptoms (Li et al., 2016; McEwen & Wingfield, 2010). Taken together, these could be a potential explanation for the differences we find for the two maltreatment sub-groups based on both type and chronicity of exposure. Even though the sexual abuse class had relatively high exposure to childhood emotional maltreatment, the emotional and physical maltreatment class had significantly higher levels of chronic emotional maltreatment exposure in comparison to the sexual abuse class – demonstrating that chronic exposure to emotional maltreatment may be more detrimental for long-term biological functioning. These differential effects by sub-groups were replicated when we assessed risk for depression diagnosis: individuals in the physical and emotional maltreatment group – but not sexual abuse group – reported more blunted cortisol response which was in turn associated with a 1.19 times greater likelihood of meeting the criteria for a depression diagnosis in late adulthood. Specifically, both perceived stress and blunted cortisol response demonstrate indirect pathways (even in the absence of direct associations; Zhao, Lynch, & Chen, 2010) through which the effects of maltreatment are transmitted to later life depressive symptoms for the physical and emotional maltreatment group.

Limitations and future directions

The findings of this research are informed by several limitations. One limitation is that we use a retrospective measure of childhood maltreatment that could potentially suffer from recall bias. However, previous studies have demonstrated the stability of retrospective childhood maltreatment reports over-time (Yancura & Aldwin, 2009) and the likelihood of under-reporting of childhood maltreatment exposures (Dube et al., 2003). Future research should collect prospective data to evaluate the long-term impacts of childhood maltreatment exposure on adult mental health. Another avenue for future research is to determine the age at which first exposure to maltreatment occurred and the duration of such exposure both of which could potentially influence the associations found and was beyond the scope of the present research. Additionally, childhood maltreatment exposures, perceived stress, and depressive symptoms are based on self-reports which could suffer from single reporter bias and inflated associations. These biased estimates are likely to influence within time associations but not longitudinal association between perceived stress and depressive symptoms evaluated in this study (Blalock, 1961). Moreover, perceived stress is measured only at one time point and could be under or overestimated and future work should consider evaluating self-reported stress at multiple timepoints to capture the phenomena

more accurately. Finally, the present study uses a normative sample with little ethnic diversity (i.e. the vast majority of the sample was White). Future work should evaluate the hypothesized pathways of this study with high-risk samples (e.g. substantiated maltreatment or foster care experience) and with other psychopathology outcomes in adulthood. It is likely that the mediation effects may vary by population of inference and outcome. Although no gender differences were found in this research, it may be beneficial to further explore gender differences.

Conclusions and implications

Despite these limitations, the present study has several strengths. First, we identified sub-groups with heterogeneous childhood maltreatment exposures (i.e. based on type and chronicity) and evaluate its direct and indirect effects via physiological stress dysregulation and perceived stress, on depressive symptoms in late adulthood with a large nationally representative sample. Second, we demonstrate the differential effects of physiological stress dysregulation and perceived stress in midlife on the association between childhood maltreatment groups and longitudinal depressive symptoms in late adulthood. Perceived stress is an important mechanism of the associations found in this study for both maltreatment groups, but physiological stress dysregulation is only an important mechanism among individuals with chronic and severe physical and emotional maltreatment exposure.

Intervention strategies could include reduction of perceived stress as a potentially critical target for the promotion of better mental health outcomes for individuals with similar maltreatment chronicity and type exposures as the two sub-groups. Cognitive behavior therapy, yoga and mindfulness meditation have proven invaluable for the reduction of perceived stress and depressive symptoms in previous research (Kimbrough et al., 2009; Wilson et al., 2012). Since perceived stress is a mechanism with similar mediating effects for both sub-groups identified in this study, such therapeutic approaches targeted at prevention of perceived stress could be critical for depressive symptoms recovery for these vulnerable sub-groups. Moreover, for the emotional and physical maltreatment group consistent and responsive caregiving in childhood is important to prevent cortisol dysregulation (Fisher et al., 2011), thereby necessitating a need for primary prevention of emotional and physical maltreatment in childhood. Cognitive behavior therapy, cognitive behavior stress management, relaxation therapy have proven invaluable to improve cortisol functioning in previous studies and could also be implemented for this group that has already been exposed to emotional and physical maltreatment in childhood (McGregor & Antoni, 2009).

Disclosure statement

The authors report no conflict of interest.

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Ethical approval

The study uses pre-existing data from the MIDUS study that was reviewed and deemed as a category 4 exemption for Human Subjects Research by the Purdue University IRB. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

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Data availability

<https://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/29282>

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