

Cluster analysis reveals distinct patterns of childhood adversity, behavioral disengagement, and depression that predict blunted heart rate reactivity to acute psychological stress

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Abstract

Background There is considerable evidence documenting associations between early life adversity, behavioral disengagement, and depression with blunted cardiovascular reactivity to acute psychological stress. However, while often examined as independent predictors, it is also likely that a combination of these factors uniquely relate to cardiovascular reactivity.

Purpose The present study employed multivariate cluster analysis to examine if distinct combinations of these outcomes relate to cardiovascular stress reactivity.

Methods Participants ($N = 467$) were predominantly female (60.6%) with a mean age of 19.30 years ($SD = 0.82$). Measures of early life adversity, behavioral disengagement, and depression were completed; in addition, participants had their blood pressure and heart rate monitored throughout a standardized stress testing session. Cardiovascular reactivity was calculated as the difference between mean stress and mean baseline cardiovascular values.

Results Analyses revealed two clusters with distinct patterns of exposure to early life adversity, levels of behavioral disengagement and depression, uniquely related to cardiovascular reactivity. In unadjusted models, Cluster

1 that was characterized by greater exposure to early life adversity, higher levels of behavioral disengagement and depression, was associated with lower systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) reactivity. Cluster 2 was characterized by reactivity values similar to the sample means. In fully adjusted models, Cluster 1 predicted heart rate reactivity to stress.

Conclusions The present study identifies a behavioral cluster that is characteristic of a blunted heart rate reactivity profile, significantly extending the research in this area.

Keywords Blunted reactivity · Early life adversity · Behavioral disengagement · Depression · Cluster analysis

Introduction

For decades, the cardiovascular reactivity (CVR) hypothesis postulated that prolonged and exaggerated responses to stress signify a vulnerability to cardiovascular disease (CVD) [1]. More specifically, it states that increased heart rate and blood pressure in response to stress alter the structure and function of the heart, leading to greater susceptibility to CVD [1, 2]. Prospective evidence links heightened stress responses with hypertension [3–6], left ventricular mass [7], atherosclerosis [8], and early cardiac morbidity and mortality [9].

However, research in recent years has found that blunted reactivity, a proposed marker for central motivational dysregulation, is also related to a range of negative health and behavioral outcomes [10, 11]. Blunted

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responders are low reactors compared with others in the sample and this type of stress response, initially considered protective, is indirectly related to CVD risk through several behavioral factors [10, 12, 13]. For example, depression [14], behavioral disengagement [11], substance abuse [15], and addictive behaviors [16] are associated with lower responses to acute psychological stress. Prospective studies show that blunted CVR predicts depressive symptoms 5 years later [14], shorter relapse in treatment programs for alcohol [17], cocaine [18], and smoking dependence [19]. Blunted reactivity is also related to a range of adverse health states [2], such as increased carotid intima-media thickness and coronary artery calcification [20]. Moreover, a recent systematic review found CVR prospectively predicts both mental and physical health consequences [13]. It is evident that the magnitude of the cardiovascular stress response, be it exaggerated or blunted, are indicative of poorer outcomes. These deviations reflect homeostatic dysfunction and signify a vulnerability to disease [21].

Psychosocial factors, such as motivation and early life adversity (ELA, e.g., abuse, neglect, and maltreatment in childhood) have been identified as risk and mediating determinants for blunted CVR. Studies show that those with depression are characterized by reduced response to reward [22–24], lower levels of motivated behavior [25] and perseverance when faced with a challenge [26, 27], and unsolvable task [28]. More recent work shows that the association between depression and blunted CVR is in part mediated by motivational factors [29]. When accounting for the mediating role of intrinsic motivation, which involves undertaking a goal or task out of personal satisfaction and interest, blunted responses become less pronounced in those with greater depressive symptoms [29]. In fact, altered stressor-evoked activation in neuroanatomical brain regions linked to motivation regulation is one proposed biological mechanism underlying blunted CVR [10, 30, 31].

Furthermore, exposure to chronic stress during critical periods of development (e.g., early life adversity) can place a strain on stress sensitive systems and cause alterations in brain regions (i.e., limbic system and prefrontal cortex) responsible for motivation and autonomic regulation [10, 30]. Without protective factors in place, ELA can become incorporated into long-term regulatory physiological processes and increase vulnerability to developmental, biological, mental, and behavioral adverse outcomes, increasing the risk of chronic disease in adulthood [32, 33, 38]. Imaging studies show deactivation in brain regions (e.g., anterior cingulate cortex, ventral striatum, amygdala, and medial prefrontal cortex) that are related to stress, motivated behavior, depression, and blunted reactivity [34–37].

This hyporesponsiveness to stimuli, which would normally motivate active coping efforts, is proposed to

be a rational explanation for the origins of blunted reactivity [10] and may lead to a greater reliance on disengagement coping strategies [39, 40]. In the short term, avoidant coping styles such as behavioral disengagement may prove beneficial with a cognitive and/or behavioral removal from the stressor [41, 42]. The immediate relief that follows reinforces the continued use of avoidant coping strategies, reducing motivation to return to the stressor [39]. Early life adversity affects self-regulatory processes, such as coping efforts, emotions and physiological reactivity [43]. Those with greater exposure to ELA may rely more on avoidant coping styles, that over time increase susceptibility to depression; with lower responses to stress indicating the physiological consequence of these health damaging behaviors [44].

Studies show that both ELA [45–47] and depression are associated with blunted reactivity to stress [14, 48–50]. Early life adversity can have a profound, long-lasting effect in adulthood. Recent research shows that the psychological impact of ELA results in higher depressive symptoms and has a knock-on effect on biological responses to stress [51]. The risk of depression increases with exposure to ELA, affecting the onset, severity, frequency, and duration of this disorder [52–55]. Furthermore, a systematic review reported that avoidant coping styles (e.g., behavioral disengagement), which arise from childhood experiences [56], were a significant predictor of depression [57].

While a substantial body of literature has demonstrated independent associations between blunted reactivity, ELA [45–47, 58], patterns of behavioral disengagement [11, 19, 59], and depression [10, 14, 48, 60, 61], how these factors cluster together, or if they indeed cluster, is unclear. Cluster analysis estimates the similarity between objects in a set, and from a clinical standpoint offers a better understanding of the heterogeneity that exists in patient characteristics in clinical populations [62]. It is a valuable data reduction analytical tool for the health sciences, as it guides research and understanding through its reliance on classification systems [63]. Classification not only allows researchers (e.g., in psychiatry) to determine which items are similar and dissimilar in a set but allows them to make and revise classifications repeatedly [62]. Therefore, it may prove useful in the development of tailored treatments and the advancement of diagnostic criteria [64]. Moreover, a recent systematic review argues adopting a clinimetric approach for assessment of not just biological vulnerability factors, but in combination with psychosocial patterns, which are more likely to be fruitful for intervention [44].

The purpose of this study is to focus on multiple variables associated with blunted CVR to acute psychological stress, to broaden the scope of our current understanding and to examine whether low reactivity

to stress is characterized by a behavioral cluster of ELA, behavioral disengagement, and depression. Specifically, the aim of the present study was (i) to identify if there was a distinct cluster of individuals who score higher on ELA, behavioral disengagement, and depression and (ii) if individuals characterized by this cluster exhibit blunted patterns of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) reactivity to stress compared with other identified clusters.

Methods

Study Sample

Participants were 467 young healthy adults who participated in a laboratory testing session between January 2019 and February 2020. Twenty-two outliers were removed for having high resting blood pressure $\geq 140/90$, which can be considered Stage 2 hypertensive [65], and 16 for missing data on study variables. This left a convenience sample of 429 healthy young adults. All participants received course credit for their participation.

The sample demographic information can be found in Table 1. To maintain a healthy sample, current illness or infection was listed in the exclusion criteria; participants were instructed in the laboratory session reminder email to reschedule if they had an illness or infection (e.g., cold, flu, strep throat). Moreover, participants were instructed to refrain from alcohol consumption and vigorous exercise 12 h prior to testing, as well as eating and drinking, not including water, 2 h before attending the laboratory [66–68]. Participants verbally confirmed they followed all eligibility criteria prior to the start of their testing session. At the time of the laboratory visit, participants ranged in age from 18 to 28 years ($M = 19.45$, $SD = 1.07$), with a mean body mass index (BMI) of 23.97 kg/m^2 ($SD = 4.70$). The sample was predominantly white ($n = 283$; 66.0%) and female ($n = 273$; 63.6%). Participants were recruited from Baylor University (Waco, TX) using the university's online psychology subject pool (SONA Systems). Participants received 2 h of SONA research credits, which were applied to their psychology and neuroscience courses. Participants provided written informed consent and this study, while not pre-registered, was approved by the university's Institutional Review Board.

Table 1 Participant Characteristics and Demographics

Items	<i>N</i>	Mean (<i>SD</i>)	Range
Age (years)	429	19.45 (1.07)	18–28 years
Body mass index (kg/m^2)	429	23.97 (4.70)	
Sex			
Male	156	19.70 (1.36)	
Female	273	19.30 (0.83)	
Race			
White	283		
Black/African American	34		
American Indian/Alaska Native	1		
Asian	80		
Multiracial/Other	31		
Ethnicity			
Hispanic/Latino	78		
Not Hispanic/Latino	345		
Smoking Status			
Nonsmoker	420		
Smoker	9		
Medication use			
Yes	84		
No	345		
HADS-D cutoff (≥ 8)			
Depressed	68		
Nondepressed	361		

Measures

Childhood adversity

The Childhood Trauma Questionnaire (CTQ) was administered to assess the frequency of childhood maltreatment, including abuse and neglect [69, 70]. The CTQ is a retrospective assessment comprised of 28 items, including five clinical scales that measure occurrence of ELAs (i.e., emotional abuse [EA], physical abuse [PA], sexual abuse [SA], emotional neglect [EN], and physical neglect [PN]), with an additional three item minimization-denial scale to detect underreporting of abuse [71]. Items are scored on a 5-point scale, ranging from 1 (*never true*) to 5 (*very often true*). Reliability and validity of the CTQ have been previously established [72–74]. For the current study, the five clinical scales were analyzed. The Cronbach's alpha for the scales exceeded .73, except for the physical neglect scale which yielded an α of .50.

Brief COPE

Participants completed the Brief Coping Orientation to Problems Experienced Scale [75], which is a 28-item self-report measure of coping responses to stressful life events. Items are scored on a 4-point scale ranging from 1 (I haven't been doing this at all) to 4 (I've been doing this a lot). The present study focused on examining the two-item behavioral disengagement subscale, which is a measure of general levels of behavioral disengagement and consists of "I have been giving up the attempt to cope" and "I have been giving up trying to cope with my problems" [75]. This subscale has been found to be a reliable measure for predicting health outcomes [76]. The Cronbach's alpha for the behavioral disengagement subscale was .72.

Depression measure

Depression was evaluated using the Hospital Anxiety and Depression Scale [77], which consists of 14 items, 7 that measure anxiety (HADS-A; e.g., "Worrying thoughts go through my mind") and 7 that measure depression (HADS-D; e.g., "I feel as if I am slowed down"). Items are scored on a 4-point scale, ranging from 0 to 3, with higher scores signifying greater symptoms of anxiety and depression. Data were analyzed as both continuous symptom scores and a binary variable using cutoff scores ≥ 8 to indicate possible cases of depression [77, 78]. The HADS has acceptable psychometric properties and good concurrent validity [78]. For the present study, the depression subscale was analyzed and yielded a Cronbach's α of .72, while the HADS-A anxiety subscale, analyzed as a covariate in the regression models, yielded an α of .81.

Psychological Ratings of Stress

A two-item questionnaire was administered directly before and after completing the stress task to assess task stressfulness and adjust for individual differences in perception of stress to the task [11]. Participants had to rate whether the task was demanding and stressful. Examples of these questions include, "How stressed do you feel about the upcoming task?", and "How stressed did you feel during the task?" Responses were rated on a 7-point Likert scale (1 = not at all to 7 = extremely).

Cardiovascular Measures

SBP and DBP were measured discontinuously by a research assistant using an automated blood pressure cuff (Carescape, V100, GE; produced in El Paso, TX), which is attached above the brachial artery of the nondominant hand. Automated sphygmomanometers are widely used in stress reactivity research [28, 79, 80], are recommended for clinical use in hospital care settings [81], and previously validated as an accurate measure of cardiovascular assessment [82]. Heart rate was continuously recorded using electrocardiogram (ECG), signals digitized at 500 Hz using BioLab, a MindWare acquisition and laboratory integration platform (MindWare Technologies LTD, Westerville, OH). Following automated R-peak detection, research staff visually inspected all individual HR traces for removal of artifacts using MindWare's HR/HRV analysis software, and then imported into Kubios HRV. During the session, a total of 8 readings were statistically recorded: four during the resting baseline period (2, 4, 6, and 8 min) and every minute during the stress task (0:30, 1:30, 2:30, and 3:30 min).

Procedure

Upon arrival to the laboratory, participants provided written consent. A blood pressure cuff was then attached to their nondominant hand and ECG electrodes were placed in a three-spot configuration. Participants were instructed to sit quietly for a 10-min acclimatization phase. A formal 10-min resting baseline period followed, during which time cardiovascular recording began. Participants then had to listen to a prerecorded audio of task instructions for the Paced Auditory Serial Addition Test [83]. A brief practice trial was then given to ensure participants understood the stress task instructions, which was followed by a 4-min stress task. Participants then engaged in a brief period of rest followed by an additional baseline period and acute psychological stress task (data not reported here). After this time, all physiological equipment was removed, and participants completed additional questionnaires (approximately

30–45 min). At the end of the laboratory session, participants were debriefed regarding the psychological stress task manipulations.

Stress task

Participants undertook a 4-min version of the paced auditory serial addition test (PASAT) to elicit acute psychological stress [83]. A series of single digit numbers from 1 to 9 were presented and participants had to add each consecutive number to the number they had just heard, rather than the number they had said out loud. Answers were given orally. The interval between numbers became progressively shorter each time, with a presentation rate of 2.4 for the first minute, followed by 2.0, 1.6, and 1.2 s until task completion. Elements of competition, social evaluation, and self-evaluation were included in the task [11]. Participants were informed they would lose five points for every incorrect answer or omission. All incorrect answers were recorded as an objective measure of task performance. In the context of blunted reactivity, this is proposed to be more reliable than self-report measures of engagement, given participants may be unaware of their attenuated task engagement [84]. Participants were also told they were being videotaped for assessment by “body language experts.” In reality, no such assessments were made. Finally, they were instructed to look at themselves in a mirror placed 0.5 m away for the duration of the task. The PASAT demonstrates good test-retest reliability [34, 85] and has been shown to successfully perturb the cardiovascular system [86–88].

Statistical Analyses

Data were screened prior to analyses to ensure a healthy sample of young adults. Given there were seven cluster variables, power considerations for cluster analyses identified our sample size was significantly powered to detect effects and was substantially greater than the recommended sample size of 10^m , where m represents the number of clustering variables [4, 89]. Descriptive statistics were computed for all study variables. Mean levels of SBP, DBP, and HR were computed across each phase to yield an average baseline and task measure for each cardiovascular parameter. Reactivity scores were determined by subtracting mean task from mean baseline values. Repeated measures (baseline, task) ANOVAs were conducted to confirm that the stress task successfully perturbed the cardiovascular system; partial eta squared (η_p^2) is reported as a measure of effect size. Correlational analyses were conducted to evaluate collinearity among study variables (ELA factors, behavioral disengagement, depression, and reactivity outcomes). Cluster analysis was carried out

using Ward’s method in IBM SPSS Statistics version 26.0. Lastly, hierarchical linear regressions were conducted to examine whether cluster membership was uniquely related to CVR profiles while controlling for covariates.

In line with previous research and to ensure the cluster analysis was not influenced by the scale of individual variables, raw scores for study variables were converted to standardized z -scores [4]. Prior to identification of clusters, raw data were examined for normality, which can considerably influence results [90]. Skewness (<2) and kurtosis (<3) indicated acceptable ranges of normality on all study variables [91], except for specific ELA variables (SA, PA, and PN). It is clear from Table 2, that the majority of participants did not experience these types of trauma. This is in line with previous reports of prevalence estimates for abuse and neglect, with both physical and sexual abuse and physical neglect, reportedly lower than that of other types of adversity [92–95].

No assumptions about the number of clusters were made prior to analysis. We employed a hierarchical cluster analysis to examine the standardized data and afford maximum flexibility in determining the appropriate number of clusters using Ward’s method. This begins with the same number of clusters as cases; with each step, cases are combined, forming one less cluster. The selection is based on which combination of clusters minimizes the within-cluster sum of squared Euclidean distances between individual scores and the mean of each variable in that cluster is calculated. The smaller the sum of squares, the greater the similarity between individuals in the cluster. At each step, the two clusters merged are those that minimize the increase in the total sum of squares across all variables in all clusters. Ward’s method determines which two clusters will produce the smallest increase in the total sum of squares when combined [4, 90]. To investigate the between cluster differences on general study parameters, chi-square (χ^2) and independent t tests were applied for continuous and categorical variables respectively, and cluster differences in reactivity were tested with one-way ANOVAs.

Table 2 Percentages of Trauma Not Experienced

Source of childhood adversity	Mean	SD	Cumulative % (for 5 = none)
EA	8.01	3.83	33.8
PA	6.45	2.48	50.8 [†]
SA	5.53	2.33	91.6 [†]
EN	8.54	4.20	33.6
PN	6.38	2.18	57.6 [†]

[†]ELA factors non-normally distributed.

Results

Descriptive Statistics

The descriptive statistics of study variables can be seen in Table 3. The scores for the CVR and depression variables are greater than those previously reported elsewhere [29]. In line with recent research, behavioral disengagement was related to higher symptoms of depression [11], while ELA factors had similar ranges to those seen in other studies [51].

Manipulation Check

Results from a series of repeated measures (baseline, task) ANOVAs confirmed an increase in baseline to task on each cardiovascular measure for; SBP, $F(1,427) = 1,512.07, p < .001, \eta_p^2 = .78$, DBP, $F(1,427) = 2,058.23, p < .001, \eta_p^2 = .83$; and HR, $F(1,424) = 463.77, p < .001, \eta_p^2 = .52$, demonstrating the task was physiologically stressful. Furthermore, repeated measures revealed a significant increase from pre- to post-task ratings of self-reported stress, $F(1, 422) = 537.25, p < .001, \eta_p^2 = .56$, indicating that the task was psychologically stressful. Objective stress task performance was not related to CVR or depression in the present study (all $ps > .05$). In line with previous research, there were significant sex differences in depression, $t(427) = 2.38, p = .018$, with females ($M = 4.64, SD = 3.16$) reporting higher depressive symptomology compared with males ($M = 3.92, SD = 2.80$). There were no significant differences in CVR due to smoking status or oral contraceptives (all $ps > .05$). However, there were significant differences in reactivity due to sex for DBP, $t(426) = 3.07, p < .01$; females exhibited lower DBP reactivity ($M = 12.79, SD = 5.99$) compared with males ($M = 14.66, SD = 6.25$), and for HR, $t(423) = 2.11, p = .036$; females exhibited higher HR reactivity ($M = 12.20, SD = 11.04$) compared with males ($M = 9.91, SD = 10.46$). Additionally, there were significant differences in reactivity due to medication use, for DBP, $t(426) = -2.32, p = .021$, with those taking medication ($n = 84$) having lower DBP reactivity ($M = 12.08, SD = 5.74$) compared with those not taking medication ($M = 13.81, SD = 6.20$).

Collinearity Check

As can be seen in Table 3, there are acceptable levels of collinearity among the study variables to warrant cluster analysis, with the maximum correlation coefficient being less than .90 [89].

Cluster Analysis

Two distinct clusters arose based on the criterion necessary for the selection of the appropriate number of

Table 3 Descriptive Statistics and Correlational Analysis for Study Variables

	Mean (SD)	Range	Cronbach's alpha	HADS-D subscale	CTQ-EA	CTQ-PA	CTQ-SA	CTQ-EN	CTQ-PN	Behavioral disengagement	SBP	DBP	HR
1. HADS-D subscale	4.38(3.05)	0 to 18	.72	—	.321**	.232**	.178**	.342**	.221**	.367**	-.065	-.115*	-.098*
2. CTQ-EA	8.01(3.83)	5 to 24	.86	—	.594**	—	.218**	.654**	.380**	.181**	-.095*	-.069	-.128**
3. CTQ-PA	6.45(2.48)	5 to 20	.73	—	—	—	.281**	.422**	.353**	.147**	-.068	-.039	-.149**
4. CTQ-SA	5.53(2.33)	5 to 25	.92	—	—	—	—	.143**	.210**	.094	-.050	-.121**	-.070
5. CTQ-EN	8.54(4.20)	5 to 23	.90	—	—	—	—	—	.549**	.238**	-.061	-.098*	-.099*
6. CTQ PN	6.38(2.18)	5 to 17	.50	—	—	—	—	—	—	.239**	-.073	-.116*	-.143**
7. Behav. Disengagement	3.12(1.45)	1 to 8	.72	—	—	—	—	—	—	—	-.072	-.109*	-.108*
8. SBP reactivity (mmHg)	17.13(9.11)	-4.55 to 51.50	—	—	—	—	—	—	—	—	—	.612**	.624**
9. DBP reactivity (mmHg)	13.47(6.14)	-4.30 to 33.00	—	—	—	—	—	—	—	—	—	—	.374**
10. HR reactivity (bpm)	11.36(10.88)	-11.11 to 71.64	—	—	—	—	—	—	—	—	—	—	—

The sample size was $N = 429$ on all measures of adversity, the HADS-D and behavioral disengagement, and $N = 428$ on both systolic and diastolic blood pressure, and $N = 427$ on heart rate.

* $p < .05$ level; ** $p < .01$ level.

clusters. Results from one-way ANOVAs showed the two clusters differed significantly from one another on all measures of reactivity (all $ps < .01$). As can be seen in [Table 4](#), a clear behavioral pattern emerged for reactivity profiles. In Cluster 1 ($n = 61$; 14.2%), those with greater exposure for all ELA factors, were higher on behavioral disengagement and depression. The reactivity profile for this cluster was blunted in comparison to that of Cluster 2, that is, lower than the sample average (refer to [Figure 1](#)). Respondents in Cluster 2 ($n = 368$; 85.8%) were characterized as having lower scores on ELA, behavioral disengagement, and depression, along with a relatively higher reactivity profile on all cardiovascular parameters in comparison to Cluster 1. Furthermore, Cluster 2 was characterized by reactivity values closely in line with the sample averages. The mean and standard errors are provided for study variables on each cluster (please refer to [Table 4](#)).

Analysis of general study parameters revealed significant differences between the clusters for depression and anxiety using the HADS recommended cutoffs (≥ 8) and

Table 4 Means and Standard Errors of Study Variables Across Both Clusters

	Cluster 1 ($n = 61$)		Cluster 2 ($n = 368$)	
	Mean	SE	Mean	SE
EA	15.05	0.51	6.84	0.12
PA	10.29	0.54	5.82	0.06
SA	8.16	0.70	5.10	0.03
EN	14.15	0.55	7.62	0.18
PN	8.46	0.40	6.04	0.09
Behavioral disengagement	3.39	0.19	3.07	0.07
Depression	6.28	0.44	4.06	0.15
SBP reactivity (mmHg)	14.94	1.01	17.50	0.48
DBP reactivity (mmHg)	11.89	0.77	13.73	0.32
HR reactivity (bpm)	7.49	1.14	12.01	0.58

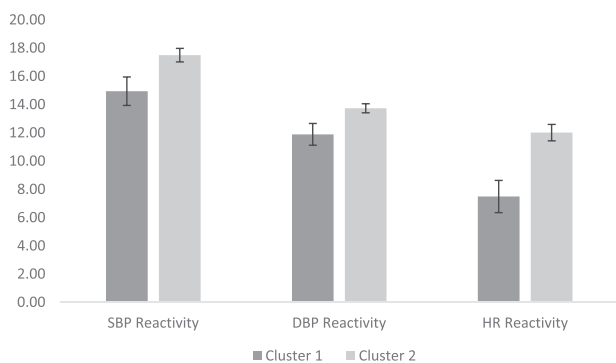


Figure 1. Means and standard errors of systolic blood pressure reactivity, diastolic blood pressure reactivity and heart rate reactivity based on cluster membership.

Table 5 General Study Parameters of Cluster 1 and Cluster 2

	Cluster 1 ($n = 61$)	Cluster 2 ($n = 368$)
Race (% White)	54.1	67.9
Sex (% Female)	73.8	62.0
HADS-D ($\% \geq 8$)	36.1*	12.5
HADS-A ($\% \geq 8$)	49.2*	27.2
Objective Task Performance	275.83 (95.23)*	334.92 (98.99)
Medication (% taking medication)	24.6	18.8
Smoking (% smokers)	3.3	1.9
BMI (kg/m^2)	24.81 (4.29)	23.83 (4.76)
Age	19.45 (0.94)	19.45 (1.09)
Baseline SBP (mmHg)	115.49 (9.22)	115.51 (9.98)
Baseline DBP (mmHg)	67.32 (5.63)	67.33 (6.55)
Baseline HR (bpm)	76.74 (10.34)	77.26 (11.39)

Values are reported as means and standard deviations, except for the explicitly stated percentages.

*Significantly different from Cluster 2.

objective task performance. Given the literature on depression, motivation, and blunted reactivity, it is not surprising that Cluster 1, characteristic of higher depressive symptoms, less engagement on the task and a blunted reactivity profile, significantly differed from Cluster 2 in this regard. There were no significant differences in baseline measures, sex, medication use, race, BMI, age, or smoking at the time of stress testing (refer to [Table 5](#)).

Linear Regression

To examine whether cluster membership was associated with CVR to stress, simple linear regressions were calculated. Prior to analyses, a binary variable was created for cluster membership (1 = Cluster 1 and 0 = Cluster 2) to assign numerical value to this categorical variable. Significant effects were found for SBP, $F(1,426) = 4.14$, $p = .042$, $r^2 = .010$, DBP, $F(1,426) = 4.78$, $p = .029$, $r^2 = .011$, and HR reactivity, $F(1,423) = 9.21$, $p = .003$, $r^2 = .021$. Cluster 1 membership was significantly associated with lower CVR to stress.

Hierarchical linear regressions followed to adjust for the potential covariates, anxiety, and objective task performance, which were entered as covariates in step 1, with our predictor variable (Cluster 1) in step 2. The Enter method was used in the two blocks. For SBP reactivity, anxiety was the significant predictor in the first block, $F(2,418) = 3.45$, $p = .033$, adjusted $r^2 = .012$; the addition of the cluster predictor did not lead to a significant change in the model ($p = .094$). A similar pattern emerged for DBP reactivity ($p = .105$). However, the opposite pattern emerged for HR reactivity, $F(2,415) = 0.86$, $p = .425$

for step 1 of the model, and $F(3,414) = 3.06$, $p = .028$, adjusted $r^2 = .015$ for step 2. Cluster 1 was significantly associated with HR reactivity to stress (refer to Table 6).

Discussion

The aim of the current study was to investigate whether there were distinct clusters characterized by a history of ELA and behavior and whether these clusters were uniquely associated with cardiovascular stress reactivity. Using multivariate cluster analysis, two distinct behavioral clusters were identified with statistically different SBP, DBP, and HR stress reactivity profiles. The cluster characterized by the largest ELA, behavioral disengagement, and depression reports had statistically lower stress responses for all cardiovascular parameters. This warrants attention given previous reports of independent associations between these behavioral factors and blunted reactivity. Moreover, our findings support the premise that ELA can disrupt the normative development of self-regulatory processes and place a strain on stress sensitive systems resulting in maladaptive responses to stress [10, 45, 58].

The current study is the first to examine how a combination of these factors, rather than studying each factor in isolation, relate to cardiovascular stress reactivity. Therefore, our findings not only provide confirmatory support for previous research reporting associations between these behaviors and lower reactivity, but also adds extensively to our understanding of how these factors cluster together in a way characteristic of a blunted heart rate reactivity profile. Identification of a behavioral cluster with distinct patterns of blunted reactivity is novel. Future research should aim to not only replicate these findings but given the negative outcomes related to exaggerated reactivity, identify a behavioral cluster characteristic of this reactivity profile.

The main findings from the present study is that a behavioral cluster emerged characteristic of a blunted heart rate reactivity profile. Upon further analyses, in unadjusted models, this behavioral cluster was associated with CVR to acute stress (i.e., SBP, DBP, and HR). In adjusted models, cluster membership was related to HR reactivity only. Results indicate that those in Cluster 1 compared with Cluster 2, had greater exposure to ELA, were more reliant on maladaptive coping, (i.e., behavioral disengagement), reported higher symptoms of

Table 6 First Block (Control), Second Block (Predictors) Hierarchical Multiple Regression of Clusters and CVR

	Model	Standardized coefficient beta	<i>t</i>	<i>p</i>
SBP reactivity (mmHg)	1 (Constant)		11.26	.000
	PASAT	0.006	0.115	.909
	HADS-A	-0.128	-2.63	.009
	2 (Constant)		11.39	.000
	PASAT	-0.012	-0.246	.806
	HADS-A	-0.114	-2.32	.021
DBP reactivity (mmHg)	Cluster 1	-0.084	-1.68	.094
	1 (Constant)		12.67	.000
	PASAT	0.025	0.516	.606
	HADS-A	-0.133	-2.74	.006
	2 (Constant)		12.76	.000
	PASAT	0.008	0.157	.875
HR reactivity (bpm)	HADS_A	-0.120	-2.44	.015
	Cluster 1	-0.081	-1.62	.105
	1 (Constant)		5.56	.000
	PASAT	0.032	0.660	.510
	HADS-A	-0.056	-1.15	.250
	2 (Constant)		6.04	.000
HR reactivity (bpm)	PASAT	0.004	0.075	.940
	HADS-A	-0.034	-0.687	.492
	Cluster 1	-0.137	-2.73	.007

Criterion variable: Cardiovascular reactivity (SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate).

Covariates: PASAT as measure of objective task performance and anxiety as measured by the HADS-A.

Predictor variable: Cluster 1 membership.

depression and exhibited lower HR reactivity to acute psychological stress. This may reflect low beta-adrenergic receptor responsiveness, which is indexed by blunted HR reactivity and evident in those with depression [14]. The findings support the proposition that lower HR responses are a byproduct of absent/reduced motivation to engage [84], given that Cluster 1 was related to lower HR reactivity and was characterized by reduced levels of behavioral engagement and lower task performance. Additionally, blunted HR reactivity is considered a hallmark for depression [49], is related to increased exposure to ELA [45, 47], lower psychological task engagement [96], and higher levels of behavioral disengagement [11].

The study also supports a growing body of literature suggesting blunted reactivity may be a peripheral marker of central dysregulation in the fronto-limbic brain regions vital for goal-directed behavior and autonomic control, such as the anterior cingulate gyrus, nucleus accumbens, and medial prefrontal cortex [10]. Not only does repeated exposure to ELA have a long-lasting impact on these brain systems, but both depression [10, 30, 97] and behavioral disengagement [11, 84] are characteristic of motivational deficits. Given that many of the adverse health and behavioral outcomes related to blunted reactivity require treatment programs which require effort, perseverance, and engagement, this impaired motivation could potentially impact treatment success [11]. Furthermore, it may offer an explanation as to how both distal and proximal factors together relate to blunted reactivity. Both biological and behavioral responses to stress are formed in early childhood [98, 99], with maladaptive coping efforts (e.g., behavioral disengagement) providing relief from distress in the short term [39]. In the long-term however, these coping styles have negative psychological consequences, e.g., depression [39]. Therefore, those exposed to adverse events in childhood rely on maladaptive coping efforts. Over time this increases susceptibility to psychological problems in adulthood that result in lower cardiovascular responses to acute stress.

Considering the particular determinants of blunted reactivity are still relatively unknown, the present findings have important practical, methodological, and theoretical implications. A practical component to this study is the value of cluster analysis in health care settings. Cluster analytical models have much to offer, particularly in the clinical field, given that no attempt is made a priori to identify the number of clusters. It helps identify subgroups within a patient population based on identifiable characteristics; and has been shown to have clinical utility in identifying asthma phenotypes [100]. This classification of distinct groups who deviate from adaptive stress responses (e.g., blunted reactivity) could potentially aid practitioners in identifying vulnerable subgroups based on behavioral factors. Whittaker et al.

[12]. suggest that while the use of CVR research as a clinical biomarker is premature, it can however elucidate as to whom may benefit from additional supports. Given the predictive utility of blunted reactivity at determining behavioral outcomes at follow-up (e.g., depression), and goal directed behaviors in clinical populations [17–19], identifying distinct behavioral profiles characteristic of lower reactivity to stress, could prove useful for tailored and targeted interventions for those most at risk [101]. Methodologically, cluster analysis is a well-established approach for identifying how different groups are similar on a set of factors compared with other groups [101] and can also establish sources of heterogeneity within samples [102]. Given the heterogeneity of patient characteristics, illness severity and response to treatment that exists in clinical populations, cluster analysis is proposed to be an effective method for understanding these differences [64]. In the present study, this analysis revealed that the influence of ELA on coping with challenges, increased psychological distress and shaped physiological sensitivity and is perhaps one step closer to integrating clinical and biological parameters [44]. Theoretically, given previous empirical observations of independent associations between the behavioral factors employed in this study and blunted CVR, the behavioral cluster that emerged extensively adds to our current understanding about how more negative behaviors cluster together and uniquely relate to lower cardiovascular responses to stress.

This study is not without limitations. Due to the cross-sectional nature of the study design, causality cannot be inferred. Second, given the use of continuous symptom scores and no information gathered on the clinical status of depression, it is not possible to signify pathology [29]. Third, although the study used a relatively homogeneous sample of undergraduate students, the sample was predominantly female (63.6%) and white, with a racial diversity observed (non-whites; 34.0%). Furthermore, 18.4% of participants reported their ethnicity as Hispanic. Significant racial differences exist in the development of CVD [103, 104] and ELA [105], and given that CVR is a pathway to CVD, future research should aim recruit a more diverse sample to examine differences in physiological responses to stress. Fourth, given the sensitivity of the questions and the length of time between event occurrence and reporting, retrospective recollection of childhood events is subject to issues of underreporting and recall bias (see 106–109) and lacks the capacity to capture effects of stress during critical developmental epochs [110]. However, there is evidence supporting the stability of retrospective assessment, with the CTQ shown to have good test-retest reliability [111]. Fifth, although recovery blood pressure is an important index of CVD, the present study did not examine this as an outcome. While the main focus

was on CVR to acute stress, this should not prevent future research from examining the effects of the recovery period. Lastly, exposure to stress activates the cardiovascular system [37] and when it exceeds a person's ability to cope, avoidant coping strategies are employed [112]. This can result in psychobiological processes that facilitate the progression of psychological distress and psychosis [113, 114]. Given that this study takes somewhat of a dichotomous view of one particular coping style (i.e., lower/higher levels of behavioral disengagement), future research may benefit from examining how people who use several types of coping strategies simultaneously, deal with adverse events and stressors [101, 112]. Some strengths of the study include the application of multivariate cluster analysis and given the study consists of a relatively large sample of young healthy adults who are free from illness, the external validity of the results are supported.

While the current study has attempted to address, in part, the complex relationship between behavioral factors and blunted reactivity, future research should aim to elucidate if these behavioral clusters are characteristic of stress reactivity in a younger sample. ELA reportedly accelerates development (e.g., behavioral, biological, psychological, and social) in adolescence [115]. Those who employ avoidant coping strategies (e.g., behavioral disengagement) report higher levels of depression [116, 117], which can predict recurrence and duration in adulthood [118]. Investigating behavioral clusters in an adolescent sample, may help identify areas where intervention may be best suited. Alternatively, given that a behavioral cluster in the current study was uniquely associated with lower cardiovascular responses and prospective studies report blunted reactivity predicts poorer behavioral outcomes at follow-up, future research could examine these biological and behavioral factors together, to determine clinical significance for future disease outcomes. The adoption of a more integrated approach that includes clinimetric evaluation with biological markers may prove fruitful.

To conclude, a behavioral cluster composed of higher levels of ELA, behavioral disengagement, and depression emerged. This cluster was characteristic of a blunted heart rate reactivity profile, even after controlling for anxiety. Given the aforementioned negative health and behavioral outcomes related to blunted reactivity, it is clear that deviations from adaptive stress responses, signify a vulnerability to disease. The study extends a growing body of research reporting independent associations between these behavioral factors and lower reactivity, to suggest that together these negative behaviors form a cluster predictive of a blunted reactivity profile.

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Compliance With Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards Keogh, Howard, Gallagher and Ginty declare they have no conflict of interest.

Ethical Approval All procedures were in accordance with the ethical standards of the institutional review board and the 1964 Helsinki declaration and its later amendments.

Informed Consent Informed consent was obtained from all participants included in the study.

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