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ARTICLE

Behavioural clusters characteristic of cardiovascular reactivity profiles relate to poorer health outcomes

Tracey M. Keogh[1,2] | **Siobhán Howard**[1,2] | **Stephen Gallagher**[1,2]

[1]Department of Psychology, Centre for Social Issues Research, Study of Anxiety, Stress and Health Laboratory, University of Limerick, Limerick, Ireland

[2]Health Research Institute, University of Limerick, Limerick, Ireland

Correspondence

Tracey M. Keogh, Department of Psychology, University of Limerick, Castletroy, Limerick, Ireland.
Email: tracey.keogh@ul.ie

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Abstract

Objectives: Blunted cardiovascular reactivity is associated with a distinct behavioural profile of greater exposure to early life adversity, coupled with higher levels of behavioural disengagement and symptoms of depression. The present study sought to extend on this work by investigating if behavioural clusters with distinct patterns of reactivity were related to health and behavioural outcomes at baseline and at a 4-year follow-up.

Methods: Hierarchical cluster analyses were conducted using longitudinal data drawn from the Midlife Development in the United States (MIDUS 2) Biomarker Project and the MIDUS 3 follow-up 4 years later. During MIDUS, 2 participants (N = 513) underwent a standardized stress testing protocol and had their blood pressure and heart rate monitored throughout. In addition, hierarchical cluster analyses were conducted on responses from measures of early life adversity, behavioural disengagement and depression. Binary logistic regressions were conducted to determine whether cluster membership was related to health and behavioural outcomes which were taken at both time points.

Results: Three behavioural clusters emerged with statistically different blood pressure reactivity patterns. The cluster characterized by greater exposure to early life adversity, higher levels of behavioural disengagement and depressive symptoms, had relatively lower blood pressure reactivity patterns compared with both the exaggerated reactivity cluster and the cluster similar to the sample mean. In fully adjusted models, this cluster was associated with hypertension (p = .050) and depressed affect (p = .033), while Cluster 1 characteristic of an exaggerated blood pressure reactivity profile was associated with depressed affect (p < .001). Cluster membership did not significantly predict future health status.

Conclusion: This study extends research on behavioural clusters characteristic of reactivity profiles to demonstrate how they relate to health and behavioural outcomes during MIDUS 2.

KEYWORDS
behavioural cluster, cardiovascular reactivity, cluster analyses, depressed affect, hypertension

Statement of contribution

What is already known on this subject?

- Early life adversity, behavioural disengagement and depression are independently associated with cardiovascular reactivity (CVR) to acute psychological stress.
- These same factors are indicative of poorer health outcomes.
- A previous study applied multivariate cluster analysis and revealed that trauma history and behavioural factors clustered together and uniquely related to blunted cardiovascular responses to stress.

What this study adds?

- This study presented the opportunity to replicate findings from the previous study reporting on a behavioural cluster characteristic of a blunted CVR profile.
- This is the first study to observe a behavioural cluster characteristic of an exaggerated reactivity profile.
- This study examined cross-sectional and prospective associations between behavioural clusters characteristic of CVR profiles and health and behavioural outcomes at the time of testing and on follow-up 4 years later.

INTRODUCTION

The cardiovascular reactivity (CVR) hypothesis postulates that metabolically maladaptive stress responses over time signify poorer health outcomes (Lovallo, 2005; O'Súilleabháin et al., 2018; Phillips et al., 2013). The magnitude of the individual stress response considered to be relatively stable (Manuck, 1994; Matthews et al., 2001), contributes to the development of cardiovascular disease (CVD; Obrist, 1981). Evidence suggests that exaggerated stress responses signify a vulnerability to CVDs; including atherosclerosis (Kamarck et al., 1997; Treiber et al., 2003) and increased left ventricular mass (Allen et al., 1997). One systematic review found exaggerated reactivity was associated with a greater risk and earlier onset of hypertension (Turner et al., 2020). Epidemiological evidence suggests exaggerated reactivity is related to higher resting blood pressure at follow-up and predicts hypertension (Brindle et al., 2016; Carroll et al., 2011; Matthews et al., 2004). However, more recent research indicates that blunted reactivity is also indicative of adverse outcomes (Carroll et al., 2008; Ginty et al., 2011; Phillips, Der, et al., 2011; Phillips, Hunt, et al., 2011).

Blunted responders are those comparatively lower to others in the sample (Whittaker et al., 2021) and low-stress responses are as problematic for health maintenance as exaggerated responses (Larkin et al., 2020; Phillips, 2011). Blunted reactivity is associated with a range of negative outcomes such as hospitalizations (Sherwood et al., 2017), impaired immunity (Carroll et al., 2009) and mortality (Kupper et al., 2015). Many behavioural factors, such as addiction (Lovallo, 2007) and behavioural disengagement (Ginty et al., 2020) act as indirect mechanisms which accentuate the effect of blunted reactivity on the

development of CVDs (Carroll et al., 2017; Whittaker et al., 2021). However, one factor that has received a lot of attention in this regard is depression (Brindle et al., 2013; Keogh et al., 2021; Phillips, Hunt, et al., 2011; Turner et al., 2020).

Prospective and cross-sectional evidence suggest depression predicts hypertension (Jonas & Lando, 2000), stroke (Gump et al., 2005), poorer cardiac prognosis (Lichtman et al., 2008) and increases the risk of CVD mortality (Brindle et al., 2013; Wulsin et al., 1999). Additionally, depression is associated with blunted responses to stress (Brindle et al., 2013; Phillips et al., 2013; York et al., 2007). Blunted reactivity is not only a proposed marker of motivational dysregulation (Phillips, 2011) but also considered a hallmark of depression (Schiweck et al., 2019) and prospectively related to depressive symptoms 5 years later (Phillips, Hunt, et al., 2011).

Motivational factors are proposed to underlie the depression–CVR relationship (Carroll et al., 2017). Given that depression is characterized by reduced levels of motivated behaviour (Franzen & Brinkmann, 2015), such as low perseverance (Chauntry et al., 2019; Van Doren et al., 2019) and response to reward (Brinkmann et al., 2014; Franzen & Brinkmann, 2016), this suggested mechanism is not that surprising. Moreover, a recent study found blunted responses were less pronounced in those with depression when accounting for motivation (Keogh et al., 2020), with a fMRI study showing that blunted responders displayed attenuated activity in brain regions involved in motivated behaviour when presented with a task (Ginty et al., 2013). This altered stressor-evoked activation is proposed to be a biological mechanism underlying blunted stress responses (al'Absi et al., 2021; Carroll et al., 2017; Ginty et al., 2017).

This motivational dysregulation may stem from exposure to early life adversity (ELA; Carroll et al., 2017), which can place a strain on stress sensitive systems and disrupt the normative development of biological, mental and behavioural regulatory processes (Suglia et al., 2018). These mechanisms may interact and impact other cardiometabolic factors (e.g., blood pressure) and become incorporated into long-term physiological processes that affect cardiac morbidity and mortality (al'Absi et al., 2021; Bucci et al., 2016; Ginty et al., 2017; Johnson et al., 2019; Suglia et al., 2018). ELA is associated with high blood pressure and increased risk of hypertension (Suglia et al., 2018). In addition, ELA can result in greater reliance on avoidant coping strategies (e.g., behavioural disengagement), which are reported more frequently in hypertensive patients (Palagini et al., 2016) and predict depression in clinical and non-clinical samples (Chen & Qu, 2021; Dempsey et al., 2000; Hagan et al., 2017; Seiffge-Krenke & Klessinger, 2000). One study found the psychological impact of ELA, resulted in higher symptoms of depression, which had a knock-on impact on cardiovascular responses to stress (Keogh et al., 2022). While the independent associations between the aforementioned ELA and behavioural factors and blunted CVR are well documented (Brindle et al., 2013; Ginty et al., 2020; Keogh et al., 2021; Phillips, Hunt, et al., 2011; Voellmin et al., 2015), recent research extends on this work through the use of cluster analysis (Keogh et al., 2022). This method is a useful data reduction tool and may advance diagnostic criteria through classifying subgroups with identifiable characteristics in patient populations (Haldar et al., 2008; Leonard & Droege, 2008; Romesburg, 1984). In that study, cluster analysis identified a behavioural cluster that consisted of greater exposure to ELA, higher levels of behavioural disengagement coupled with higher symptoms of depression that was characteristic of a blunted heart rate (HR) reactivity profile (Keogh et al., 2022). Despite this, the long-term impact of this behavioural profile on future health is yet to be examined and that study did not identify a cluster characteristic of an exaggerated reactivity profile.

The mechanistic association between behavioural clusters and CVR profiles is relatively under studied. Given the health and behavioural corollaries related to both exaggerated and blunted reactivity at follow-up [i.e., hypertension and depression (Carroll et al., 2011, Phillips, Hunt, et al., 2011)], the purpose of the current study is to extend on previous work to broaden the scope of our understanding. Specifically, this study aims to (1) determine whether behavioural clusters (i.e., ELA, behavioural disengagement and depressive symptoms) characteristic of both exaggerated and blunted CVR profiles emerge and (2) establish whether these behavioural clusters, independent of patterns of CVR, related to poorer health and behavioural outcomes (i.e., depressed affect and hypertension) at baseline and at a 4-year follow-up. Cluster analysis presents the opportunity to replicate findings from a previous study in a young healthy sample (Keogh et al., 2022), by examining this in middle-aged adults. It was hypothesized that greater exposure to ELA,

coupled with higher levels of behavioural disengagement and depressive symptoms, would be characteristic of a blunted reactivity profile. Prospective studies report on the relations between these CVR profiles and adverse health and behavioural outcomes (Brindle et al., 2016; Carroll et al., 2008; Phillips, Der, et al., 2011), yet this study is the first to examine how behavioural clusters characteristic of distinct patterns of reactivity relate to depressed affect and hypertension at two different time points (baseline and 4 years later).

MATERIALS AND METHODS

Participants

Data were drawn from the MIDUS 2 (including the Biomarker project) and MIDUS 3 datasets which were linked using the M2ID variable. Only those who went on to complete the biomarker project (n = 1155) were included (Ryff, Almeida, et al., 2019; Ryff, Seeman, & Weinstein, 2019) and this served as a baseline measure for all study variables. The Biomarker Project consisted of 970 participants from the longitudinal survey sample and 185 from the Milwaukee sample. At the time of the clinic visit, participants ranged in age from 35 to 86 years (M = 57.12, SD = 11.51), with a mean body mass index (BMI) of 29.67 kg/m^2 (SD = 6.53). The sample was predominantly female (n = 651; 56.4%) and white (n = 865; 74.9%) with a racial diversity observed (non-whites; 19.9%). Taking prescription medication was in effect normative for this sample, with over two thirds (n = 838; 72.6%) reporting taking some form of prescription medication. These participants were included and controlled for as a covariate in the regression models. Follow-up analyses were conducted using MIDUS 3, which contains behavioural, psychological, health and social factors. Informed consent was obtained prior to beginning study procedures. Based on power considerations for cluster analyses with a recommended sample size of 10^m, with m representing the number of cluster variables, the present study with its seven cluster variables is significantly powered to detect effects (Mooi & Sarstedt, 2011).

Procedure

Of the original MIDUS sample, 4963 adults completed the MIDUS 2 survey data collection, which involved a 30-min telephone interview followed by two self-administered questionnaire booklets. Those who lived in the United States and were not part of the city oversamples were then invited to participate in the Biomarker Project. Participants underwent a 2-day overnight stay at a clinical research centre that involved a comprehensive biological assessment while completing a standardized laboratory-based stress task. Indicators of beat-to-beat blood pressure and HR were measured. A complete medical history was gathered to enhance self-reported data previously collected in Project 1. The MIDUS 3 initiative returned in 2013 with similar comprehensive assessments as those gathered during MIDUS 2 being administered. A flowchart of timelines of data collection and measurements taken can be found in Figure 1. MIDUS data collection is reviewed and approved by the Education and Social/Behavioural Sciences and the Health Sciences IRBs at the University of Wisconsin-Madison.

Measures

Depression measure

Depression was evaluated using the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). The scale consists of 20 items pooled from previously validated scales to measure current depressive symptoms, for example 'my sleep is restless' (Radloff, 1977). Using a four-point scale (0 = rarely or none of the time to 3 = most or all of the time), participants report the occurrence of symptoms in the preceding week, with higher scores signifying higher symptoms of depression. The CES-D has accept-

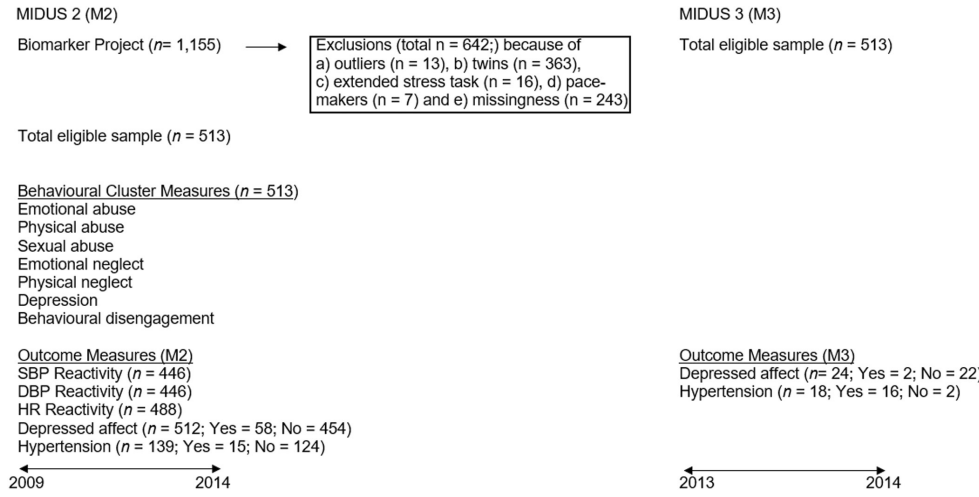

FIGURE 1 Flowchart of timelines, participants and measures used in MIDUS 2 and MIDUS 3

able psychometric properties, excellent concurrent validity and is sensitive to discerning between general and psychiatric populations (Brindle et al., 2013; Radloff, 1977). The total scores range from 0 to 60 and scores greater than 16 are used as an indicator of clinical significance (Radloff, 1977). In the current study, the total CES-D scale yielded Cronbach's alpha of .67.

ELA measure

The Childhood Trauma Questionnaire (CTQ) is a self-report retrospective assessment used to evaluate experiences of childhood abuse and neglect (Bernstein et al., 1994; Lambert et al., 2019). It is comprised of 28 items, consisting of five clinical scales measuring the frequency of childhood adversities [i.e., emotional abuse (EA), physical abuse (PA), sexual abuse (SA), emotional neglect (EN) and physical neglect (PN)], with a further three item minimization-denial scale to identify underreporting of abuse (Bernstein et al., 2003). The occurrence of these experiences is scored on a 5-point scale, (1 = never true to 5 = very often true). The CTQ has excellent reliability and validity (Bernstein et al., 1994, 1997; Carballedo et al., 2012; Fink et al., 1995). For this study, the five clinical scales were analysed and Cronbach's alpha for the each of the five scales exceeded .70.

Behavioural disengagement measure

Coping responses to stressful events were assessed using the 28-item Brief Coping Orientation to Problems Experienced Scale (Carver, 1997). Participants answer questions on a 4-point scale (1 = a lot to 4 = not at all). The current study examined the behavioural disengagement subscale, which is found to be a reliable measure for predicting health outcomes (Bose et al., 2015). This subscale consists of 4-items (e.g., 'I have been giving up the attempt to cope'). Cronbach's alpha for the behavioural disengagement subscale (.73) was similar to previous reports (Ginty et al., 2020; Keogh et al., 2022).

Health and behavioural outcomes

Depressed affect and hypertension were measured in MIDUS 2 and MIDUS 3 and assessed as primary dependent measures. Participants indicated if they were taking medication for high blood pressure which

was used as a proxy for hypertension status. Responses were derived as yes/no at the time of testing and at follow-up. A short seven-item questionnaire was used to assess depressed affect based on yes/no responses to having experienced depressed affect (i.e., feelings of being sad, blue or depressed) during a 2-week period in the previous 12 months. Some examples of questions include, did you 'think a lot about death?' and 'lose interest in most things?'

Cardiovascular measurement

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were assessed with a Finometer (Finapres Medical Systems), which derives from the volume-clamp method (Penaz, 1973). Using a finger cuff to evaluate continuous blood pressure, any increases in arterial pressure cause the cuff to adjust and reflect alterations in blood pressure. An electrocardiogram (ECG) recorded HR, with beat-to-beat signals digitized at 500 Hz and collected in a microcomputer. ECG waveforms were submitted to detection software to identify R waves and MIDUS research staff then visually inspected all ECG waveforms to revise software errors in identifying normal R waves. The subsequent series of normal R intervals were used to establish HR and were converted to beats per minute (Ryff et al., 2011).

Stress task

Participants attended a clinical research centre for a 2-day overnight stay. On Day 2 participants completed a 90-min standardized stress testing protocol. Given that details for the session have been described in detail elsewhere (Coyle et al., 2020; Ryff et al., 2011), we can be reasonably brief. Upon arrival to the laboratory, cardiovascular equipment was calibrated and to ensure task instructions were understood, participants completed practice trials for the stress task. After this, a formal 11-min resting baseline period began, which was then followed by the first of two 6-min cognitive stress tasks. A 6-min recovery period followed, after which the second cognitive task began. Cardiovascular variables were averaged across the two stress tasks (Stroop and MATH), as previously reported elsewhere (Coyle et al., 2020; Keogh et al., 2021).

The cognitive stress tasks consisted of the Stroop colour/word task and the Morgan and Turner Hewitt (MATH; Turner et al., 1986) mental arithmetic task. These tasks were presented in random order and each lasted 6 min. No evaluative component was included. For the Stroop task, one of four colour name words were shown in either a congruent or incongruent font to the name on the screen (e.g., the word blue was written in blue font versus the word blue was written in red font). Participants had to use one of four keys on a keypad that related to the colour of the letters but not the colour name. As rate of presentation was based on task performance, greater accuracy led to increased presentation rates.

For the MATH task, a number of addition and subtraction problems were presented on screen for 2.0 s, followed by the word equals for 1.5 s, with the answer then being displayed for 1.0 s. Participants had to press one of two keys (equivalent to yes or no) to signify whether the solution presented to the problem was correct. Problem difficulty varied across five levels, ranging from level 1 (*1-digit ± 1-digit numbers*) to level 5 (*3-digit ± 3-digit numbers*), with correct responses leading to an increase in difficulty level. The total number of problems presented are determined by response accuracy to each trial.

Statistical analyses

Data were screened for outliers and assumptions of fit. Outliers deviating ±3 SDs from the mean on CVR values were excluded ($n = 13$). Furthermore, as a consideration of the assumption of independence in analyses, a decision was made a priori to exclude the total number of twins in the sample ($n = 363$). Additional exclusions include those who completed an extended version of the stress task ($n = 16$; Ryff et al., 2011), those with pacemakers ($n = 7$) and missingness on study variables ($n = 243$). This left a total of 513 participants and demographic information for the sample can be found in Table 1.

Mean levels of SBP, DBP and HR were computed across each phase to yield an average for baseline, task and recovery. Reactivity scores were calculated by the difference between task and baseline values. Repeated measures (baseline, task) ANOVAs were conducted to establish whether the stress task successfully elicited a stress response; partial eta squared (η_p^2) is reported as a measure of effect size. Correlational analyses evaluated associations between ELA, behavioural disengagement, depressive symptoms and reactivity outcomes. The raw scores for ELA, behavioural disengagement and depressive symptoms from the CES-D were converted to standardized z-scores and hierarchical cluster analysis using Ward's method was conducted in IBM SPSS Statistics version 26.0.

Ward's method begins with the same number of clusters as cases; and with each additional step the cases combine and form one less cluster. This selection is based on the within-cluster sum of squared Euclidean distances calculation between the mean of each variable and individual scores. The smaller the sum of squares represents the greater the similarity between individuals in the cluster. Chi-square (χ^2) and independent *t*-tests were used to examine between cluster differences on general study parameters for continuous and categorical variables respectively. Lastly, one-way ANOVAs were conducted to determine any differences in CVR between the behavioural clusters at MIDUS 2. Binary logistic regressions followed to assess whether cluster membership in MIDUS 2 was related to depressed affect and hypertension at the time of reporting. This same model was revisited while controlling for a range of covariates [SBP baseline, age, smoking, taking medications, BMI, antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs)]. Following this, an uncontrolled logistic regression was used to evaluate whether cluster membership at baseline was related to these same health and behavioural outcomes at a 4-year follow-up.

TABLE 1 Participant characteristics and demographics

Items	*N*	Mean (*SD*)	Range
Age (years)	**513**	**58.16 (11.44)**	**35–86 years**
BMI (kg/m^2)	513	29.42 (6.19)	14.99–60.39
Sex			
Male	240	57.50 (11.59)	
Female	273	56.67 (11.26)	
Race			
White	447		
African American	18		
Native American	4		
Asian/Pacific Islander	1		
Multiracial	7		
Other	10		
Employment status			
Employed	344		
Unemployed	158		
Education level	503	7.63 (2.42)	3–12
High school	134		
College (attending)	107		
Associates degree	36		
Bachelor's degree	122		
Some graduate school	15		
Masters	65		
PhD	24		

Note: For sex, age and BMI, *N* = 513. For race, *N* = 487 and for socioeconomic measures, education level, *N* = 503 and employment status, *N* = 502.

RESULTS

Descriptive statistics

The descriptive statistics and correlational analysis of study variables can be reviewed in Table 2. With the maximum correlation coefficient being less than .90, there are acceptable levels of collinearity among the study variables to warrant cluster analysis (Mooi & Sarstedt, 2011).

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, $F(1,445) = 743.52$, $p < .001$, $\eta_p^2 = .63$, DBP, $F(1,445) = 1197.19$, $p < .001$, $\eta_p^2 = .73$; and HR, $F(1,487) = 556.03$, $p < .001$, $\eta_p^2 = .53$, demonstrating the task was physiologically stressful. There were no significant differences in CVR due to sex or for those who reported taking medication for depression ($n = 44$). Furthermore, CVR did not predict future hypertensive status (all ps > .05). However, there were significant differences in reactivity due to smoking for SBP, $t(444) = -2.87$, $p < .01$; smokers exhibited lower SBP reactivity ($M = 9.65$, $SD = 10.38$) compared to non-smokers ($M = 14.00$, $SD = 10.36$). Additionally, there were significant differences in reactivity due to medication use, for HR, $t(486) = -1.98$, $p = .048$, with those taking medication ($n = 364$) having lower HR reactivity ($M = 3.31$, $SD = 3.22$) compared with those not taking medication ($M = 3.98$, $SD = 3.35$). These potential confounds were also associated medication ($n = 364$) having lower HR reactivity ($M = 3.31$, $SD = 3.22$) compared with those not taking medication ($M = 3.98$, $SD = 3.35$). These potential confounds were also associated with baseline cardiovascular measures and as a result were controlled for in our main analyses.

Cluster analysis

Three distinct clusters arose based on the necessary selection criteria for the correct number of clusters that included dendogram inspection and agglomeration schedule coefficients. A clear behavioural pattern emerged for reactivity profiles. In Cluster 1 ($n = 273$; 53.2%), those with less exposure to ELA were low on behavioural disengagement and depressive symptoms. The reactivity profile for this cluster was higher in comparison with the other two clusters. Cluster 2 ($n = 175$; 34.1%) was characterized by moderate levels of ELA, behavioural disengagement and symptoms of depression with a reactivity profile similar to the sample mean. In contrast, respondents in Cluster 3 ($n = 65$; 12.7%), reported greater exposure for all ELA factors, were higher on behavioural disengagement and depressive symptoms and were characteristic of a blunted reactivity profile; that is, lower than the sample average (please refer to Figure 2). The mean and standard errors are provided for study variables on each cluster (please refer to Table 3).

Analysis of general study parameters revealed significant cluster differences for age, smoking, medication use, BMI and baseline SBP (ps < .05). There were no significant differences in baseline measures (DBP and HR), sex, race or socioeconomic status at the time of stress testing which are provided in Table 4.

Cluster membership and CVR in MIDUS 2

Results from a series of one-way ANOVAs confirmed significant between cluster differences in CVR for; SBP, $F(2,443) = 4.21$, $p = .015$, and for DBP, $F(2,443) = 5.71$, $p = .004$. Tukey HSD post-hoc tests were carried out to establish where the significant differences were. The Tukey HSD post-hoc tests revealed a significant difference in SBP reactivity ($p = .012$) between Cluster 1 ($M = 14.48$, $SD = 10.61$) and Cluster

TABLE 2 Descriptive statistics and correlational analysis for study variables

	Mean (*SD*)	Range	Cronbach's alpha	CES-D	CTQ-EA	CTQ-PA	CTQ-SA	CTQ-EN	CTQ-PN	Behavioural disengagement	SBP reactivity	DBP reactivity	HR reactivity
1.CES-D	8.40 (7.99)	0–45	.67	–	.269**	.177**	.205**	.318**	.288**	.224**	−.151**	−.191**	−.146**
2. Emotional abuse	8.19 (4.23)	5–25	.88	–	–	.657**	.374**	.710**	.566**	.107*	−.170**	−.142**	−.037
3. Physical abuse	6.86 (3.07)	5–25	.79	–	–	–	.377**	.538**	.535**	.131**	−.140**	−.140**	−.051
4. Sexual abuse	6.56 (3.89)	5–25	.94	–	–	–	–	.282**	.353**	.182**	−.040	−.036	−.070
5. Emotional neglect	10.01 (4.60)	5–25	.89	–	–	–	–	-	.629**	.156**	−.155**	−.165**	−.031
6. Physical neglect	6.83 (2.84)	5–21	.70	–	–	–	–	–	–	.210**	−.079	−.112*	−.157**
7. Behave. disengagement	6.85 (2.22)	4–16	.76	-	-	-	-	-	-	-	−.084	−.029	−.090*
8. SBP reactivity	13.48 (10.44)	−21.60 to 46.95	–	–	–	–	–	–	–	–	–	.783**	.124**
9. DBP reactivity	6.35 (3.88)	−6.20 to 17.60	–	–	–	–	–	–	–	–	–	–	.305**
10. HR reactivity	3.48 (3.26)	−6.40 to 13.60	–	–	–	–	–	–	–	–	–	–	–

Note: The sample size was $N = 513$ on all measures of adversity, the CES-D (Center for Epidemiological Depression) scale and behavioural disengagement, and $N = 446$ on both SBP (systolic blood pressure) and DBP (diastolic blood pressure) reactivity, and $N = 488$ on HR (heart rate) reactivity. *$p < .05$ level; **$p < .01$ level.

3 (M = 10.09, SD = 8.25) and in DBP reactivity (p = .005) between Cluster 1 (M = 6.86, SD = 3.95) and Cluster 3 (M = 5.10, SD = 3.35). No significant effects were observed for HR reactivity.

Associations between cluster membership and health/behavioural outcomes in MIDUS 2

To assess whether cluster membership in MIDUS 2 was associated with depressed affect and hypertension at the time of testing, binary logistic regressions were calculated given these were categorical outcomes, and Cluster 2, which was similar to the sample mean, was used as a reference cluster. For hypertension status, inclusion of cluster membership to the model was significantly related to hypertension, X^2 (2) = 6.55, p = .038, with between 4.6% and 9.3% of the variance explained. Cluster 3 membership made a statistically significant contribution to the model (Wald X^2[1, N = 139] = 5.89, p = .015). Those in Cluster 3 were 6.25 times (95% CI [1.42, 27.45]) more likely to have hypertension compared to those in Cluster 2. A similar pattern emerged in the fully adjusted model that controlled for NSAIDs, BMI, smoking, baseline SBP and taking prescription medication. Though the overall model was non-significant, X^2 (7) = 11.59, p = .115, Cluster 3 membership made a statistically significant contribution to the model (Wald X^2[1, N = 119] = 3.83, p = .050). Those in Cluster 3 were 6.30 times (95% CI [.998, 39.74]) more likely to have hypertension, when controlling for covariates compared with those in Cluster 2. No significant effects were observed for Cluster 1.

For depressed affect, the model was statistically significant, X^2 (2) = 42.26, p < .001, with between 7.9% and 15.6% of the variance explained by adding cluster membership to the model. Cluster 3 made a statistically significant contribution to the overall model (Wald X^2[1, N = 512] = 6.15, p = .013). Those in Cluster 3 were 2.32 times (95% CI [1.19, 4.50]) more likely to report depressed affect compared with those in Cluster 2; while Cluster 1 also made a statistically significant contribution to the overall model (Wald X^2[1, N = 512] = 17.89, p < .001). Compared with Cluster 2, those in Cluster 1 were .198 times (95% CI [.094, .420]) less likely to report depressed affect.

A similar pattern emerged for Cluster 1 which in the fully adjusted model, was significantly associated with depressed affect (Wald X^2[1, N = 448] = 12.09, p < .001). Again, those in Cluster 1 were

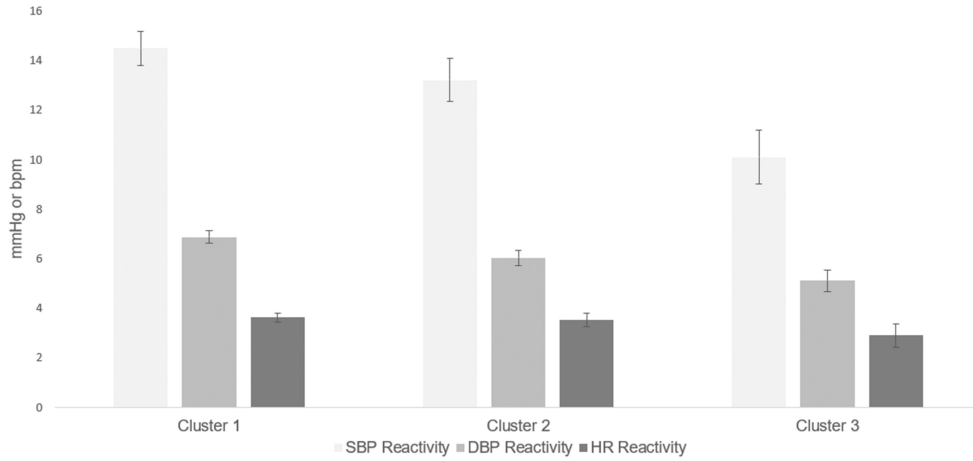

FIGURE 2 Means and standard errors of SBP (systolic blood pressure) reactivity, DBP (diastolic blood pressure) reactivity and HR (heart rate) reactivity in millimetres of mercury (mmHg) or beats per minute (bpm) based on cluster membership. Cluster 1 had the lowest reports on factors of ELA (early life adversity), CES-D (depression) and behavioural disengagement and was characteristic of patterns of exaggerated blood pressure reactivity. Cluster 2 reports were similar to the sample means as was blood pressure reactivity. Cluster 3 had the highest reports on behavioural factors and was characteristic of a blunted blood pressure reactivity profile. Significant differences were observed between Cluster 1 and Cluster 3 for both SBP and DBP reactivity.

TABLE 3 Means and standard errors of study variables across the three clusters

	Sample (n = 513)			Cluster 1 (n = 273)			Cluster 2 (n = 175)			Cluster 3 (n = 65)		
	Mean	SE	95% CI	Mean	SE	95% CI	Mean	SE	95% CI	Mean	SE	95% CI
EA	8.19	.19	[7.82,8.55]	6.03[b,c]	.09	[5.84,6.21]	8.66[a,c]	.24	[8.20,9.13]	15.98[a,b]	.60	[14.78,17.19]
PA	6.86	.13	[6.60,7.12]	5.75[b,c]	.06	[5.63,5.87]	6.62[a,c]	.15	[6.23,6.91]	12.15[a,b]	.64	[10.87,13.44]
SA	6.56	.17	[6.22,6.90]	5.15[b,c]	.04	[5.07,5.22]	6.49[a,c]	.21	[6.07,6.91]	12.68[a,b]	.89	[10.90,14.45]
EN	10.01	.20	[9.61,10.41]	7.07[b,c]	.14	[6.80,7.35]	12.04[a,c]	.27	[11.49,12.58]	16.87[a,b]	.48	[15.90,17.84]
PN	6.83	.12	[6.59,7.08]	5.44[b,c]	.06	[5.32,5.56]	7.37[a,c]	.18	[7.01,7.72]	11.26[a,b]	.48	[10.30,12.23]
Behav.disen	6.85	.10	[6.66,7.05]	6.83[c]	.13	[6.57,7.09]	6.39[c]	.16	[6.08,6.70]	8.19[a,b]	.29	[7.62,8.77]
Depression	8.40	.35	[7.71,9.09]	4.75[b,c]	.25	[4.26,5.24]	11.81[a,c]	.63	[10.56,13.06]	14.52[a,b]	1.36	[11.80,17.25]
SBP reactivity	13.45	.50	[12.47,14.43]	14.48	.69	[13.13,15.84]	13.20	.87	[11.48,14.91]	10.09[a]	1.09	[7.90,12.28]
DBP reactivity	6.36	.18	[6.00,6.72]	6.86[c]	.26	[6.36,7.37]	6.03	.31	[5.41,6.64]	5.10[a]	.44	[4.21,5.98]
HR reactivity	3.55	.15	[3.24,3.85]	3.61	.19	[3.24,3.98]	3.51	.27	[2.98,4.04]	2.89	.46	[1.98,3.80]

Note: N = 513 on all behavioural factors. EA (emotional abuse), PA (physical abuse), SA (sexual abuse), EN (emotional neglect) and PN (physical neglect), behav.disen = behavioural disengagement. SBP (systolic blood pressure) reactivity, DBP (diastolic blood pressure) reactivity, and HR (heart rate) reactivity in mmHg or bpm. N = 237 for SBP reactivity for Cluster 1 and Cluster 2, N = 152 for DBP reactivity for Cluster 1 and Cluster 2 and N = 57 for Cluster 3 for SBP and DBP reactivity. N = 256 for Cluster 1, N = 169 Cluster 2 and N = 63 for Cluster 3 for HR reactivity.

[a]Different from cluster 1.

[b]Different from cluster 2.

[c]Different from cluster 3.

TABLE 4 General study parameters of Cluster 1, Cluster 2 and Cluster 3

	Cluster 1 (n = 273)	Cluster 2 (n = 175)	Cluster 3 (n = 65)
Age	59.62 (11.34)[b]	57.53 (11.56)	53.74 (10.33)
Sex (% female)	50.2	53.1	66.2
Race (%)			
White	244 (89.4)	150 (85.7)	53 (81.5)
African American	7 (2.6)	8 (4.6)	3 (4.6)
Native American	2 (.7)	0	2 (3.1)
Asian/Pacific Islander	0	1 (.6)	0
Multiracial	4 (1.5)	2 (1.1)	1 (1.5)
Other	3 (1.1)	6 (3.4)	1 (1.5)
Education level (%)			
High school	56 (20.6)	54 (30.9)	24 (36.9)
College (attending)	51 (18.7)	41 (23.5)	15 (23.1)
Associate degree	16 (5.9)	16 (9.1)	4 (6.2)
Bachelor's degree	74 (27.1)	34 (19.4)	14 (21.5)
Some graduate school	13 (4.8)	2 (1.1)	0
Masters	40 (14.7)	19 (10.9)	6 (9.2)
PhD	18 (6.6)	6 (3.4)	0
Employed (%)			
Yes	181 (66.3)	122 (69.7)	41 (63.1)
No	87 (31.9)	49 (28.0)	22 (33.8)
CES-D (% > 16)	1.5[a],[b]	26.9[b]	36.9
Medication (% taking medication)	73.3[a]	80.6[b]	64.6
Smoking (% smokers)	7.7[b]	12.6	26.2[a]
BMI (kg/m^2)	29.17 (5.50)	29.04 (5.76)	31.48 (9.10)
Baseline SBP (mmHg)	125.36 (17.78)[b]	124.64 (17.44)	118.74 (16.70)
Baseline DBP (mmHg)	60.97 (10.76)	61.21 (11.87	61.27 (11.88)
Baseline HR (bpm)	71.70 (10.46)	73.45 (10.90)	74.32 (9.62)

Note: Values are reported as means and standard deviations, except for the explicitly stated percentages. Education level and employment status are used as measures of socioeconomic status. Baseline SBP (systolic blood pressure), baseline DBP (diastolic blood pressure) and baseline HR (heart rate).

[a]Different from Cluster 2.

[b]Different from Cluster 3.

.220 times (95% CI [.094, .517]) less likely to report depressed affect compared to those in Cluster 2, while controlling for covariates (antidepressants, smoking, baseline SBP, taking prescription medication and age). Cluster 3 membership made a statistically significant contribution to the model (Wald X^2[1, N = 448] = 4.54, p = .033). Compared with Cluster 2, those in Cluster 3 were 2.29 times (95% CI [1.07, 4.90]) more likely to report depressed affect.

Cluster membership predicting health and behavioural outcomes in MIDUS 3

Binary logistic regressions were again conducted to assess whether cluster membership in MIDUS 2 predicted health status at a 4-year follow-up. Missingness was considerably high for both primary outcomes (95.3%), so responses are limited to small sample sizes (please refer to Figure 1). No statistically significant effects were observed for hypertension or depressed affect.

DISCUSSION

The present study sought to determine whether there were distinct behavioural clusters characteristic of CVR profiles that related to health and behavioural outcomes at baseline and follow-up. Three distinct behavioural clusters emerged with statistically different CVR profiles. Cluster 1 was characterized by the lowest ELA and behavioural factors and had statistically higher blood pressure responses to stress. Cluster 2 was characteristic of reactivity values similar to the sample mean with moderate levels of ELA and behavioural factors observed. Lastly, Cluster 3 was characterized by greater reports of ELA, coupled with higher levels of behavioural disengagement and higher symptoms of depression, with statistically lower blood pressure responses to stress.

Cluster 3 was associated with hypertension and depressed affect at baseline and withstood adjustment for several covariates. The findings for depressed affect are not surprising given that maladaptive coping efforts arise from experiences of ELA (Fluharty et al., 2021; Luecken et al., 2006) which over time can increase the risk of depression (Luecken et al., 2006). In the adjusted model, this behavioural cluster remained significantly associated with hypertension which seems somewhat nuanced given research on exaggerated reactivity and hypertension. However, when accounting for the associations between ELA (Suglia et al., 2018), depression (Jonas & Lando, 2000) and disengagement coping strategies (Gleiberman, 2007; Palagini et al., 2016) with hypertension, it is plausible that these behavioural factors exert an influence that moderates the relationship between reactivity and hypertension. It is also worth noting that not all studies find exaggerated reactivity to be related to hypertension on follow-up (e.g., Bourassa et al., 2021). Additionally, other studies found exaggerated responses were related to lower risk of early mortality (Kupper et al., 2015) and improved disease markers (Heponiemi et al., 2007). In addition, Cluster 1 which was characteristic of an exaggerated reactivity profile, was also associated with depressed affect and withstood adjustment for several covariates. While this is in contrast with research on depression and blunted reactivity, it lends support to previously reported associations between depression and exaggerated reactivity (Kaushik et al., 2019; Kibler & Ma, 2004; Matthews et al., 2005). Furthermore, depression has been found to be related to a range of physiological adjustments, with the present findings reflecting altered autonomic function (Phillips, 2011). Notably, cluster membership was not found to be predictive of future health status 4 years later. Considering the sample sizes for these health and behavioural outcomes at follow-up were markedly small and in adjusted models cluster membership was related to these outcomes at baseline, future research should aim to recruit larger sample sizes to test the effects of behavioural clusters on future health status. Given recent findings of a behavioural cluster characteristic of a blunted HR reactivity profile in a young healthy sample (Keogh et al., 2022), the findings merit attention. Through the use of cluster analysis this study sought to replicate these findings, and while a behavioural cluster emerged with a distinct pattern of blunted CVR, this was observed for blood pressure rather than the previously reported HR. This may be a result of the types of stress tasks used or differences in sample profiles, with personal salience argued to be an important moderator of blunted cardiovascular reactions to stress (Bourassa & Sbarra, 2022). Although the previous study (Keogh et al., 2022) arguably involved a task of low personal salience (i.e., mental arithmetic), components of competition and evaluation were included which may have influenced levels of personal salience and explain the differences in physiological findings between the two studies. Furthermore, the current study analysed data from a midlife sample where chronic health conditions were considered normative, while the previous study recruited young healthy participants free from illness and disease. Therefore, the differences between studies may reflect age-dependent changes which affect the structure and function of the heart (Kane & Howlett, 2018). Nevertheless, the present study extends research by identifying behavioural clusters characteristic of both blunted and exaggerated CVR profiles in a mid-life sample related to poorer health and behavioural outcomes at the time of testing, suggesting that behavioural clusters indicative of CVR profiles may signify psychological and physiological vulnerabilities.

This study has some notable strengths. Compared with other CVR studies, the sample for baseline analyses is quite large and a range of covariates were controlled for, including NSAIDs, which with

continued use can increase blood pressure and risk for hypertension (Morrison et al., 2007). In addition, we extend on previous research reporting a behavioural cluster characteristic of a blunted HR reactivity profile in a healthy young sample, to include lower blood pressure (SBP and DBP) responses to stress in a midlife sample, using a cross-sectional and prospective design. Moreover, to the best of our knowledge this study is the first to identify a behavioural cluster characteristic of an exaggerated reactivity profile. Despite the strengths, the study is not without limitations. First, due to reliance on self-report measures, presumptions about the clinical status of depression cannot be made (Carroll et al., 2009). Furthermore, retrospective recollection of ELA cannot capture time-specific effects of stress, is subject to recall bias and issues of underreporting (Campbell et al., 2014; Hammen, 2015; Hanson et al., 2016; McLaughlin et al., 2010). However, evidence suggests recollection of events in adulthood is relatively reliable (Bifulco et al., 1997), with the CTQ reported to be a stable measure of ELA over time (Paivio, 2001). Second, a racial diversity was observed and given that CVR is a pathway to future cardiac illness and racial differences exist in both ELA (Slopen et al., 2010) and CVD (Hackler III et al., 2019; O'Neal et al., 2019), future studies should recruit a more racially diverse sample to explore differences in biological responses to stress. Third, taking medication for chronic health problems was normative given the midlife sample. However, this was controlled for and effects were still present at the time of testing. Moreover, while taking medication was used as a proxy for general medications that may affect cardiac activity, there are many individual medications that may have a differential impact on the cardiovascular system. However, this study controlled for both antidepressants and NSAIDs which can affect blood pressure activity and increase the risk of hypertension (Morrison et al., 2007; Salomon et al., 2009). Fourth, the study focused on behavioural disengagement as an avoidant coping strategy; future research could examine the role of other coping styles. Finally, the sample size for follow-up outcomes were notably small, and future research should recruit larger samples, better powered to detect effects.

To conclude, a behavioural cluster emerged characteristic of a blunted blood pressure reactivity profile, partially replicating previous research on behavioural clusters in this context (Keogh et al., 2022). To the best of our knowledge, this is the first study to identify a behavioural cluster characteristic of an exaggerated reactivity profile. More importantly the findings suggest that behavioural clusters characteristic of patterns of blood pressure reactivity relate to both hypertension and depressed affect at the time of testing. Applying cluster analysis to behavioural factors which may precede patterns of CVR may provide a clinical utility to future CVR research by indicating those most vulnerable and in need of treatment efforts. Adopting a clinimetric approach for assessment of not just psychosocial factors but in combination with biological factors would allow for a more comprehensive appraisal of the cumulative burden of stress and could set the use of biomarkers in a clinical context (Guidi et al., 2021; Whittaker et al., 2021). Lastly, this study somewhat replicates previous findings (Keogh et al., 2022), albeit for blood pressure rather than HR reactivity. The findings suggest behavioural clusters are associated with different CVR in samples of different age and health profiles. Nevertheless, the study extends research (Keogh et al., 2022) by identifying behavioural clusters characteristic of blood pressure reactivity profiles and advances our understanding of how these clusters relate to depressed affect and hypertension.

AUTHOR CONTRIBUTIONS

Tracey Mary Keogh: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; validation; visualization; writing – original draft; writing – review and editing. **Siobhán Howard:** Conceptualization; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing. **Stephen Gallagher:** Conceptualization; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST

All authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in ICPSR at http://www.icpsr.umich.edu/, reference number [ICPSR 4652, ICPSR 29282, ICPSR 36346].

ORCID

Tracey M. Keogh https://orcid.org/0000-0002-4189-5926
Siobhán Howard https://orcid.org/0000-0002-1689-0867
Stephen Gallagher https://orcid.org/0000-0002-5471-7774

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