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Cardiovascular Reactivity Patterns and Pathways to Hypertension: A Multivariate Cluster Analysis

RUNNING HEAD: REACTIVITY PATTERNS AND HYPERTENSION

Ryan C. BRINDLE[a], Annie T. GINTY[a,b], Alexander JONES[c], Anna C. PHILLIPS[a], Tessa J. ROSEBOOM[d,e], Douglas CARROLL[a], Rebecca C. PAINTER[e], Susanne R. DE ROOIJ[d]

[a]School of Sport, Exercise, and Rehabilitation Sciences, University of Birmingham, Birmingham, B15 2TT, UK

[b]Department of Psychiatry, School of Medicine, University of Pittsburgh, USA, 15260

[c]Centre for Cardiovascular Imaging, University College London Institute of Cardiovascular Science, London W1T 7HA, United Kingdom

[d]Department of Clinical Epidemiology, Biostatistics & Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

[e]Department of Obstetrics & Gynecology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

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Address correspondence to:

Ryan C. Brindle, School of Sport, Exercise, and Rehabilitation Sciences, University of Birmingham, Birmingham, B15 2TT, UK: Email Address: RCB236@bham.ac.uk: Telephone: +44 121 414 8745

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Abstract

Substantial evidence links exaggerated mental stress induced blood pressure reactivity to future hypertension but the results for heart rate reactivity are less clear. For this reason multivariate cluster analysis was carried out to examine the relationship between heart rate and blood pressure reactivity *patterns* and hypertension in a large prospective cohort (age range 55-60 years). Four clusters emerged with statistically different systolic and diastolic blood pressure and heart rate reactivity patterns. Cluster 1 was characterised by a relatively exaggerated blood pressure and heart rate response while the blood pressure and heart rate responses of cluster 2 were relatively modest and in line with the sample mean. Cluster 3 was characterised by blunted cardiovascular stress reactivity across all variables and cluster 4, by an exaggerated blood pressure response equal to that of cluster 1 and a modest heart rate response equal to that of cluster 2. Membership to cluster 4 conferred an increased risk of hypertension at five year follow-up, HR = 2.98 (95%CI: 1.50-5.90), p <.01, that survived adjustment for a host of socio-demographic variables. These results further specify the established link between blood pressure reactivity and hypertension and support the use of multivariate approaches to stress psychophysiology.

Keywords: Psychological Stress, Multivariate Cluster Analysis, Hypertension, Blood Pressure, Heart Rate, Body Mass Index

Introduction

The association between exaggerated blood pressure (BP) reactions to acute psychological stress and hypertension is well established. Supporting evidence comes from several independent epidemiological datasets that have shown exaggerated systolic (SBP) and/or diastolic (DBP) BP reactivity to acute psychological stress to be linked with increased resting BP at 6.5- and 12-year follow-up[1-2] and to predict hypertension diagnosis at 13-year follow-up[3]. In addition, being "high risk" for developing hypertension based on parental history or having elevated resting BP are associated with exaggerated BP stress reactivity[4]. Importantly, a large meta-analysis also has established a positive association between BP stress reactivity and hypertension[5].

In contrast, the relationship between stress-induced heart rate (HR) reactivity and hypertension remains equivocal. Relatively increased HR reactivity has been observed among individuals with parental history of hypertension[6] and several small scale studies have reported a positive association between HR stress reactivity and increased 1-year ambulatory SBP[7] and incident mild hypertension[8]. However, a relationship between HR reactivity and elevated BP has failed to emerge from epidemiological studies[3] or meta-analysis[5]. Further complexity is added by findings of negative associations between HR stress reactivity and hypertension risk factors such as obesity and the use of addicting substances such as alcohol and tobacco. In each case, the obese[9], smokers[10], and those dependent on alcohol[11] all exhibited blunted rather than exaggerated HR responses to acute psychological stress. Accordingly, it may be timely to take a more nuanced look at the relationship between cardiovascular stress reactivity and hypertension.

It has been suggested that focusing on a single cardiovascular reactivity variable may be limiting in scope, as evidence has shown that different patterns of end-organ responses have differential risk for disease[12] and that focusing on multivariate patterns of stress

reactivity may be more informative[12]. With regard to BP and HR this makes sense given that these variables are not independent but, in fact, profoundly influence each other; increases in cardiac output increase BP and changes in BP influence HR via baroreceptor mechanisms[13]. However, the wide interindividual variation in normal patterns of HR and BP stress responses makes it challenging to define homogeneous groups of subjects. Cluster analysis offers a solution to this problem by assigning subjects from a single large cohort into clusters based on their statistical similarity on a set of variables defined *a priori*. This approach was undertaken with two goals: 1) to identify clusters of individuals who exhibit significantly different patterns of BP and HR stress reactivity, and 2) assess whether membership to a particular cluster conferred increased/decreased risk of hypertension diagnosis at 5-year follow-up.

Methods

Participants

Participants were from the Dutch Famine Birth Cohort, which comprised 2414 men and women born in Amsterdam during 1943-1947. The study was designed to examine the health consequences of prenatal famine exposure. Hence, it may be suggested that this population characteristic may limit the generalizability of the present study results. However, this is unlikely as, predominantly, famine exposure early in gestation, defined as a 13 week period where daily caloric intake was below 1000 calories[14] (Roseboom, van der Meulen, Raveli, Osmond, Barker, & Bleker, 2001), was associated with poorer adult health[15] (Roseboom, Painter, van Abeelen, Veenendaal, & de Rooij, 2011); only 58 (8.6%) individuals in the present sample were exposed to famine during early gestation. Reasons for loss at follow-up include: 160 babies were not registered in Amsterdam, 328 individuals had died at follow-up, 213 had emigrated, 157 refused to have their addresses collected, 125 were untraceable at follow-up, and 8 requested to be removed from the study database[16,17]. All

1423 members of the cohort who lived in the Netherlands on September 1, 2002 were invited to the clinic to undergo stress testing from 2002-2004; 740 attended. Follow-up analyses comparing individuals who refused to participate in the stress testing wave (n = 683) with those who participated in the follow-up showed that there were no differences in sex (p = .49) or birth weight (p = .42). There was a significant difference in age ($mean_{refused}$ = 58.3yrs, $mean_{attended}$ = 59.2yrs, $p < .01$).

In the 2008-2009 follow-up interviews were conducted. Participants self-reported reported whether or not they had ever received a diagnosis of hypertension from a physician. The mean (SD) temporal lag between stress testing and the hypertension follow-up interview was 5.5 years (range: 4 – 6.8 years). Dropout between stress testing and hypertension follow-up interview was 232 participants (34.6%). The study was approved by the local Medical Ethics Committee, carried out in accordance with the Declaration of Helsinki, and informed consent was obtained from all participants.

General Study Parameters

In the 2002-2004 stress testing sessions, research nurses gathered anthropometric measurements and collected socioeconomic status (SES), education, and lifestyle data during a standardized interview. Height was measured twice using a fixed or portable stadiometer and weight was measured twice using Seca and portable Tefal scales. Body mass index (BMI) was calculated as weight (kg)/height (m^2) from the averages of the two height and weight measures. SES was defined according to the International Socio-Economic Index (ISEI)-92, which is based on the participant's or their partner's occupation, whichever has the higher status[18]. Values on the ISEI-92 range from 16 (low status) to 87. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression[19]. Education level was measured on a 10-point scale (1 = primary education not completed, 10 = university completed). Alcohol consumption was recorded as the number of units

consumed per week; one unit was defined as one glass of an alcoholic beverage. On the basis of self-report, participants were characterized as current, ex, or never smokers and also indicated whether or not they were currently taking anti-hypertensive medication.

Psychological Stress Protocol

Stress testing was carried out in the afternoon between the hours of 12:00-14:00 following a light lunch. A formal 20-minute baseline was followed by three psychological stress exposures: Stroop, mirror-tracing, and a speech task. Each task lasted 5 minutes and was separated by 6-minute between-task intervals; a 30-minute recovery phase followed the final stress task. The Stroop task was a computerised version of the classic Stroop colour-word conflict task. After instruction, participants were allowed to practise until they fully grasped the requirements of the task. During the task, a mistake or response over the time limit (5s) triggered a beep. The mirror-tracing task required participants to trace a star that could only be seen in a mirror image (Lafayette, IN, USA). Participants were allowed to practice one circuit. They were told to give priority to accuracy over speed and that most people could perform five circuits without diverging from the line. Every divergence from the line induced a short beep. Prior to the speech task, participants listened to a pre-recorded scenario in which they were told to imagine that they were falsely accused of pick-pocketing. Participants were instructed to give a 3-minute response to the accusation and were given 2 minutes to prepare a response. The responses were recorded on video and participants were told that the number of repetitions, the eloquence and the persuasiveness of their performance would be marked by a team of communication-experts and psychologists.

Continuous measures of BP and HR were made during the stress test protocol using a Finometer or Portapres Model-2 (Amsterdam, The Netherlands). There was no difference in reactivity as a function of the two different measurement instruments. Four 5-minute blocks were defined as follows: baseline (final 5 minutes in baseline period), Stroop, mirror-tracing,

and speech task (including preparation time). Mean SBP, DBP, and HR were calculated for each period.

Statistical Analysis

Baseline SBP, DBP, and HR were the averages of measures recorded during the 5-minute period 15 minutes into the formal baseline. Cardiovascular measures were averaged across the three tasks to obtain a stress period average for each variable. Stress reactivity was defined as the difference between stress and baseline averages for SBP, DBP, and HR. A repeated-measures ANOVA, comparing baseline and stress task values, was carried out to confirm that the stress tasks perturbed cardiovascular activity. Partial eta squared and hazard ratios are reported as the measure of effect size.

Cluster analysis was carried out using Ward's method[20] in SPSS version 22 (Chicago, IL, USA). Raw reactivity scores for SBP, DBP, and HR were converted to z-scores to ensure that the cluster analysis was not influenced by the scale of individual variables. Ward's method begins with the same number of clusters as cases. In each subsequent step, cases are combined, forming one less cluster than before. For each cluster, a within-cluster sum of the 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. A total sum of squares is then calculated across all clusters. Ward's method determines which two clusters will produce the smallest increase in the total sum of squares when they are merged. Eventually, the merger of two dissimilar clusters will cause a substantial increase in the total sum of squares. The state of the clusters just prior to this point is considered the "natural solution" to the clustering process. Follow-up one-way ANOVAs were carried out to determine whether clusters differed significantly on mean SBP, DBP, and HR reactivity. As data was normally distributed, between cluster differences in general study parameters were tested with one-way ANOVAs and Chi-squared analysis.

Binary logistic regression was used to assess whether cluster membership in 2002-2004 predicted reported physician diagnosis of hypertension at the 2008-2009 follow-up. Following tests of unadjusted models, models were adjusted for education, SES, BMI, sex, age, HADS-depression score, smoking status, and alcohol consumption, and self-reported anti-hypertension medication use at stress-testing to assess the influence of potential confounders.

Results

Study Population

Of the 740 cohort members, 721 completed the stress protocol. Cardiovascular data were unavailable for four participants. Incomplete cardiovascular data due to technical problems, participant exclusion, due to significant arrhythmia, determined during cardiovascular data processing, and removal of two statistical outliers (> 5 standard deviations above mean) left an effective sample size of 669 which is substantially above the suggested sample size of 2^m needed for cluster analysis, where m is the number of clustering variables[21].

Stress Reactivity

The stress task battery significantly perturbed SBP, $F(1, 668) = 2511.21$, $p < .001$, $\eta^2 = .79$, DBP, $F(1, 689) = 579.69$, $p < .001$, $\eta^2 = .47$, and HR, $F(1, 668) = 165.48$, $p < .001$, $\eta^2 = .20$; in all cases cardiovascular activity increased in response to stress. The overall magnitude of the cardiovascular perturbations is shown in Figure 1.

Cluster Analysis

Based on the criterion discussed for selecting the appropriate number of clusters, SBP, DBP, and HR reactions to the stress task battery were found to resolve to four distinct clusters. The means and standard errors for SBP, DBP, and HR reactivity for each cluster can be found in Figure 1. Results of independent one-way ANOVAs and *post-hoc* analyses

showed that all the clusters were significantly different from each other on all cardiovascular variables ($p < .05$) with a few exceptions: clusters 1 and 4 did not significantly differ in SBP or DBP reactivity (both $p > .45$), and clusters 2 and 4 did not significantly differ in HR reactivity ($p = .56$). Whereas cluster 2 was characterised by reactivity values mostly in line with the sample averages, the other clusters were different in several respects. Individuals in cluster 1 registered exaggerated HR and BP responses while individuals in cluster 3 exhibited an overall blunted reactivity profile. Finally, individuals in cluster 4 mounted an exaggerated BP response equal to that of cluster 1 but only a modest HR response statistically equal to that of cluster 2.

Analysis of general study parameters revealed several significant differences between the clusters (Table 1). Significant between-cluster differences ($p < .05$) were found for education, SES, BMI, HADS-depression score, baseline DBP, gender, and smoking status. There were no significant cluster differences in baseline SBP or HR, age, alcohol consumption, dropout, and hypertension medication use at the time of stress testing.

[Insert Figure 1 about here]

[Insert Table 1 about here]

Cluster Risk for Hypertension

Hypertension status was recorded for 438 participants in 2008-2009. There was no significant difference in HR or BP stress reactivity between those who participated in the follow-up and those who did not. Analysis of general 2002-2004 study parameters in the follow-up sample revealed significant differences between the clusters in education, SES, BMI, HADS-depression score, hypertension medication use at time of stress testing, and smoking status; age, gender, baseline cardiovascular variables, and alcohol consumption did not significantly vary across clusters (Table 2). In all, 211 (48%) reported having received a diagnosis of hypertension from a physician in the 2008-2009 follow-up. Binary logistic

regression confirmed a relationship between 2002-2004 cluster 4 membership and increased risk of hypertension at 2008-2009 follow-up (Table 3). To assure that this relationship was not influenced by those already hypertensive at the 2002-2004 stress testing session, this analysis was revisited and adjustment for hypertension medication use at the time of stress testing; results survived adjustment (Table 3). Finally, to explore potential mediators education, SES, BMI, HADS-depression score, and smoking status were inserted as covariates; cluster 4 membership was still significantly related to increased risk of hypertension at follow-up (Table 3).

[Insert Table 2 about here]

[Insert Table 3 about here]

Exploratory Analyses of Task Specificity

Given that the current study aimed to determine if stable individual differences in stress reactivity predicted individual differences in hypertension risk we chose to aggregate reactivity measures across the tasks as task aggregation has been shown to result in a more reliable measure of individual differences in stress reactivity[22]. However, we acknowledge that stress tasks differ in their provoked responses and in their relevance to disease. Consequently, we undertook exploratory cluster and binary logistic regression analyses for each task individually. Individual cluster analyses for the speech and Stroop tasks resulted in the same clusters as the main analysis and in both cases the cluster characterized by exaggerated BP, but only modest HR reactivity had significantly increased risk of hypertension (both HRs > 1.96 & both p <.013). Cluster analysis of reactivity values to the mirror tracing task also revealed four distinct groups that qualitatively were similar in pattern to the other tasks but cluster membership failed to predicted hypertension.

Discussion

Using multivariate cluster analysis, four homogenous clusters of individuals with statistically different SBP, DBP, and HR stress reactivity patterns were identified. Further, cluster membership was found to predict increased risk of a physician diagnosis of hypertension at 5 year follow-up. Interestingly, a dichotomy emerged whereby cluster 1 and 4 garnered the smallest and greatest risk of hypertension, respectively, despite mounting statistically equal exaggerated BP stress responses; the only between-cluster difference was in HR reactivity where cluster 1 mounted an exaggerated HR response and individuals in cluster 4 registered small HR responses equal to the sample mean. This relationship withstood adjustment for various potential anthropometric and socio-demographic confounders and hypertension medication use at time of stress testing. By showing that only individuals characterized by an exaggerated BP reaction and relatively small HR reaction are at increased risk of hypertension, these results support, but also more specifically characterize the previously reported prospective relationship between exaggerated BP reactivity and hypertension. Lastly, these results critically emphasize the role of multivariate analyses in stress psychophysiology research.

That the cluster characterized by the largest SBP and DBP stress responses had the greatest risk of hypertension at 5-year follow-up was not unexpected. Moreover, this relationship withstood adjustment for hypertension medication use at stress testing and several potential anthropometric and socio-demographic confounders. Although mediation by some other unmeasured factor is possible, it is unlikely, as previous studies have shown the association between exaggerated BP stress reactivity and hypertension to withstand statistical adjustment for other variables such as age, gender, and baseline BP[3]. What is more likely is that repeated large magnitude surges in BP, induced by mental stress, engage local BP regulatory mechanisms and lead over time to upward structural resetting of the peripheral vasculature[23,24]. Specifically, elevated resting BP results from a positive feedback cycle in

which frequent acute surges in BP promote vascular hypertrophy which decreases lumen diameter and increases vessel stiffness, in turn, amplifying future BP fluctuations. Evidence of such processes lies in the reported association of exaggerated BP reactivity with increased carotid intima-media thickness in children[25], adolescents[26,27], and adults[28,29], and with increased vascular stiffness[30] as well as the propensity for BP reactivity to increase with age[31]. It is likely that such physiological processes underlie the development of hypertension in the individuals contained in the cluster that displayed exaggerated BP responses to mental stress[1-3].

An unexpected finding was that the cluster of individuals carrying the least risk of hypertension did not have reactivity values located at the mean but instead had the most exaggerated HR and BP reactions. Hence, compared to the cluster at highest risk of hypertension, which had an equally exaggerated BP response but only modest cardiac response, it would appear that the presence/absence of a robust HR response is, to some extent, a factor in determining hypertension risk. One possible interpretation relates to the early observation that similar BP reactions can result from significantly different changes in cardiac output and total peripheral resistance[12]. A spectrum exists in which individuals at the extreme ends modulate BP by primarily augmenting either cardiac output (CO; *cardiac reactors*) or total peripheral resistance (TPR; *vascular reactors*). Going further, it has been suggested that not only is the magnitude of reactivity significant in the context of disease but that different underlying mechanisms (i.e., relative degree of CO/TPR modulation) may carry differential hypertension risk[12]. The present results accord with this framework as the individuals in the highest risk cluster registered an exaggerated BP reaction despite only a modest increase in HR, whereas the cluster carrying the least amount of risk mounted an equally exaggerated BP response but also recorded a HR reaction almost 3x larger than the sample mean. With such differences in cardiac activity between the clusters, it may be that

individuals in the cluster with the least risk increased BP by augmenting cardiac output through beta-adrenergic activation and/or vagal withdrawal mechanisms, while the high-risk cluster increased BP primarily through alpha-adrenergic vasoconstriction[32,33]. It is also possible that the reaction patterns exhibited by individuals in clusters 2 and 3 resulted from variations, not only in the degree of mixed alpha/beta -adrenergic activation, but also in overall magnitude of autonomic reactivity. Hence, these data suggest that not only is the magnitude with which an individual responds to mental stress significant in the context of disease, but also underlying multivariate hemodynamic and autonomic mechanisms carry differential risk and should be considered.

The current study is not without limitations. First, it could be argued that an element of subjectivity exists in choosing the clustering algorithm and the final number of reactivity profile clusters. These are issues with all forms of cluster analysis. We chose Ward's method as it has been widely used in health psychology research[34] and precedence for its use exists in stress psychophysiology; two previous studies have used Ward's method to cluster stress reactivity patterns according to autonomic activity[33] and stress task[32]. Four clusters were selected for two reasons: a substantial increase in total sum of squares was observed during the iteration decreasing the sample from five clusters to four, and outputs with five or three clusters either had very small clusters with extreme individuals or large, heterogeneous clusters, respectively. Second, the effect sizes in in the current study are small. However, they are consistent in magnitude with those observed in other studies[3], and this is not unexpected as hypertension is multiply determined, having etiological roots in the vascular, autonomic, genetic, and metabolic domains[35]. Finally, the possibility exists that famine exposure *in utero* could influence the present results and limit generalizability. However, chi square analysis revealed that famine exposure did not differ across the clusters (p = .25) nor did it relate to hypertension diagnosis (p = .17).

In conclusion, using multivariate cluster analysis, four distinct HR and BP reactions patterns were identified that differed in relative risk of hypertension diagnosis at 5 year follow-up. A profile characterized by exaggerated BP but only modest HR reactivity conferred the greatest risk, while individuals mounting relatively exaggerated BP and HR responses carried the least amount of risk. These results support, but more importantly, add specificity to the established relationship between blood pressure stress responses and hypertension and provide positive reinforcement for the use of multivariate statistical approaches in psychophysiology research.

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Figure 1. Means of systolic (SBP), diastolic (DBP), and heart rate (HR) reactivity in mmHg or beats per minute for overall sample and individual clusters. HR reactivity is significantly different across all clusters, with the exception of clusters 2 and 4. SBP and DBP reactivity is significantly different across clusters with the expectation of clusters 1 and 4. Error bars represent standard error.

Summary Table

What is known about the topic

- Exaggerated blood pressure reactions to acute psychological stress are associated with increased risk of hypertension
- Links between exaggerated heart rate stress responses and hypertension are inconsistent and blunted heart rate stress reactions have been linked to hypertension risk factors (e.g., obesity, smoking, heavy alcohol consumption). This creates a paradox since heart rate and blood pressure stress reactions are not mutually exclusive, but are linked through cardiovascular regulatory mechanisms.
- Multivariate patterns of heart rate and blood pressure stress reactivity have been seldom explored with regard to disease risk.

What this study adds

- Using multivariate cluster analysis, four unique clusters of individuals were identified that statistically differed in the magnitude of heart rate and blood pressure reactivity to a battery of mental stress tasks.
- The cluster with the least amount of risk mounted a relatively exaggerated heart rate and blood pressure response while the cluster with the greatest risk mounted an exaggerated blood pressure, but relatively small heart rate response.
- This study adds specificity to the already established link between blood pressure stress reactivity and hypertension and reinforces the use of multivariate approaches to stress psychophysiology.

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Table 1: General Study Parameters of Clusters 2002-2004 Wave (N = 669)

	Cluster 1 (N = 85)	Cluster 2 (N = 268)	Cluster 3 (N = 184)	Cluster 4 (N = 132)
Education	5.2 (2.3)†	4.5 (2.1)	4.1 (2.2)*	4.7 (2.2)
SES	55.0(11.8)# †‡	49.9 (14.2)*	47.3 (14.3)*	49.8 (14.0)*
BMI (kg/m^2)	26.8 (3.6)#† ‡	28.5 (4.6)*†	29.4 (5.2)*#	29.2 (4.6)*
HADS-Depression	2.3(2.3) †	3.3 (3.2)	3.8 (3.0)* ‡	2.8 (2.7)†
Smoking (% smokers)[a]	7.1	22.8	38.3	15.2
Hypertension Medication Use[b]	15.3%	17.9%	26.1%	33.3%
Sex (% female)[a]	50.6%	46.6%	60.3%	53.0%
Age	58.5 (1.0)	58.2 (0.9)	58.3 (1.0)	58.2 (0.9)
Alcohol	10.5 (11.6)	10.0 (14.2)	8.9 (12.9)	10.1 (15.1)
Dropout[c]	32.9%	35.8%	37.0%	29.5%
Baseline SBP	133.2 (22.3)	127.3 (19.9)	127.7 (20.2)	126.9 (21.8)
Baseline DBP	70.3 (11.6)# ‡	66.0 (11.0)*	67.2 (12.1)	65.2 (13.9)*
Baseline HR	75.4 (10.1)	73.4 (10.2)	74.7 (11.0)	73.3 (10.8)

Note: Values are reported as Mean (SD). *different from Cluster 1, #different from Cluster 2, †different from Cluster 3, ‡different from Cluster 4

[a] denotes significant Chi-Square (p <.05)

[b] denotes those reporting medication usage

[c] denote percent not returning in 2008-2009

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Table 2: General Study Parameters of Clusters 2008-2009 Wave (N = 438)

	Cluster 1 (N = 57)	Cluster 2 (N = 172)	Cluster 3 (N = 116)	Cluster 4 (N = 93)
Education	5.3 (2.2)†	4.6 (2.1)†	3.9 (1.9)*#	4.6 (2.1)
SES	54.7 (11.2)†	51.2 (14.0)	47.0 (13.7)*	50.3 (14.0)
BMI (kg/m^2)	26.9 (3.2)#†‡	28.5 (4.7)*	29.3 (5.2)*	29.2 (4.5)*
HADS-Depression	2.1 (1.8) †	3.2 (3.3)	3.6 (2.9)*	2.7 (2.8)
Smoking (% smokers)[a]	5.3	23.8	36.5	15.1
Hypertension Medication Use[ab]	12.3%	18.0%	30.2%	33.3%
Sex (% female)	52.6%	47.7%	58.6%	53.8%
Age	58.5 (1.0)	58.2 (0.9)	58.2 (0.9)	58.1 (0.9)
Alcohol	9.9 (9.4)	10.3 (15.9)	9.7 (14.4)	8.7 (15.6)
Baseline SBP	132.6 (20.1)	127.1 (19.7)	127.4 (19.4)	127.4 (20.1)
Baseline DBP	70.0 (10.7)	66.4 (11.2)	67.4 (12.7)	66.4 (11.9)
Baseline HR	75.8 (9.5)	73.8 (10.0)	74.2 (10.7)	7.4 (10.1)

Note: Values are reported as Mean (SD). Differences denote p <.05 *different from Cluster 1, #different from Cluster 2, †different from Cluster 3, ‡different from Cluster 4

[a] denotes significant Chi-Square (p <.05)

[b] denotes those reporting medication usage

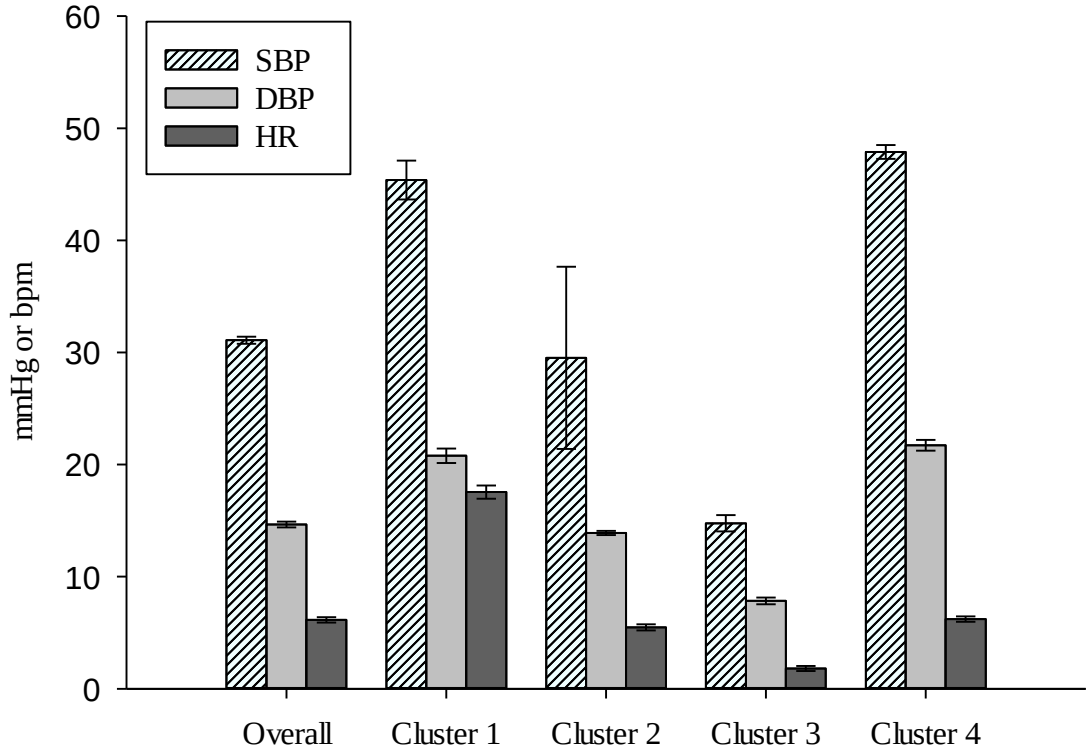
Table 3: Hazard Ratio of Physician Diagnosis of Hypertension by Stress Reactivity Cluster

Reactivity Clusters	HR[a] (95% CI), *p* Value	HR[b] (95% CI), *p* Value	HR[c] (95% CI), *p* Value
Cluster 1	1.00 (reference)	1.00 (reference)	1.00 (reference)
Cluster 2	1.23 (0.66-2.29), 0.50	1.11 (0.57-2.15), 0.77	0.88 (0.45-1.73), 0.70
Cluster 3	1.71 (0.90-3.28), 0.10	1.22 (0.60-2.48), 0.59	1.17 (0.56-2.47), 0.68
Cluster 4	2.98 (1.50-5.90), <.01	2.24 (1.07-4.69), 0.03	2.17 (1.04-4.55), 0.04

[a]HR, unadjusted

[b]HR, adjusted for hypertension medication at stress testing phase 2002-2004

[c]HR, adjusted for education, SES, BMI, HADS-depression score, and smoking status


60
50
40
30
20
10
0
mmHg or bpm
SBP
DBP
HR
Overall
Cluster 1
Cluster 2
Cluster 3
Cluster 4

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