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Metabolically exaggerated cardiac reactions to acute psychological stress:
the effects of resting blood pressure status and possible underlying
mechanisms

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Running head: Exaggerated cardiac reactivity

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Abstract

The study aimed to: confirm that acute stress elicits metabolically exaggerated increases in cardiac activity; test whether individuals with elevated resting blood pressure show more exaggerated cardiac reactions to stress than those who are clearly normotensive; and explore the underlying mechanisms. Cardiovascular activity and oxygen consumption were measured pre-, during, and post- mental stress, and during graded submaximal cycling exercise in 11 young men with moderately elevated resting blood pressure and 11 normotensives. Stress provoked increases in cardiac output that were much greater than would be expected from contemporary levels of oxygen consumption. Exaggerated cardiac reactions were larger in the relatively elevated blood pressure group. They also had greater reductions in total peripheral resistance, but not heart rate variability, implying that their more exaggerated cardiac reactions reflected greater β -adrenergic activation.

Descriptors: Additional cardiac output; Blood pressure; Exercise; Heart rate variability; Psychological stress; Total peripheral resistance;

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The reactivity hypothesis considers that large magnitude cardiovascular reactions to psychological stress contribute to cardiovascular pathology (Lovallo & Gerin, 2003; Schwartz, et al., 2003) and several prospective studies have shown that high reactivity confers an additional risk for outcomes such as hypertension, atherosclerosis, and increased left ventricular mass (e.g. Allen, Matthews, & Sherman, 1997; Barnett, Spence, Manuck, & Jennings, 1997; Carroll, Ring, Hunt, Ford, & Macintyre, 2003; Kamarck, et al., 1997; Lynch, Everson, Kaplan, Salonen, & Salonen, 1998; Markovitz, Raczynski, Wallace, Chettur, & Chesney, 1998; Treiber, et al., 2003). There is an apparent paradox, however; why should cardiovascular perturbations to psychological stress be associated with increased cardiovascular risk when broadly similar adjustments during physical exercise are rightly regarded as health protective and beneficial? One major possible difference is that the latter are ‘metabolically appropriate’ whereas the former may not be (Obrist, 1981). The earliest indications of such cardiac-metabolic uncoupling and ‘additional cardiac activity’ during stress came from two field studies. Heart rate and oxygen consumption were recorded in pilots during difficult flight manoeuvres (Blix, Stromme, & Ursin, 1974) and in novice parachutists just prior to jumping (Stromme, Wikeby, Blix, & Ursin, 1978); they were also measured during dynamic exercise. Heart rate increased to these stress exposures more than would be expected from contemporary levels of oxygen consumption and the association between cardiac changes and energy expenditure during exercise. Between the early 1980s and the early 1990s, there was a small flurry of laboratory studies suggesting that ‘additional heart rate’ (e.g., Carroll, Turner, & Hellawell, 1986; Carroll, Turner, & Prasad, 1986; Langer, et al., 1985; Turner & Carroll, 1985), as well as ‘additional cardiac output’ (e.g., Carroll, Harris, & Cross, 1991; Sherwood, Allen, Obrist, & Langer, 1986) was evident during various stress tasks including mental arithmetic, video games, and aversive reaction time avoidance tasks.

However, others remained skeptical (Brener, 1987) and given the continuing popularity of the reactivity hypothesis and the importance of the presumption that, in contrast to physical activity, psychological stress elicits metabolically-exaggerated cardiac adjustments, we recently revisited the issue. Cardiac output was measured

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using Doppler echocardiography, and oxygen consumption using mass spectrometry, at rest, during and after a mental stress task and during graded sub-maximal exercise (Carroll, Phillips, & Balanos, 2009). Large increases in cardiac output were observed during stress exposure in the context of very modest rises in energy expenditure; observed cardiac activity during stress exceeded by 2.6 L/min that predicted on the basis of contemporary levels of oxygen consumption.

Numerous further questions arise. For example, what are the mechanisms underlying such metabolically exaggerated cardiac responses? Two candidates immediately present themselves: increased β -adrenergic activation and parasympathetic withdrawal. Propranolol, a β -adrenergic antagonist, has been observed to block the exaggerated cardiac output reaction to an aversive reaction time task (Sherwood et al., 1986). However, others have observed that respiratory sinus arrhythmia decreased during a mental arithmetic stress, signifying parasympathetic withdrawal, but only when there was no requirement to vocalise the answers (Sloan, Korten, & Myers, 1991). The present study sought to further examine mechanisms underlying metabolically exaggerated cardiac responses by measuring heart rate variability to index parasympathetic withdrawal and blood pressure to allow the derivation of total peripheral resistance; decreases in resistance signify reduced α -adrenoreceptor activation and/or increased β -adrenoreceptor activation whereas increases in resistance implicate α -adrenergic activation (Joyner & Dietz, 2003). It was hypothesised that exaggerated cardiac activity would largely be a function of increased β -adrenergic activation, with a minor contribution from parasympathetic withdrawal.

The case control design, in which those at increased risk of developing, for example, hypertension as a result of parental hypertension or because they have elevated, although sub-hypertensive, blood pressure levels are compared with those at lower risk, offers one means of testing the association between exaggerated cardiac activity and likely future pathology. On balance, previous studies point to higher cardiovascular reactivity in those, who although normotensive, are at higher risk of developing hypertension (for a meta-analytic review, see Fredrikson & Matthews, 1990). However, only two studies have examined this issue in the specific context of

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additional cardiac activity. The first showed that young healthy participants with mildly elevated resting blood pressure showed greater additional heart rate reactions to stress than unambiguously normotensive controls (Sims & Carroll, 1990). The second demonstrated that the same was true for additional cardiac output (Carroll et al., 1991). We decided to re-visit this issue with the technology used in our recent study of additional cardiac activity (Carroll et al., 2009).

The present study had several aims. First, we were concerned to independently replicate our recent findings that increases in cardiac activity during acute psychological stress were metabolically exaggerated (Carroll et al., 2009). Second, the present study also examined, in the context of additional cardiac activity, whether individuals with mildly elevated but normotensive resting blood pressures showed greater additional cardiac reactions than unambiguously normotensive individuals. Third, interest also lay in the mechanisms underlying additional cardiac activity. By deriving total peripheral resistance and measuring heart rate variability, it was possible to examine both increased β -adrenergic activation and enhanced vagal withdrawal as possible mechanisms. Fourth, we were interested not only in the role of these mechanisms in helping generate additional cardiac reactivity but also in the extent to which differential β -adrenergic activation or differential vagal withdrawal best explained the expected differences in additional cardiac reactivity between individuals with high and low resting blood pressure. It was hypothesised that: 1) cardiac reactions to acute psychological stress would be metabolically exaggerated; 2) normotensive participants with mildly elevated resting blood pressure would show greater additional cardiac output during stress than controls who were unambiguously normotensive; 3) there would be evidence of increased β -adrenergic activation and enhanced vagal withdrawal during the stress task; 4) the greater additional cardiac activity in participants with mildly elevated resting blood pressure would largely reflect increased β -adrenergic drive (Schneider, Jacobs, Gevirtz, & O'Connor, 2003).

Methods

Participants

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An initial pool of 246 healthy male undergraduates was recruited from notice board advertisements across the University of Birmingham to an initial blood pressure screening session. After a 5-minute period of relaxed sitting, three blood pressure readings were taken at 1-minute intervals from the left arm using a brachial cuff and an Omron (model M5-I) semi-automatic sphygmomanometer. Resting systolic (SBP) and diastolic (DBP) blood pressure were determined as the average of the last two readings. Twenty-two of those screened were invited and agreed to participate in a laboratory stress and exercise testing session; 11 were regarded as having relatively high blood pressure (SBP > 130 mmHg) but below accepted criteria for the diagnosis of hypertension and 11 were deemed to be unambiguously normotensive (SBP < 120 mmHg). The summary characteristics of the two groups are presented in Table 1. They did not differ in age, height, weight, or body mass index. As would be expected, they differed on screening SBP, $F(1,20) = 50.97$, $p < .001$, $\eta^2_p = .718$, and DBP, $F(1,20) = 7.84$, $p = .01$, $\eta^2_p = .282$. Women were excluded from the study for four reasons: their low prevalence of elevated resting blood pressure (Carroll et al., 1991); the possibility of variations in reactivity with menstrual cycle phase (Hastrup & Light, 1984; Stoney, Matthews, McDonald, & Johnson, 1988); the sensitivities involved in thoracic scanning; and our aim to replicate our previous study (Carroll et al., 2009). None of the participants smoked, had a history of cardio-respiratory disease, a current illness or infection, nor was taking prescribed medication. They were required to refrain from consuming food or caffeine within two hours and from alcohol intake and vigorous exercise within 12 hours of the laboratory testing session. The study was approved by the relevant Research Ethics Committee.

[Insert Table 1 about here]

Design

This was a multi-condition within-subject study. Briefly, following instrumentation and instruction, participants were allowed approximately 20 minutes to adapt to the laboratory environment. This was followed by an 8-minute formal resting baseline, an 8-minute psychological stress task, and a 20-minute resting recovery period (since

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recovery for most of the variables of interest occurred within the first eight minutes of the recovery period, only these minutes feature in the analyses). Finally, another 4-minute resting baseline period was followed by four 4-minute bouts of cycle exercise of incrementally increasing demand.

Stress and Graded Sub-maximal Exercise Tasks

The psychological stress task was the paced auditory serial addition test (PASAT) (Gronwall, 1977) which demonstrates good test-retest reliability (Willemsen, et al., 1998). Briefly, via audio CD, participants were presented with a series of single digit numbers and required, in each case, to add any given number to the number presented next while in each case retaining the prior number in memory in order to add it to the next number presented. They indicated their answer by depressing the appropriate number (2 through 18) on a locally fabricated key pad, and this answer was then relayed to a computer screen in view of both participant and experimenter. This version of the PASAT consisted of four consecutive 2-minute periods of 50, 65, 75 and 100 digits at presentation rates of 2.4, 2.0, 1.6, and 1.2 seconds, respectively. An experimenter stood 1-metre distant from and adjacent to the participants and ostentatiously scored their answers. The task also involved elements of competition, reward, and punishment. A leader board was displayed prominently and participants informed that they should attempt to beat the five scores on the board. They were awarded 1000 points at the start of the task but lost five points for every addition they got wrong or omitted to answer. The final points total served as the performance score. Finally, they received a brief burst of loud, aversive noise once during the first five of every ten trials, coincident with an error where one was made or at the end of the series of five if no errors were made. This ensured that each participant received the same number of noise bursts. The addition of the loud noise component has been found to increase the effects of the PASAT on cardiovascular activity (Veldhuijzen van Zanten, et al., 2004). The mean performance score was 826 ($SD = 108.76$). On task completion, participants indicated on a 7-point rating scale (0 = not at all, 6 = extremely), how stressful and how difficult they found the task.

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Throughout the four 4-minute continuous bouts of sub-maximal aerobic exercise, participants pedaled at a constant 50 revolutions *per* minute, using the tachometer provided. For the first 4-minutes, there was no friction load on the wheel, but for the subsequent three exercise bouts increasing friction loads were applied to yield exercise power demands of 30, 60, and 90 watts respectively. All participants were able to meet these requirements.

Apparatus and Procedure

The study was conducted in a temperature controlled ($20 \pm 2^{\circ}\text{C}$) laboratory. Throughout the session, participants semi-reclined on a couch specifically designed for exercise echocardiography (Ergoselect 1000L, Ergoline GmbH, Bitz, Germany). The couch had an integrated cycle ergometer and the facility to tilt laterally to allow participants' hearts to be imaged. Participants remained tilted to the left for all measurements. Echocardiographic measurements were performed using a Philips Sonos 7500 ultrasound machine with an S3 two-dimensional transducer (1-3 MHz). Digital images of spectral waveforms were recorded continuously for later analysis. For each measurement point, averages were obtained from three or more spectral waveforms recorded at end-expiration or as close as possible to it. Measurements of aortic blood flow could be averaged across 60-second intervals. The electrocardiogram (ECG) and a respiratory waveform were also recorded. An apical five-chamber view of the heart was used with Doppler mode to identify flow through the aortic valve during systole. The velocity profile of the aortic flow was obtained using pulsed-wave spectral mode at a screen sweep speed of $100 \text{ mm}\cdot\text{s}^{-1}$, Doppler sampling of the flow was taken immediately below the orifice of the aortic valve. The flow was quantified automatically using the velocity time integral, which is the mean distance through which blood travels in the outflow tract during ventricular contraction. Each measurement of velocity time integral was made from at least three velocity profiles taken towards the end of expiration. The diameter of the aortic valve was measured from a parasternal long axis view and the aortic valve area was calculated. Stroke volume (SV) was calculated from velocity time integral \times the aortic valve area; cardiac output (CO) was calculated as heart rate (HR) \times SV. Heart

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rate variability (HRV) was obtained by sampling the ECG over 60-second epochs. Each R-wave to R-wave interval (IBI) was used to calculate the square root of the mean of the sum of the squared successive differences (RMSSD), using the formula $RMSSD (ms) = \sqrt{(1/n)\sum IBI_i - IBI_{i-1}^2}$, where i = the current IBI and n is the number of IBIs in a 60-second epoch. Blood pressure was recorded every two minutes throughout the protocol using the same device employed in the screening session. From mean arterial pressure (MAP), computed as $1/3SBP + 2/3 DBP$, total peripheral resistance (TPR) was calculated using the formula: $TPR = (MAP/CO) \times 80$.

Metabolic rate, indexed by oxygen consumption (VO_2), was measured on a breath-by-breath basis by assessing ventilation and analyzing inspired and expired gas composition using an integrated system. The apparatus used to supply air and measure ventilation was the mouthpiece assembly. Its key components were a turbine (VMM 400, Interface Associates, Laguna Niguel, CA, USA) to measure the volume of inspired and expired gas and a pneumotachograph (Hans Rudolf, KS, USA) to determine flow and respiratory timings. Gas composition was analyzed by a fast responding quadrupole mass spectrometer (Airspec, QP2000, Airspec, Kent, UK). All data were recorded on a computer running proprietary software.

Data Reduction and Statistical Analyses

Cardiac and metabolic data are presented on a minute-to-minute basis, blood pressure and TPR every two minutes. The psychological stress (8-minute baseline, 8-minute stress task, and 8-minute recovery) and exercise (4-minute rest, and four 4-minute exercise bouts) data were analysed separately using repeated measures ANOVA, with blood pressure status groups as a between subject factor. The Greenhouse-Geisser correction was applied and partial η^2 is reported as a measure of effect size. Predicted CO during initial baseline, the stress task, and recovery were computed from the individual regressions of VO_2 on CO during the last two minutes of the pre-exercise rest and the last two minutes of each of the four exercise bouts. The final two minutes were chosen in each case as this would assure a steady state. The 22 regression coefficients were uniformly large (β s ranged from 0.82 to 1.00, and the mean β , calculated using the z transformation, was 0.97). By entering VO_2 values separately

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for each minute of the 8-minute baseline, 8-minute stress task, and 8-minute recovery into the individual regression equations, predicted CO values were generated for each of these minutes. Additional CO is the difference between actual and predicted CO. Again, repeated measures ANOVA, with blood pressure status group as a between subjects factors, was applied to the additional CO data. Finally, average additional CO values during stress were computed as the overall mean of the eight values. Reactivity values for TPR and HRV were calculated as the mean of the values during the stress task minus the mean of the baseline values. ANCOVA was applied to determine the extent to which any group differences in additional CO during stress could be accounted for by variations in TPR and HRV reactivity. Inspection of the raw ECG indicated that one of the participants had a high frequency of ectopic beats and, accordingly, was excluded from the analysis.

Results

Stress task impact

The high resting blood pressure group did not differ significantly from the unambiguously normotensive group in terms of stress task performance, 835 (106.99) versus 819 (120.02), nor on the ratings of task stressfulness, 4.0 (1.25) versus 3.7 (0.90), and difficulty, 3.8 (1.13) versus 4.2 (0.87), F_s all < 1 .

Cardiac activity

The HR, SV, and CO data for the two blood pressure status groups before, during, and after the stress task are depicted in Figure 1. For HR and SV, there were significant main effects of time, $F(23,437) = 78.12$, $p < .001$, $\eta^2_p = .804$ and $F(23,437) = 68.55$, $p < .001$, $\eta^2_p = .779$ respectively, and significant time \times groups interaction effects, $F(23,437) = 8.85$, $p < .001$, $\eta^2_p = .318$ and $F(23,437) = 2.80$, $p = .03$, $\eta^2_p = .128$. The relatively high blood pressure group showed greater increases in HR and SV to the stress task. In neither case was the main effect of groups significant. For CO, there was a main effect of time, $F(23,437) = 119.79$, $p < .001$, $\eta^2_p = .863$, a near significant main effect of groups, $F(1,19) = 3.77$, $p = .07$, $\eta^2_p = .166$, and a significant time \times groups interaction effect, $F(23,437) = 11.45$, $p < .001$, $\eta^2_p = .376$. Thus, as

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would be expected from the outcome of the analyses of CO's constituent parts, the relatively high blood pressure group exhibited larger increases in CO to the PASAT. The summary HR, SV, and CO data for the exercise phase of the study are also presented in Figure 1. In each case, there was a significant effect of time, $F(19,361) = 263.59$, $p < .001$, $\eta^2_p = .933$, $F(19,361) = 44.70$, $p < .001$, $\eta^2_p = .702$, and $F(19,361) = 211.31$, $p < .001$, $\eta^2_p = .918$, for HR, SV, and CO, respectively. There were no main effects for groups and only for HR was there a significant time \times groups interaction effect, $F(19,361) = 2.47$, $p = .04$, $\eta^2_p = .115$; HR tended to rise faster at the beginning of each exercise level for the relatively high blood pressure group.

[Insert Figure 1 about here]

Metabolic activity

The VO_2 data for the two blood pressure status groups before, during, and after the stress task are presented in Figure 2. The only significant effect to emerge from ANOVA was a main effect of time, $F(23,437) = 9.24$, $p < .001$, $\eta^2_p = .327$. VO_2 rose during the stress task. The exercise data are also summarised in Figure 2. As can be seen, VO_2 increased in a progressive fashion with increasing exercise load, $F(19,361) = 712.19$, $p < .001$, $\eta^2_p = .974$. There was no main effect for groups, nor a significant time \times groups interaction effect.

[Insert Figure 2 about here]

Additional cardiac output

The summary data for additional CO, derived as the difference between actual cardiac activity during the stress phase of the study and cardiac output predicted on the basis of individual VO_2 and CO regressions during exercise and stress phase VO_2 values, are presented in Figure 3 for each of the blood pressure groups. Analysis revealed a main effect of time, $F(23,437) = 100.25$, $p < .001$, $\eta^2_p = .841$, and a significant time \times groups interaction effect, $F(23,437) = 11.83$, $p < .001$, $\eta^2_p = .384$. The relatively high

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blood pressure group showed almost twice the additional CO during the stress task as the unambiguously normotensive group. There was no main effect of groups.

[Insert Figure 3 about here]

Blood pressure and total peripheral resistance

The patterns of SBP, DBP, and TPR at baseline, during stress, and in recovery for the two groups are displayed in Figure 4. For SBP and DBP, only the effect of time was significant, $F(11,209) = 32.43$, $p < .001$, $\eta^2_p = .631$ and $F(11,209) = 15.97$, $p < .001$, $\eta^2_p = .457$, respectively. Analysis of TPR also yielded a significant effect of time, $F(11,209) = 59.05$, $p < .001$, $\eta^2_p = .757$. However, in this instance there was also a significant time \times groups interaction effect, $F(11,209) = 4.36$, $p = .002$, $\eta^2_p = .186$; the relatively high blood pressure group showed a more profound decrease in TPR during the stress task. The summary statistics for SBP, DBP, and TPR during exercise are also presented in Figure 4. Only the main effects of time were significant, $F(9,171) = 27.91$, $p < .001$, $\eta^2_p = .595$ for SBP, $F(9,171) = 10.91$, $p < .001$, $\eta^2_p = .365$ for DBP, and $F(9,171) = 74.01$, $p < .001$, $\eta^2_p = .796$ for TPR.

[Insert Figure 4 about here]

Heart rate variability

Figure 5 presents the summary HRV data during all conditions of the study. Analysis of the baseline, stress, and recovery values yielded only a significant main effect of time, $F(23,437) = 7.68$, $p < .001$, $\eta^2_p = .288$. However, there was a tendency for the normotensive group to show a larger reduction in RMSSD HRV during stress, which was reflected in a nearly significant time \times groups interaction effect $F(23,437) = 2.19$, $p = .08$, $\eta^2_p = .103$. During exercise, only the effect of time was significant, $F(19,361) = 19.37$, $p < .001$, $\eta^2_p = .505$; RMSSD HRV declined with the onset of exercise.

[Insert Figure 5 about here]

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Accounting for additional cardiac activity

As indicated, two candidate mechanisms underlying additional cardiac activity during acute stress are alpha withdrawal/ β -adrenergic activation, as indexed by reduced TPR, and parasympathetic withdrawal, as indexed by decreases in RMSSD HRV. First, a simple ANOVA was run to compare the two blood pressure groups on the average additional CO during the stress task. As would be expected, there was a significant group difference, $F(1,19) = 15.46, p = .001, \eta^2_p = .449$; the additional CO means (SD) for the relatively high blood pressure group and the normotensive group were 3.5 (0.97) L/min and 1.8 (0.94) L/min, respectively. This analysis was repeated but with TPR reactivity entered as a covariate. The group difference in additional CO was no longer statistically significant and the effect size was attenuated by 66%, $F(1,18) = 3.24, p = .09, \eta^2_p = .152$. Average additional CO and TPR reactivity were strongly negatively correlated, $r(19) = -.81, p < .001$; the greater the additional CO, the larger the decrease in TPR. A somewhat different picture emerged when HRV was examined in a similar fashion. The blood pressure status group difference in additional CO during stress remained significant following adjustment for HRV reactivity, $F(1,18) = 12.25, p = .003, \eta^2_p = .405$, and the effect size was only marginally attenuated. The correlation between additional CO during stress and HRV stress reactivity was positive, but not statistically significant, $r(19) = .27, p = .23$.

Correcting for Body Surface Area

CO and TPR values were individually corrected for body surface area calculated as $\sqrt{(\text{height (cm)} \times \text{weight (kg)}) / 3600}$ (Mosteller, 1987). The mean (SD) surface area in metres² for the relatively high and relatively low blood pressure groups was the same for the two groups: 1.95 (0.12) m² in both cases. Accordingly, it is hardly surprising that when we re-visited the stress task analyses using these corrected values for CO and TPR virtually identical outcomes emerged to those reported above.

Discussion

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Using relatively novel technology (Doppler echocardiography and mass spectrometry) in this context, the present results confirm that cardiac reactions to acute psychological stress are metabolically exaggerated. They also showed that normotensive individuals with mildly elevated resting blood pressure exhibited greater additional cardiac output during stress than controls who were unambiguously normotensive. Further, there was evidence of both increased β -adrenergic activation and enhanced vagal withdrawal during acute stress. Finally, the greater additional cardiac activity in participants with mildly elevated resting blood pressure was largely explained by increased β -adrenergic drive and not by greater vagal withdrawal.

As such, the present results confirm those reported from earlier research (e.g., Carroll et al., 1991; Sherwood et al., 1986) as well as the findings of our recent study (Carroll et al., 2009). Whereas during graded exercise cardiac activity increased progressively with increased exercise load and the concomitant changes in VO_2 , psychological stress provoked substantial increases in cardiac activity in the context of very modest rises in metabolic activity. Thus, the changes in cardiac activity during psychological stress would indeed appear to be metabolically exaggerated. The extent of this exaggeration can be gleaned from the derived additional CO values; the mean additional CO during psychological stress was 2.6 L/min. Not only does this indicate that the extent of exaggerated cardiac reactions to psychological stress is far from trivial, it precisely replicates the mean value that we observed in our previous study using the same methodology (Carroll et al., 2009). Our stress task was also unsurprisingly associated with increases in SBP and DBP, as well as decreases in TPR and reduced RMSSD HRV. The 8-minute PASAT has previously been shown to elicit a decrease in TPR (Ring, et al., 1999), although with longer exposure, there is an eventual increase in TPR (Ring, Burns, & Carroll, 2002). Similarly, we have previously demonstrated a decrease in RMSSD HRV to the 8-minute PASAT (Ring, et al., 1999) as have others using different stress tasks (e.g., Sloan et al., 1991).

As hypothesised, the group with relatively elevated resting SBP at screening exhibited greater cardiac responses to the stress task than the group who were unambiguously normotensive. The groups did not, however, differ in VO_2 during stress. Thus, as confirmed by the additional CO data, the elevated resting blood

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pressure group showed more exaggerated CO reactions during stress. Indeed, their average stress-induced additional CO was almost twice that of the unambiguously normotensive group. This extends the findings of our earlier study (Carroll et al., 1991) in which additional CO to mental stress was observed for participants who had mildly elevated blood pressure but not for those who were normotensive. However, the magnitude of the cardiac perturbations elicited by the present stress task was substantially greater than those apparent in the earlier study. Thus, it would appear that with a sufficiently provocative stress exposure, even normotensive individuals show an exaggerated cardiac response, albeit to a much lesser extent than those with moderately elevated resting blood pressure. Contrary to expectations, the groups did not differ in their blood pressure reactions to stress (Fredrikson & Matthews, 1990). However, this result finds support in our earlier study comparing similar resting blood pressure status groups; as now, the time \times groups interaction effects for SBP and DBP were not significant (Carroll et al., 1991). In the present study, the TPR data afford an explanation. In addition to more exaggerated cardiac output reactions to stress, the moderately elevated resting blood pressure group showed more marked decreases in TPR: the net effect of this was a broadly similar blood pressure response in the two groups. It is worth emphasising here that our participants were all healthy undergraduate students with a healthy distensible vasculature. The question arises as to whether such off-setting would occur in older individuals with increased arterial wall stiffness. The two groups showed similar cardiovascular reactions to exercise, with one exception. HR tended to rise faster at the beginning of each exercise level for the relatively high blood pressure group. Thus, on the whole, the marked group differences in cardiac reactivity would seem to be mainly manifest during exposure to psychological stress.

The TPR data also provide a clue as to the mechanisms underlying the greater additional cardiac reactions to stress observed in those with mildly elevated screening blood pressures. The pattern of results for TPR, particularly the findings that adjustment for TPR reactivity abolished the significant group difference in additional CO during stress and the substantial negative correlation between average additional CO during stress and TPR reactivity, implicates variations in β -adrenergic activation

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as a major determinant of individual variations in exaggerated cardiac reaction. However, caution needs to be exercised, given that TPR is not directly measured but derived from MAP and CO and thus the group differences in TPR reactivity almost inevitably flow from the group differences in CO reactivity and the failure to find group differences in blood pressure reactivity. Although, as indicated, RMSSD HRV decreased during stress, indicative of vagal withdrawal, the groups did not differ significantly in HRV during stress. Further, adjustment for HRV reactivity had little impact on the group difference in additional CO during stress and HRV reactivity was not significantly correlated with stress-induced additional CO. Thus, although vagal withdrawal would appear to contribute to the overall cardiac response to stress, variations in vagal withdrawal would not seem to underlie, to any great extent, individual variations in the magnitude of exaggerated cardiac reactions to stress. These novel findings add considerably to our understanding of the mechanisms underlying enhanced cardiac reactivity in individuals with mildly elevated resting blood pressure. That the greater additional cardiac reactions in those with mildly elevated resting blood pressure is best accounted for by increased β -adrenergic activation also resonates with the contention that individuals with elevated but sub-clinical resting blood pressure are often characterised by a hyperkinetic cardiovascular state caused by excessive sympathetic drive (Julius et al., 1991). In the young and healthy, it would appear to be the β -adrenergic branch of the sympathetic nervous system that is especially hyperkinetic. However, in future studies, the measurement of systolic time intervals especially the pre-ejection period of the heart would help further resolve matters of mechanism.

The conclusions above are subject to a necessary *caveat*. Although the blood pressure groups differed in both resting SBP and DBP at screening, they did not differ in terms of baseline blood pressure during the stress testing session. However, it was not that blood pressure levels dropped between screening and stress testing for the group with moderately elevated blood pressure at screening. Rather, resting blood pressure levels were higher in the laboratory than at screening for the other group. One explanation here is that formal laboratory setting and the anticipation of the impending stress task differentially raised resting blood pressure in the group with

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lower pressure at the more informal screening session. This could be regarded as an instance of the 'white coat' effect, where individuals have transient and context-specific elevations in resting blood pressure. Alternatively, it is also possible that the group with the elevated screening blood pressure experienced a 'white coat' effect at screening and that their elevated screening blood pressures were not necessarily representative. However, this seems the less likely alternative given that normotensives who display such 'white coat' elevations in resting blood pressure have been found not to differ from other normotensives in the magnitude of their cardiovascular reactions to psychological stress (Pickering, et al., 1988). Were the 'white coat' participants those with the elevated screening blood pressure, they would not have been expected to show such markedly higher CO reactivity than the other group. Thus, the most parsimonious explanation for the present pattern of results is that it is those with consistently elevated resting blood pressure, both at screening and in the laboratory, who showed more exaggerated cardiac reactivity. It is perhaps worth noting that screening SBP and mean additional CO during stress were, as might be expected, correlated, $r(19) = .53, p = .01$; no such correlation was evident between average laboratory baseline SBP and additional CO during the stress task, $r(19) = -.19, p = .41$.

The study has a number of other limitations. First, the sample size was small. Nevertheless, it was of the same order as that tested in previous studies of additional cardiac activity in participants with and without moderately elevated resting blood pressure (Carroll et al., 1991; Sims & Carroll, 1990). Importantly, the sample was clearly sufficient to detect medium to large effects, as indicated by the effect sizes that characterise the key interactions. Indeed, the size of the key effects observed serve to strengthen the conclusions drawn. Second, we tested only men and this raises the issue of generalisability. Men and women have been found to differ in their HR reactions to the PASAT (Carroll, Phillips, Hunt, & Der, 2007) and thus the inclusion of women may have proved informative. However, testing men in this context is probably ecologically appropriate, as men have higher resting blood pressures than women at all adult ages and are more likely to develop hypertension (see, e.g., Wolf-

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Maier, et al., 2003). Nevertheless, it should be conceded that cardiovascular disease is a prominent cause of death in women across all age groups (CDC, 2010).

In conclusion, acute laboratory stress provoked increases in cardiac output that were substantially greater than would be expected on the basis of contemporary levels of energy expenditure. In addition, such exaggerated cardiac reactions were larger in individuals identified at screening to have relatively elevated resting blood pressure. Although the stress task elicited changes in both HRV and TPR, those with relatively elevated screening blood pressure showed greater reductions in TPR, but not HRV, during the psychological stress task. This implies that their more exaggerated stress-induced cardiac reactions for the most part reflected greater β -adrenergic activation.

Authors' Notes

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Table 1. Baseline characteristics of the two resting blood pressure group.

Variable	Relatively high BP group		Normotensive group	
	Mean	SD	Mean	SD
Age years	19.8	1.72	20.6	1.13
Height cm	178.8	7.79	181.5	5.07
Weight kg	76.3	7.17	75.7	8.25
Body mass index, kg/m ²	23.9	2.00	23.0	2.20
Screening SBP mmHg	137.1	8.51	112.7	7.53
Screening DBP	76.3	7.01	66.5	9.21

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Figure 1: Time course of cardiac activity (group means and standard errors)

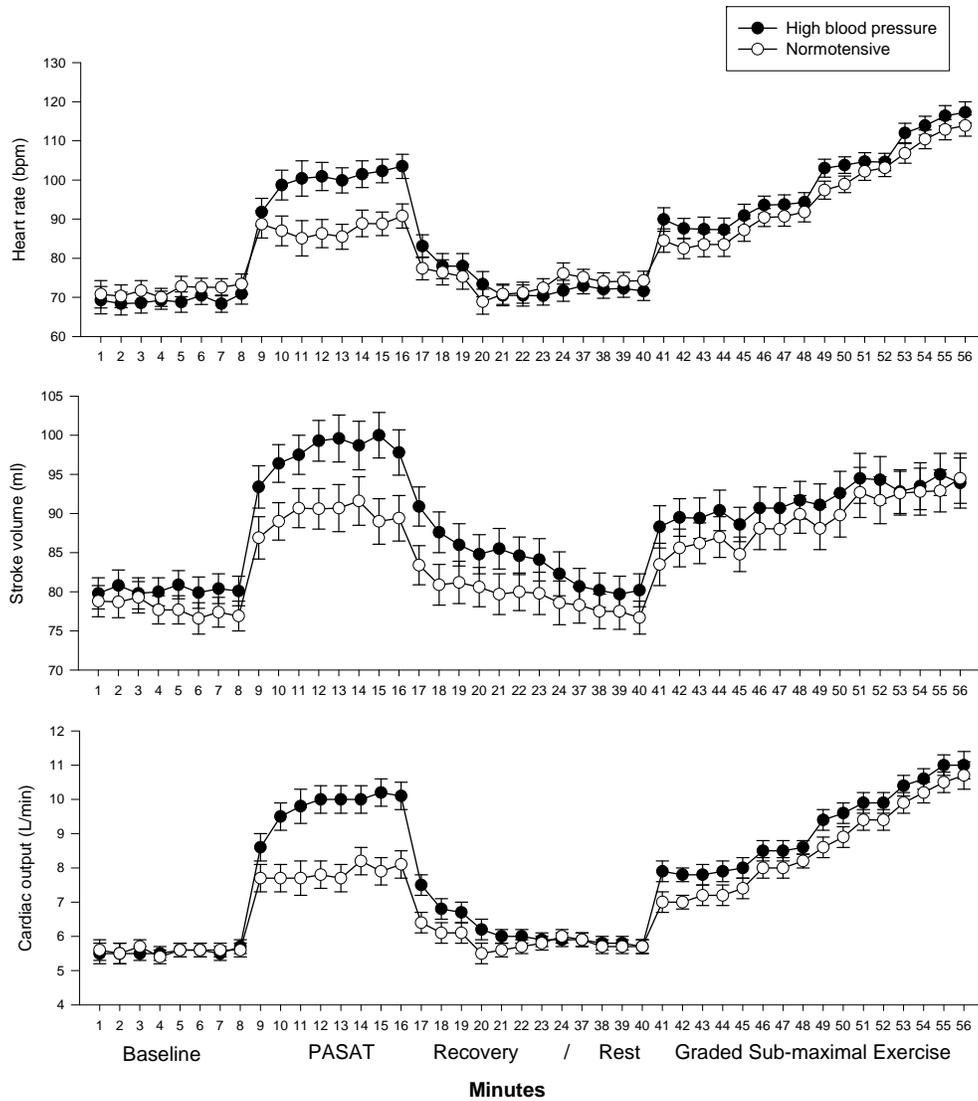
Figure 2: Time course of oxygen consumption (group means and standard errors)

Figure 3: Time course of additional cardiac output (group means and standard errors)

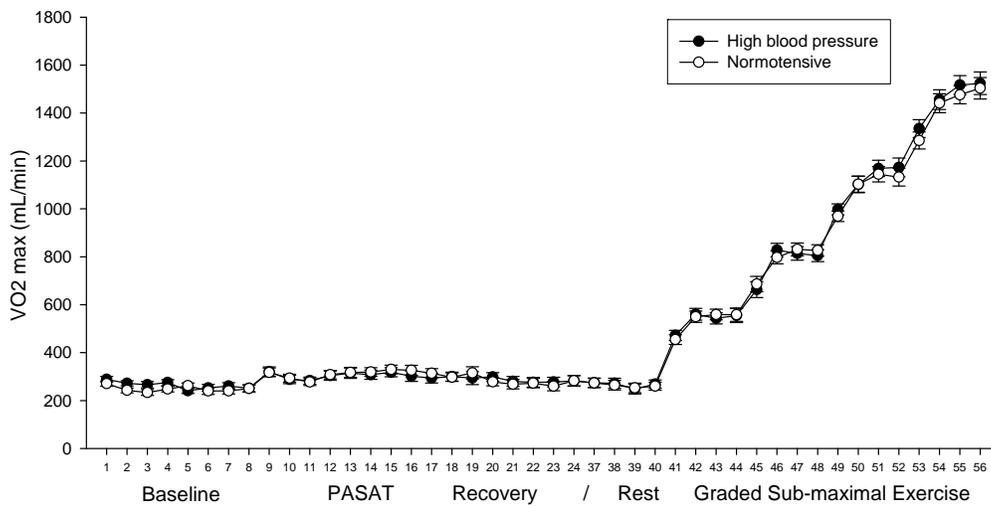
Figure 4: Time course of blood pressure and total peripheral resistance (group means and standard errors)

Figure 5: Time course of heart rate variability (group means and standard errors)

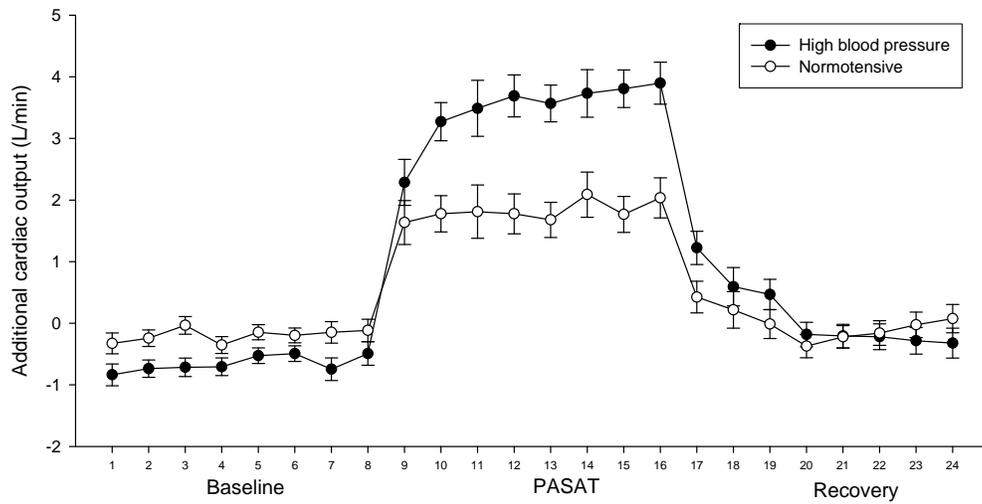
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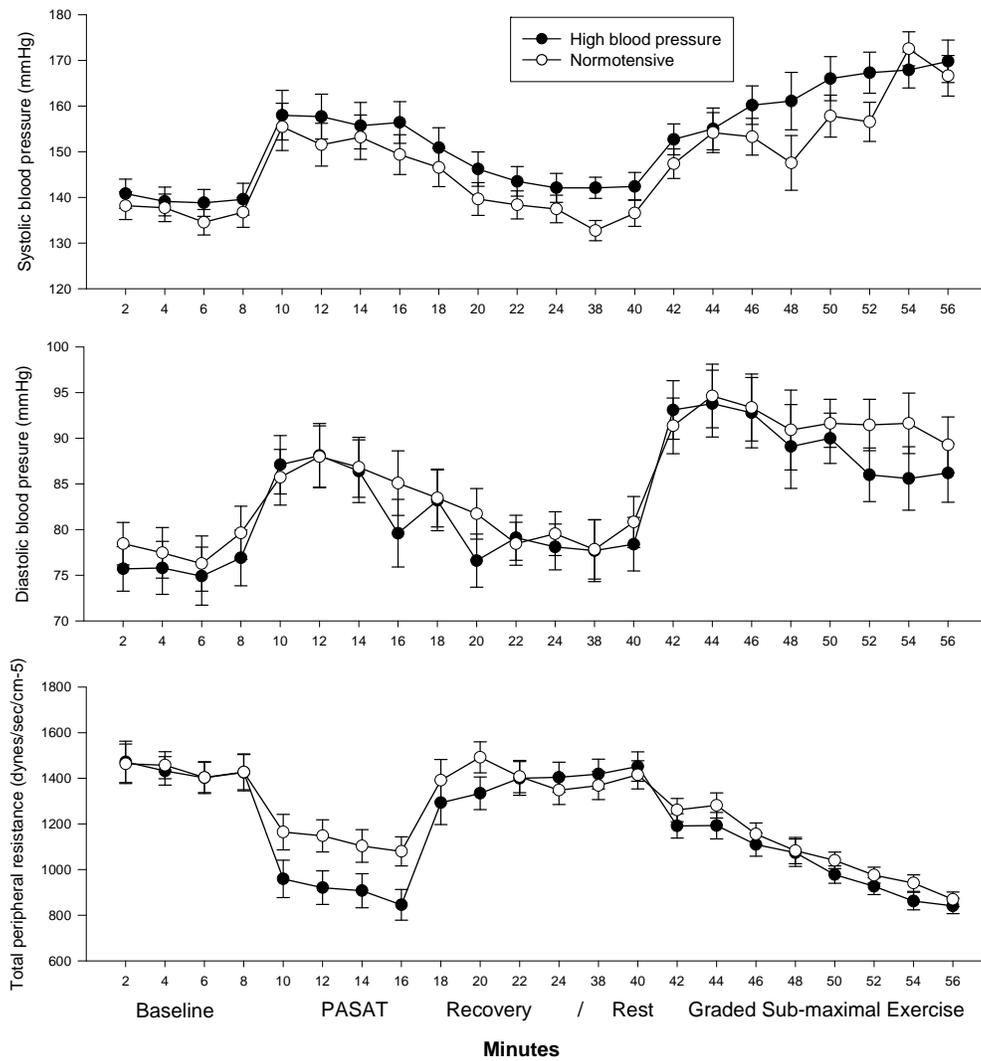
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