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Running Head: Cardiac Reactivity and Depression

Blunted cardiac reactions to acute psychological stress predict symptoms of depression five years later: Evidence from a large community study.

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Abstract

We recently reported a cross-sectional negative relationship between cardiovascular reactivity and depressive symptoms. The present analyses examined the prospective association between reactivity and symptoms of depression five years later. At the earlier time point depressive symptoms, using the Hospital Anxiety and Depression Scale (HADS), and cardiovascular reactions to a standard mental stress were measured in 1608 adults comprising three distinct age cohorts: 24-, 44-, and 63-year olds. Depression was re-assessed using the HADS five years later. Heart rate reactions to acute psychological stress were negatively associated with subsequent depressive symptoms; the lower the reactivity the higher the depression scores. This association withstood adjustment for symptom scores at the earlier time point, and for socio-demographic factors and medication status. The mechanisms underlying this prospective relationship remain to be determined.

Key words: Blood pressure; depression; heart rate; psychological stress; prospective study

Depression has been linked prospectively to mortality in general and death from cardiovascular disease in particular (for reviews, see Hemingway & Marmot, 1999; Wulsin, Vaillant, & Wells, 1999). However, the mechanisms underlying this association have yet to be established. Autonomic dysregulation remains a possibility, and depression has been associated with a variety of adaptations that suggest altered autonomic function. For example, enhancement of cardiac sympathetic activity relative to vagal tone has been reported in those with depression and subclinical depressive symptoms (Carney, et al., 1988; Light, Kothandapani, & Allen, 1998), as have increased plasma noradrenalin concentrations in patients with major depression (Rudorfer, Ross, Linnoila, Sherer, & Potter, 1985). Thus, the hypothesis that such autonomic dysregulation in depression may also be manifest as exaggerated cardiovascular reactivity (Kibler & Ma, 2004), which in turn increases the risk of cardiovascular pathology, is intuitively appealing.

First, exaggerated cardiovascular (blood pressure and heart rate) reactions to acute psychological challenge have long been considered a risk factor for cardiovascular pathology (Lovallo & Gerin, 2003; Schwartz, et al., 2003) and several prospective studies have now shown consistently that higher cardiovascular reactivity (most commonly blood pressure and heart rate, and additionally cardiac output, stroke volume, total peripheral resistance, and pre-ejection period when measured) confers a modest additional risk for a range of cardiovascular outcomes, such as high blood pressure, carotid atherosclerosis, carotid intima-thickness, 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). Second, a meta-analysis of 11 relevant studies found moderate effect sizes indicative of a positive relationship between depressive symptomatology and heart rate reactivity, and small effect sizes linking more depressive symptoms with higher systolic and diastolic blood pressure reactions to acute psychological stress (Kibler & Ma, 2004). However, none of the aggregate effect sizes from the meta-analyses were statistically significant at conventional levels. In addition,

the studies included in the meta-analysis generally tested fairly small samples and were often conducted on patients with established cardiovascular disease. Further, few of these studies adjusted for potential confounding variables such as demographic factors and medication status.

Two subsequent larger scale studies have addressed the issue, one in a large community sample of over 1600 participants from the West of Scotland Twenty-07 Study measuring depressive symptoms and blood pressure and heart rate reactions to acute stress (Carroll, Phillips, Hunt, & Der, 2007) and the other in a coronary artery disease patient sample of over a 100 again measuring depressive symptoms and blood pressure and heart rate reactivity (York, et al., 2007). In both studies, higher depressive symptom scores were associated with lower, not higher, cardiovascular reactions to acute psychological stress. In the former, cardiovascular reactivity and symptoms of anxiety were also negatively related. What is especially compelling about these findings is that the associations were still evident following adjustment for a relatively comprehensive range of covariates. Nevertheless, both studies were cross-sectional and so direction of causality was impossible to determine. Below we report a prospective analysis from the Twenty-07 Study. The associations between cardiovascular reactivity and symptoms of depression and anxiety five years later were examined. Based on our previous cross-sectional findings, it was hypothesised that participants with higher reactivity would be less, not more, likely to report symptoms of depression and anxiety at subsequent follow-up.

Methods

Participants

Participants were resident in Glasgow and the surrounding areas in Scotland at the baseline survey of the West of Scotland Twenty-07 Study in 1987; they have been followed up at regular intervals since (Benzeval, et al., 2008). The achieved sample size at entry to the Regional study was 3036. Cardiovascular reactions to an acute psychological challenge were measured at the third follow-up in 1995-7 (Carroll, et al., 2000; Carroll, et al., 2003). Reactivity data were available for 1647 participants, with

scores for depression and anxiety symptomatology recorded for 1608 and 1607 of these respectively. Participants comprised three distinct age cohorts born in the early 1970s, 1950s and 1930s: of the 1608, 575 (36%) were aged around 24-years, 606 (38%) 44-years, and 427 (26%) 63-years; 875 (54%) were women and 733 (46%) men; and 746 (47%) were from manual and 851 (53%) non-manual occupation households. Household occupational status, an accepted index of socio-economic position, was classified as manual or non-manual from the occupational status of the head of household, using the Registrar General's (1980) classification of occupations. For the youngest of the three cohorts, head of household was either the participant, if working and living independently, or the parent, if the participant was a student or lived with their parents. For the other two cohorts, head of household was either the participant or his/her spouse/partner, depending on which of the two held or had held the highest occupational status; this was usually the man. A comparison of the three cohorts with equivalent samples drawn from the 1991 UK census revealed equivalence in terms of sex, occupational group, and home ownership (Der, 1998). The sample was almost entirely Caucasian, reflecting the West-of-Scotland population from which it was drawn. As revealed during structured interview conducted by nurses trained in survey techniques, only 71 (4%) and 46 (3%) of the sample were taking antidepressants and anxiolytic medication, respectively. The mean age of the whole sample at the third follow-up was 42.3 (SD = 15.48) years.

Measurement of depression and anxiety

Symptoms of depression and anxiety were measured at both the third and fourth follow-ups using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). At the fourth follow-up, data were available for 1245 participants. Thus, the attrition rate was 23% between these two time points. The mean (SD) temporal lag between the two follow-ups was 5.5 (SD = 1.00) years. The HADS is a well-recognised assessment instrument that comprises 14 items, seven measuring depression and seven measuring anxiety. The depression subscale emphasises anhedonia and largely excludes somatic items. Items are scored on a 4-point scale, 0 to 3; the higher the score, the greater the depression and anxiety. The HADS has good concurrent validity (Bramley,

Easton, Morley, & Snaith, 1988; Herrmann, 1997), performs well as a psychiatric screening device (Bjelland, Dahl, Haug, & Neckelmann, 2002; Herrmann, 1997), and boasts acceptable psychometric properties; for example, a Cronbach's α of .90 for the depression items and .93 for the anxiety items has been reported (Moorey, et al., 1991) and test-retest reliability coefficients as high as .85 for depression and .84 for anxiety have been found over two weeks, and .70 for over periods greater than six weeks (Herrmann, 1997).

Apparatus and procedure

Participants were tested in a quiet room in their own homes by trained nurses. Demographic information was obtained by interview. At the end of a lengthy interview and questionnaire session, participants undertook an acute psychological challenge: the paced auditory serial addition test (PASAT), which has been shown in numerous studies to reliably perturb the cardiovascular system (Ring, Burns, & Carroll, 2002; Ring, et al., 1999; Winzer, et al., 1999) and to demonstrate good test-retest reliability (Willemsen, et al., 1998). Participants were presented with a series of single digit numbers by audiotape and requested to add sequential number pairs while retaining the second of the pair in memory for addition to the next number presented, and so on throughout the series. Answers were given orally and, if participants faltered, they were instructed to recommence with the next number pair. The total number of correct answers was recorded as a measure of performance. The first sequence of 30 numbers was presented at a rate of one every four seconds, and the second sequence of 30 at one every two seconds. The whole task took three minutes, two minutes for the slower sequence and one minute for the faster sequence. The nurses were all trained in the PASAT protocol by the same trainer. They followed a written protocol during every testing session. In the present sample, all participants registered a score and completed the whole PASAT. Out of a possible score of 60, the median score was 45 (Inter-quartile range = 11).

Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were determined by an Omron (model 705CP) sphygmomanometer. This is one of the semi-automatic blood pressure measuring devices recommended by the European

Society of Hypertension (O'Brien, Waeber, Parati, Staessen, & Myers, 2001). Following interview (which took at least an hour), there was then a formal 5-minute period of relaxed sitting, at the end of which a resting baseline reading of SBP, DBP, and HR was taken. Task instructions for the PASAT were then given and the participant allowed a brief practice to ensure that they understood task requirements. Two further SBP, DBP, and HR readings were taken during the task, the first initiated 20 seconds into the task (during the slower sequence of numbers), and the second initiated 110 seconds later (at the same point during the fast sequence). For all readings, the nurses ensured that the participant's elbow and forearm rested comfortably on a table at heart level. The two task readings were averaged and the resting baseline value subsequently subtracted from the resultant average task value to yield reactivity measures for SBP, DBP, and HR for each participant.

Data reduction and analyses

Differences in depression and anxiety at the fourth follow-up between age cohorts, sexes, and household occupational groups were explored using ANOVA. The main analysis was by regression, where symptoms of depression and anxiety at the later follow-up were the dependent variables. Initially, the bivariate associations between cardiovascular reactivity and symptomatology were examined using linear regression. Sensitivity analyses, using logistic regression, were then undertaken using binary variables derived from applying a cut-off of ≥ 8 on the depression and anxiety subscales of the HADS as an indicator of possible pathology (Zigmond & Snaith, 1983). Significant associations between reactivity and symptomatology emerging from the initial simple linear regression were then re-visited adjusting for HADS scores at the earlier follow-up. This was entered at step one in the hierarchical model, with reactivity entered at step 2. Next, a model was tested which additionally adjusted for age cohort, sex, household occupational group, PASAT performance score as an indicator of task engagement, anti-depressive medication status, and anti-hypertensive medication status.

Results

Socio-demographics, depression and anxiety

Since we have already reported the socio-demographic patterning of symptoms of depression and anxiety at the third follow-up in our earlier paper (Carroll, et al., 2007), the analyses reported below are necessarily restricted to the fourth follow-up HADS scores. The overall mean depression and anxiety scores at the fourth follow-up were 3.72 (SD = 3.14) and 6.77 (SD = 3.77), respectively. ANOVA yielded main effects for all three independent variables: the older two cohorts recorded higher depression scores than the youngest cohort, $F(2,1242) = 3.26, p = .04, \eta^2 = .005$; women had higher scores than men, $F(1,1243) = 6.66, p = .01, \eta^2 = .005$; those from manual occupational households had higher scores than those from non-manual households, $F(1,1243) = 9.12, p = .003, \eta^2 = .003$. The summary statistics are presented in Table 1. Analyses of the anxiety data also revealed significant main effects for cohort, $F(2,1242) = 8.78, p < .001, \eta^2 = .014$, sex, $F(1,1243) = 53.94, p < .001, \eta^2 = .042$, and occupational status, $F(1,1243) = 6.54, p = .01, \eta^2 = .005$. As with depression, women and those in the manual occupational group reported more symptoms of anxiety than men and those in the non-manual group. However, in the case of anxiety, the oldest cohort had lower scores than the other two cohorts. There were no significant interactions between age cohort, sex, and household occupational group for depressive or anxiety symptoms.

[Insert Table 1 about here]

Cardiovascular reactions to acute psychological stress

Two-way (baseline \times task) repeated measures ANOVAs indicated that, on average, the PASAT significantly increased cardiovascular activity: for SBP, $F(1,1607) = 1564.08, p < .001, \eta^2 = .493$, for DBP, $F(1,1607) = 1048.71, p < .001, \eta^2 = .395$, and for HR, $F(1,1607) = 1108.77, p < .001, \eta^2 = .408$. The mean (SD) increases were 11.6 (11.72) mmHg SBP, 7.0 (8.61) mmHg DBP, and 8.2 (9.82) bpm HR. The mean baseline and stress values are presented in Table 2.

[Insert Table 2 about here]

Cardiovascular reactivity and future depression and anxiety symptomatology

In bivariate analyses, neither SBP nor DBP reactivity were related to HADS depression and anxiety scores five years later. However, HR reactivity was negatively associated with both depression, $\beta = -.10$, $t = 3.65$, $p < .001$, $R^2 = .010$, and anxiety symptomatology, $\beta = -.07$, $t = 2.50$, $p = .01$, $R^2 = .005$. These associations are shown in Figure 1. It is worth noting that all significant reported associations remained significant following supplementary analysis without individuals who could be deemed as outliers although their reactivity values were physiologically possible. The same associations were evident in the analyses of possible caseness; 180 (11%) and 606 (43%) met the possible caseness criteria for depression and anxiety, respectively, at wave 3, and 158 (13%) and 469 (38%) participants at wave 4, respectively. High HR, but not blood pressure, reactivity was protective against future depression and anxiety caseness; OR for each unit increase in HR reactivity (95%CI) = .98 (.97 – 1.00), $p = .05$, and OR (95%CI) = .99 (.97 – 1.00), $p = .02$, respectively.

[Insert Figure 1 about here]

Next we revisited the linear associations for HR reactivity above, but this time adjusting for HADS scores at the earlier follow-up. As indicated, we have already shown a cross-sectional relationship between cardiovascular reactivity and depression and anxiety (Carroll, et al., 2007). HADS scores at the two follow-ups were, as expected, correlated, $r(1218) = .53$, $p < .001$ and $r(1217) = .60$, $p < .001$ for depression and anxiety scores respectively. There was a significant increase in depressive symptoms, $F(1,1219) = 6.57$, $p = .01$, $\eta^2 = .005$, and decrease in anxiety scores, $F(1,1218) = 7.51$, $p = .01$, $\eta^2 = .006$, for the whole cohort over time. Thus, adjusting for HADS scores at the third follow-up will indicate whether HR reactivity predicts symptomatology at the fourth follow-up independently. In essence, this amounts to examining whether reactivity predicts the change in depression and anxiety symptoms between follow-ups. For depression scores, a significant negative association with HR reactivity was still evident following such adjustment, $\beta = -.05$, $t = 2.19$, $p = .03$, $\Delta R^2 = .003$. However, the prospective association between HR reactivity and future anxiety symptoms was no longer significant, $\beta = -.03$, $t = 1.61$, $p = .11$, $\Delta R^2 = .001$.

In a model which additionally adjusted for age cohort, sex, household occupational group, PASAT performance score, anti-depressant medication, and anti-hypertensive medication, HR reactivity continued to predict future depression scores, $\beta = -.05$, $t = 2.05$, $p = .04$, $\Delta R^2 = .002$. The statistics for the full model are shown in Table 3.

[Insert Table 3 about here]

Discussion

The mean HADS depression and anxiety scores for participants in the present study at the fourth follow-up were much the same as those we reported previously at the third follow-up (Carroll, et al., 2007). They were also broadly similar to those reported by others in large non-clinical adult samples (Crawford, Henry, Crombie, & Taylor, 2001). In addition, the socio-demographic patterning of symptoms of depression and anxiety reported earlier (Carroll, et al., 2007) was also evident at the fourth follow-up. Depression scores were higher in women, participants from manual occupational households, and those in the middle and oldest cohorts. Variations in depression and depressive symptomatology with sex (e.g., Maier, et al., 1999; Piccinelli & Wilkinson, 2000; Weissman & Merikangas, 1986) and socioeconomic status (e.g., Bruce, Takeuchi, & Leaf, 1991; Dohrenwend, et al., 1992; Stansfeld, Head, Fuhrer, Wardle, & Cattell, 2003) are well documented. However, previous data on age and depression are inconsistent. Although studies have observed an increase in depression in the elderly (Kessler, Foster, Webster, & House, 1992; Mirowsky & Reynolds, 2000), others report a negative relationship between age and depression and symptoms of depression (Charles, Reynolds, & Gatz, 2001; Turner & Noh, 1988). It has been argued the former can be attributed to age variations in chronic health and that normally functioning older adults are at no greater risk for depression than younger adults (Roberts, Kaplan, Shema, & Strawbridge, 1997). It is worth noting here that the association between age cohort and depressive symptom score at wave four in the present study was attenuated when self-

reported disability status was taken into account (analysis not reported). Anxiety levels varied similarly with sex and occupational status: again results not without precedent (e.g. Fryers, Melzer, & Jenkins, 2003; Reich, 1986). In the case of HADS anxiety, levels declined with age; this has also been reported by others (e.g. Weissman & Merikangas, 1986).

As indicated in earlier reports from this study (Carroll, et al., 2007; Carroll, Phillips, Ring, Der, & Hunt, 2005; Phillips, Carroll, Hunt, & Der, 2006; Phillips, Carroll, Ring, Sweeting, & West, 2005), the acute stress was successful in perturbing cardiovascular activity. In addition, in earlier cross-sectional analyses of these data, cardiovascular reactivity was found to be negatively related to symptoms of depression and anxiety (Carroll, et al., 2007). The present analyses, though, is the first we know to demonstrate a prospective association between HR reactivity and symptoms of depression; those with high HR reactivity exhibited lower depression scores five years later. This association remained significant following adjustment for depression scores at the earlier time-point. Thus, our results amount to more than a replication of our earlier findings. Even taking into account the correlation between symptom scores at the two follow-ups, HR reactivity was still associated with depressive symptomatology at the later time point. The analogous negative association between HR reactivity and symptoms of anxiety was no longer statistically significant following such adjustment. In addition, the relationship with depression additionally survived adjustment for both socio-demographics and medication status. The relative effect sizes for HR reactivity compared to socio-demographic variables also suggest that when earlier symptoms of depression are taken into account, low reactivity is as important, if not more so, than age and gender in the prediction of future depressive symptoms, at least in the present sample.

Whereas high cardiovascular reactivity would appear to hold implications for the development and course of inflammatory disease (Carroll, Phillips, & Lovallo, in press), low reactivity is not without its health and behavioural correlates. For example, we have recently found that individuals who mounted a poor antibody response to influenza

vaccination showed lower and less sustained cardiovascular reactions to acute stress than those who mounted a good antibody response (Phillips, Carroll, Burns, & Drayson, 2009). Further, habitual smokers have been consistently found to show blunted cardiovascular reactivity (Girdler, Jamner, Jarvik, Soles, & Shapiro, 1997; Phillips, et al., 2009; Roy, Steptoe, & Kirschbaum, 1994). It is unlikely that these effects reflect temporary abstinence during stress testing, as low cardiovascular reactivity has been observed in female smokers regardless of whether they were wearing a nicotine replacement patch or not (Girdler, et al., 1997). In addition, blunted reactivity has been found to predict relapse among smokers who have recently quit smoking (al'Absi, 2006; al'Absi, Hatsukami, & Davis, 2005). Those addicted to alcohol have also been found to exhibit blunted cardiovascular reactivity (Lovallo, Dickensheets, Myers, Thomas, & Nixon, 2000; Panknin, Dickensheets, Nixon, & Lovallo, 2002), and relatively low reactivity would appear to be a characteristic of non-alcoholics with a family history of alcoholism (Sorocco, Lovallo, Vincent, & Collins, 2006). Thus, low reactivity not only characterises those addicted to smoking and alcohol; it may also be a risk marker of some prognostic significance (Lovallo, 2006). In short, cardiovascular disease outcomes aside, low reactivity would appear to be associated with a number of negative health outcomes.

What might be the mechanisms underlying this prospective link between HR reactivity and symptoms of depression? One possibility is altered sympathetic nervous system function. However, the prevailing wisdom is that depression and symptoms of depression are associated with increased, not decreased, sympathetic nervous system activity, as indexed by a shift enhanced cardiac sympathetic activity relative to vagal tone (Carney, et al., 1988), increased plasma noradrenaline concentrations (Rudorfer, et al., 1985), and increased 24-hour urinary noradrenaline excretion (Hughes, Watkins, Blumenthal, Kuhn, & Sherwood, 2004) in individuals with depression or depressive symptomatology. However, this tells us only about the tonic state. It does not indicate how the system responds to challenge. More pertinent to reactivity is the status and responsiveness of β -adrenergic receptors. There is some evidence that individuals with depression or depressive symptomatology have fewer β -adrenergic receptor binding sites (Pandey, Janicak, & Davis, 1987) and show decreased β -adrenergic receptor

responsiveness (Mazzola-Pomietto, Azorin, Tramoni, & Jeanningros, 1994; Yu, Kang, Ziegler, Mills, & Dimsdale, 2008). What we might tentatively speculate is that blunted β -adrenergic receptor responsiveness, as indexed by low HR reactivity to acute stress in the present study, may be a risk marker for developing high levels of depressive symptomatology. However, mental stress tasks have been shown to be associated with vagal withdrawal as well as beta-adrenergic activation (Sloan, Korten, & Myers, 1991). There is also evidence that individuals with less vagal withdrawal during a film clip have higher levels of depressive symptoms (Gentzler, Santucci, Kovacs, & Fox, 2009). Indeed, depressed individuals with greater vagal withdrawal during film clips were more likely to subsequently recover from depression (Rottenberg, Salomon, Gross, & Gotlib, 2005). Thus, it is possible that there is a common brain mechanism regulating vagal nerve activity and depressive symptoms. However, in the absence of a measure of parasympathetic withdrawal in the present study, we are reluctant to speculate further.

Another possible explanation for the observed association between HR reactivity and symptoms of depression is a common genetic pathway. For example, polymorphisms of the serotonin transporter gene (5HTTLPR), which plays a key role in determining the magnitude and duration of both the central and peripheral actions of serotonin, would appear to be implicated in emotional regulation and physiological reactivity. Activity of the 5HTTLPR long allele is almost twice that of the short allele. Those with long alleles have also been found to exhibit higher blood pressure and heart rate reactions to a laboratory stress task (Williams, et al., 2001; Williams, et al., 2008). Further, men who are homozygous for the long allele have been found to score lower on measures of anxiety and depression (Lesch, et al., 1996). However, a recent meta-analysis reported that the 5HTTLPR genotype did not appear to be associated with major depression, particularly in association with high life events (Risch, et al., 2009). Nevertheless, since symptoms of depression in the general population and major depressive disorder may be distinct phenomena, this avenue seems worthy of further investigation.

The present study suffers from a number of limitations. First, the effect sizes were small. This, though, was our *a priori* expectation based on previous research and reinforces the value of large samples when examining some of the more subtle correlates of cardiovascular reactivity. However, with such small effects, it is difficult to discern their clinical significance. Nevertheless, were this finding to be replicated, low HR reactivity might afford a further, albeit modest, risk marker for the development of depressive symptomatology. Second, there remains the possibility of residual confounding as a result of some poorly measured or unexamined variable (Christenfeld, Sloan, Carroll, & Greenland, 2004). However, we did adjust for the most likely candidates, and although the negative association between HR reactivity and subsequent symptoms of depression was attenuated, it remained statistically significant. Finally, only blood pressure and HR were measured. Although, it would have been useful to have a more comprehensive assessment of haemodynamics of the sort afforded by impedance cardiography, the large sample and the decision to test participants in their homes precluded this.

In conclusion, cardiac reactions to acute psychological stress were negatively associated with depressive symptomatology five years later. This association withstood adjustment for symptom scores at the earlier time point, as well as for socio-demographic factors and medication status. The mechanisms underlying this prospective relationship remain to be determined, but blunted β -adrenergic receptor responsiveness and common genetic pathways would seem worthy of further study.

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Table 1: Mean (SD) HADS depression and anxiety scores at the third and fourth follow-ups by cohort, sex, and occupational status.

	Wave 3		Wave 4	
	Depression	Anxiety	Depression	Anxiety
<i>Age Cohort:</i>				
Youngest (N = 419)	3.1 (2.60)	7.3 (3.78)	3.4 (3.00)	6.9 (3.72)
Middle (N = 497)	3.9 (3.00)	7.4 (3.88)	4.0 (3.38)	7.1 (3.85)
Eldest (N = 329)	4.0 (2.94)	6.7 (3.71)	3.7 (2.91)	6.0 (3.62)
<i>Sex:</i>				
Male (N = 559)	3.5 (2.71)	6.5 (3.56)	3.5 (2.92)	5.9 (3.48)
Female (N = 686)	3.8 (2.98)	7.7 (3.93)	3.9 (3.30)	7.5 (3.86)
<i>Occupational Group:</i>				
Manual (N = 550)	3.9 (2.96)	7.3 (3.98)	4.0 (3.27)	7.1 (3.89)
Non-manual (N = 690)	3.5 (2.77)	7.1 (3.65)	3.5 (3.02)	6.5 (3.67)

Table 2. Mean (SD) SBP, DBP, and HR, baseline and stress values for the sample as a whole.

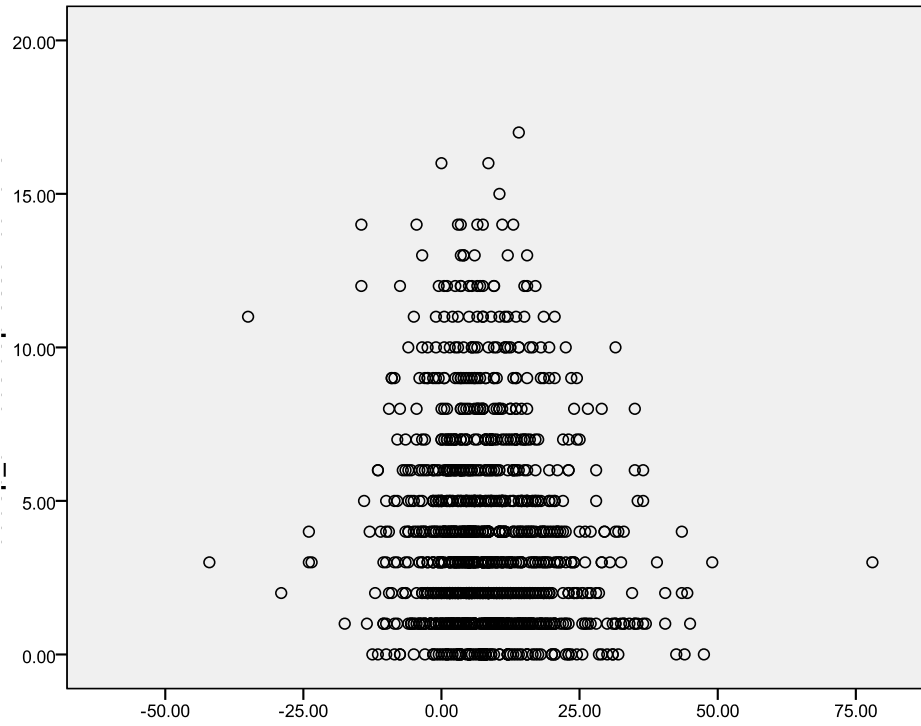
SBP		DBP		HR	
<i>Baseline</i>	<i>Stress</i>	<i>Baseline</i>	<i>Stress</i>	<i>Baseline</i>	<i>Stress</i>
129.1 (20.50)	140.6 (21.63)	78.9 (11.60)	85.7 (12.30)	66.7 (10.80)	74.8 (12.33)

Table 3: Final regression models predicting depressive symptoms at wave 4, adjusting for depressive symptoms at baseline and covariates.

Model	β	t	p	R ²
1: HADS depression baseline	.53	21.75	<.001	.281
2: HADS depression baseline	.53	21.43	<.001	
Age cohort	-.02	-0.81	.42	
Sex	.03	1.37	.17	
Occupational group	.06	2.46	.01	.285
3: HADS depression baseline	.52	20.74	<.001	
Age cohort	-.02	-0.95	.34	
Sex	.03	1.27	.21	
Occupational group	.06	2.40	.02	
PASAT score	.002	0.06	.95	
Anti-depressant medication	.06	2.27	.02	
Anti-hypertensive medication	.01	0.36	.72	.288
4: HADS depression baseline	.51	20.61	<.001	
Age cohort	-.03	-1.21	.23	
Sex	.03	1.17	.24	
Occupational group	.06	2.29	.02	
PASAT score	.01	0.45	.66	
Anti-depressant medication	.06	2.22	.03	
Anti-hypertensive medication	.01	0.28	.78	
HR reactivity	-.05	-2.05	.04	.291

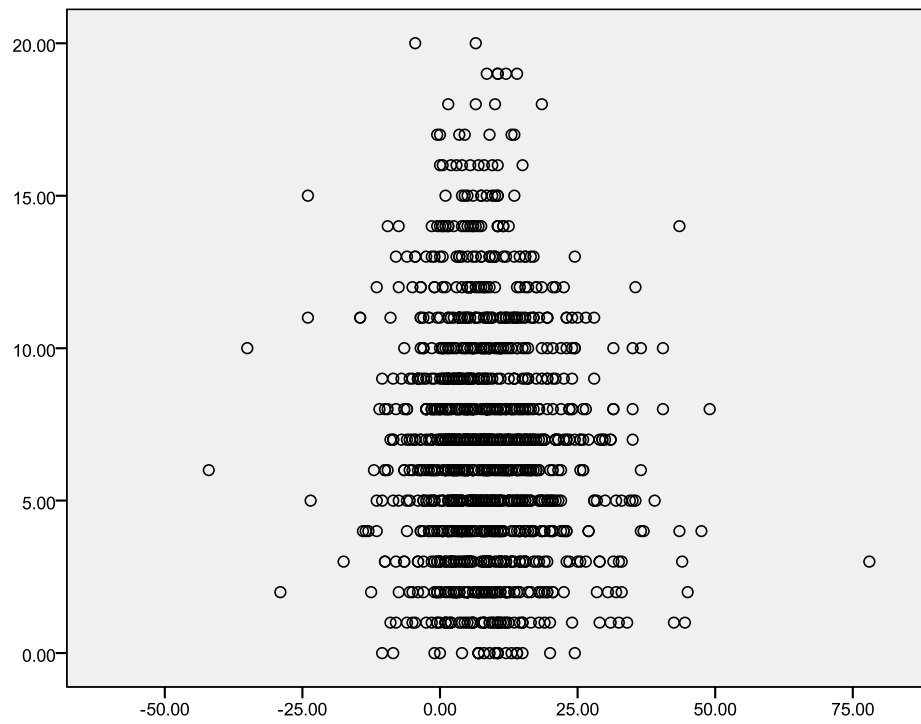
Figure 1: Associations between cardiovascular reactivity at wave 3 and HADS scores at wave 4

HADS depression score at wave 4



Heart rate reactivity at wave 3

HADS depression score at wave 4



Heart rate reactivity at wave 3