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Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample

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Running title: Reactivity and cognitive ability

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Abstract

The relationship between cardiovascular reactions to acute mental challenge in the laboratory and cognitive ability has received scant attention. The present study examined the association between reactivity and future cognitive ability. Heart rate and blood pressure reactions to a mental stress task were measured in 1647 participants comprising three distinct age cohorts. Cognitive ability was assessed using the Alice Heim-4 test of general intelligence and choice reaction time five and 12 years later. High heart rate reactivity was related to higher general intelligence scores and faster choice reaction times at both follow-ups. High heart rate reactivity was also associated with a smaller decline in cognitive ability between assessments. These associations were still evident following adjustment for a wide range of potentially confounding variables. The present results are consistent with the notion that high reactivity may not always be a maladaptive response and that low or blunted reactivity may also have negative corollaries.

Keywords: Blood pressure, cognitive ability, cognitive change, heart rate, reactivity

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1. Introduction

Little is known about the association between cardiovascular stress reactivity and cognitive function. In a study of infants, greater suppression of a heart period based index of vagal tone during the cognitive challenge afforded by the Bayley Scale of Infant Development was associated with more mature cognitive skills and more coordinated motor behaviour (DeGangi et al., 1991). A broadly similar outcome emerged from a more recent study of cardiovascular reactions to a task in which young adults were required to identify a target stimulus among a variety of distractor items (Duschek et al., 2009): R-wave to pulse interval, an index of sympathetic activity, was negatively associated with task performance, whereas respiratory sinus arrhythmia, an index of vagal tone, was positively related to performance. The authors interpret these outcomes as suggesting an association between enhanced sympathetic and reduced vagal cardiovascular influences and improved cognitive-attentional functioning. In contrast, no association between cardiovascular reactivity to memory tasks and task performance has been reported in studies of young (Backs & Seljos, 1994) and older adults (Wright et al., 2005), although in the latter study, superior memory performance was associated with faster heart rate recovery following task exposure. Given the variations in study samples, the physiological parameters measured, and the cognitive tasks employed, it is not surprising that no clear consensus emerges from these studies. With one exception (Wright et al., 2005), all of the studies were small scale and did not adjust for potential confounding variables. More importantly, all of these previous studies measured cognitive ability as performance on the stress reactivity challenge. Stronger tests of the association between cognitive ability and cardiovascular reactivity to mental stress would be afforded by using measures of cognitive ability that are independent of the mental stress task employed to elicit reactivity.

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In the present study, cardiovascular reactions to acute stress were assessed in a substantial community sample and cognitive ability was then measured five and 12 years later using a standard measure of general intelligence and choice reaction time. Thus, cognitive ability was measured independently of and at different times from mental stress task exposure. We have recently reported from analyses restricted to the oldest of three age cohorts in the West of Scotland study, retrospective associations between reactivity and cognitive ability measured seven years earlier; low heart rate reactivity was characteristic of those with relatively low prior cognitive ability (Ginty et al., 2011). The present analyses are prospective with respect to cognition and data were available for all three age cohorts. Thus, in our previous study we established the possibility of a causal pathway from low cognitive ability to blunted heart rate reactivity. In the present analyses, we test the additional possibility that reactivity predicts cognitive ability in the future, as well as any change in cognitive performance between the two follow-ups. It is also worth noting that choice reaction time has been found to correlate negatively with more traditional measures of general intelligence and indeed has been regarded as a measure of cognitive ability (Rabbit & Goward, 1994). Based on the balance of previous evidence, including our own recent finding of a retrospective positive association between heart rate reactivity and cognitive ability, as well as research testifying to an association between low or blunted reactivity and a number of adverse health and behavioural outcomes (Carroll et al., 2009a; Carroll et al., in press; Phillips, 2011), it was hypothesised that lower heart rate reactivity would be associated prospectively with relatively lower cognitive ability and slower choice reaction times. Thus, what we are hypothesising is that there might be a bi-directional relationship between cognitive ability and reactivity.

2. Method

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2.1. Participants

Data were collected as part of the West of Scotland Twenty-07 Study. Participants were from Glasgow and surrounding areas in Scotland, and have been followed up at regular intervals since the baseline survey in 1987 (Ford et al., 1994). The study's principal aim was to investigate the processes that generate and maintain socio-demographic differences in health (Macintyre, 1987). Participants were chosen randomly with probability proportional to the overall population of the same age within a post code area (Ecob, 1987). Thus, this is a clustered random stratified sample. Three narrow age cohorts were chosen (aged 15, 35, and 55 years at entry). More complete details of the study are available elsewhere (Carroll et al., 2008; Ford et al., 1994; Phillips et al., 2009).

The data reported here are from the third, fourth, and fifth follow-ups. The mean (SD) temporal lag between the third and fourth follow-up visits was 5.5 (1.00) years and between the third and fifth follow-up visits was 12.4 (0.40) years. Cardiovascular stress reactivity was assessed for 1647 participants at the third follow-up. The sample at this time point comprised 592 (36%) 24-year-olds, 624 (38%) 44-year olds, and 431 (26%) 63-year-olds. There were 890 (54%) women and 757 (46%) men, and 772 (47%) were from manual and 870 (53%) from non-manual occupation households. Household occupational status was unavailable for five participants. Overall mean (SD) age at the third follow-up visit was 42.2 (15.44) years. The mean (SD) ages of the young, middle-aged, and older age cohorts were 24.2 (0.45), 44.56 (0.84), and 63.57 (0.61) years. Cognitive ability, using the Alice Heim-4 (AH-4) test and choice reaction time (CRT), was assessed at the fourth and fifth follow-ups. The attrition rate, largely as a result of relocation, between the third and fourth follow-ups was 23%; CRT data were available for 1251 participants at the fourth follow-up. There was little attrition (5%) between the fourth and fifth follow-up and reaction time data were

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available for 1189 participants at the fifth follow-up. AH-4 scores were available for 1170 and 1148 participants at the fourth and fifth follow-ups respectively. This study was approved by the appropriate Ethics Committees.

2.2. Apparatus and procedure

Participants were interviewed and tested in a quiet room in their homes by trained nurses. During the third follow-up visit household occupational group was classified as manual or non-manual from the occupation of the head of household, using the Registrar General's Classification of Occupations (1980). Head of household was usually the man. Long-standing illness or disability status, hereafter referred to by the latter term, was determined by response to the question, 'Do you have any long-standing illness, disability, or infirmity? By long-standing I mean anything that has troubled you over a period of time or that is likely to affect you over a period of time?' Height and weight were measured and body mass index (BMI) computed. Symptoms of depression were assessed using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The HADS is a well-recognized assessment instrument that comprises 14 items, 7 measuring depression and 7 measuring anxiety. The depression subscale emphasises anhedonia and largely excludes somatic items.

Participants then undertook an acute psychological stress task, the paced auditory serial addition test (PASAT), which has been shown in numerous studies reliably to perturb the cardiovascular system (Ring et al., 2002; Winzer et al., 1999) and to demonstrate good temporal stability of reactivity (Willemsen et al., 1998). The task comprised a series of single digit numbers presented by audiotape and participants were requested to add sequential number pairs, and at the same time retain 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 the participants faltered, they were instructed to recommence with the next number pair. The first sequence of 30 numbers was presented at a rate of one every 4 seconds, and the second sequence of 30 numbers was presented at a rate of one every 2 seconds. The whole task took 3 minutes, 2 minutes for the slower sequence, and 1 minute for the faster sequence. A brief practice was given to ensure that participants understood the requirements of the task.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) values were determined by a semiautomatic sphygmomanometer (model 705CP, Omron, Weymouth, UK), a device recommended by the European Society of Hypertension (O'Brien et al., 2001). After the interview (at least an hour), there was a formal 5-minute period of relaxed sitting, at the end of which a resting baseline reading of SBP, DBP, and HR was taken. PASAT instructions were then given, followed by a brief practice. Two SBP, DBP, and HR readings were taken during the PASAT, 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 faster 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 was subsequently subtracted from the resultant average task value to yield reactivity measures for SBP, DBP, and HR for each participant.

At both the fourth and fifth follow-up visits, the Alice Heim-4 (AH-4) test, a measure of general mental ability (Deary et al., 2001), was administered; administration and scoring were carried out as described in the test manual (Heim, 1970). The test consisted of 12 practice questions followed by 33 items measuring numerical reasoning ability and 32 items measuring verbal reasoning ability.

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The test has been used in other population studies of individuals in the same age range (Singh-Manoux et al., 2005; Rabbitt et al., 2001). At the fourth and fifth follow-ups, participants undertook a CRT task using a portable device originally designed for the UK Health and Lifestyle Survey (Cox et al., 1987). The device consisted of five keys arranged in a shallow arc; the keys were numbered 1, 2, 0, 3, 4. Participants were asked to rest the 2nd and 3rd finger of each hand on the keys labelled 1,2,3,4 and press the corresponding key when one of the four digits appeared above. Participants were given eight practice trials and 40 test trials; the digits 1-4 appeared 10 times during the 40 trials in a random order. The amount of practice given to participants is similar to most studies that relate reaction times to intelligence differences (Deary, 2000). CRT was measured in milliseconds.

2.3. Statistical analysis

Differences in AH-4 scores and CRTs between sexes, household occupational group, and age cohort were explored using analysis of variance (ANOVA). Repeated- measures ANOVAs, using baseline and task values, were undertaken to confirm that the PASAT perturbed cardiovascular activity. Partial eta squared (η^2) is used as a measure of effect size. The relationship between AH-4 scores and CRTs were investigated by Pearson's correlation. Linear regression analyses were used to determine whether cardiovascular reactivity were associated with AH-4 score and CRT five and 12 years later. A series of hierarchical linear regressions were undertaken to determine whether any effects that emerged from the primary analyses withstood adjustment for potential confounding variables. The possible confounders selected were age cohort, sex, household occupational group, disability status, HADS depression, BMI, and baseline cardiovascular levels. All of these have been related to reactivity and/or cognitive ability in this cohort (Carroll et al., 2000, 2007, 2008; Phillips et al., 2011). The main regression analyses were repeated separately for numerical reasoning and verbal reasoning at the two time points testing both unadjusted and fully adjusted models. Finally, regression models were tested that examined the change in cognitive ability over time. In these, AH-4 score and CRT at the fifth follow-up were the dependent variables, cardiovascular reactivity was the independent variable, and we adjusted for earlier AH-4 score and CRT at the fourth follow-up in each case. Again, we also tested models that additionally adjusted for all the other covariates.

3. Results

3.1. Socio-demographics and cognitive ability

The overall mean (SD) AH-4 scores and mean (SD) CRTs at the fourth and fifth follow-ups were 35.28 (11.41) and 35.34 (11.31) respectively and 619.8 (153.31), and 629.5 (153.31) milliseconds respectively. The non-manual household group registered higher AH-4 scores than the manual occupational group at both follow-ups, $F(1,1164) = 189.25$, $p < .001$, $\eta^2 = .140$, $F(1, 1143) = 115.65$, $p < .001$, $\eta^2 = .092$, respectively, as well as faster CRTs, $F(1, 1245) = 39.26$, $p < .001$, $\eta^2 = .031$, $F(1, 1184) = 15.60$, $p < .001$, $\eta^2 = .013$, respectively. Males displayed significantly higher AH-4 scores at the fourth follow-up than females, $F(1,1169) = 3.95$, $p = .05$, $\eta^2 = .003$; there were no significant difference between genders at the fifth follow-up, nor for CRT at either follow up. The younger cohort registered higher AH-4 scores and faster CRTs than the middle cohort who, in turn, registered higher AH-4 scores and shorter CRTs than the oldest cohort at the fourth follow-up, $F(2,1169) = 73.96$, $p < .001$, $\eta^2 = .112$, and $F(2,1249) = 398.47$, $p < .001$, $\eta^2 = .390$, respectively, and fifth follow-up, $F(2, 1147) = 122.71$, $p < .001$, $\eta^2 = .177$, and $F(2, 1187) = 354.64$, $p < .001$, $\eta^2 = .370$, respectively. Individuals who reported long-standing illness or disability scored substantially lower on the AH4, $F(1,1169) = 22.43$, $p < .001$, $\eta^2 = .019$, and $F(1,1147) = 28.80$, $p < .001$, $\eta^2 = .025$, and had markedly slower CRTs, $F(1, 1249) = 45.86$, $p < .001$, $\eta^2 = .035$, F(1, 1187)

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= 41.40, p <.001, $\eta^2 = .034$, at the fourth and fifth follow-ups, respectively. The summary statistics are reported in Table1. AH-4 scores at the two follow-ups were positively correlated, r(1146) = .87 , p <.001, as were CRTs, r(1030) = .70, p < .001. AH4 scores correlated negatively with CRT at both the fourth, r(1123) = -.53, p < .001, and fifth, r(1136) = -.55, p < .001, follow-ups.

[Insert Table 1 about here]

3.2. Cardiovascular reactions to acute stress

Two-way (baseline x task) repeated measures ANOVA indicated that on average the PASAT significantly increased cardiovascular activity: for SBP, F(1,1646) = 1562.32, p <.001, $\eta^2 = .487$, for DBP, F(1,1646) = 1066.62, p <.001, $\eta^2 = .393$; and for HR, F(1,1646) = 1132.96, p < .001, $\eta^2 = .408$. The mean baseline and reactivity values are presented in Table 3. HR reactivity declined with age, F (2, 1644) = 21.11, p < .001, $\eta^2 = .408$; with the youngest cohort exhibiting higher reactivity than the middle cohort who, in turn showed higher reactivity than the eldest cohort (p <.05 in each case). HR reactivity was also greater in men, F(1,1645) = 5.23, p = .02, $\eta^2 = .003$, and in participants from non-manual occupational group households, F(1,1640) = 21.08, p < .001, $\eta^2 = .013$. SBP reactivity varied significantly among the age cohorts, F(2,1644) = 6.81, p < .001., $\eta^2 = .008$, with the youngest cohort having significantly lower reactivity than the other two cohorts (p < .05 in both cases). Women had smaller SBP reactions than men, F(1,1645) = 16.61, p < .001., $\eta^2 = .010$. DBP reactivity did not vary significantly with age cohort, sex, or household occupational group. The statistics reported above relate to significant group by baseline/task condition interactions. However, for the sake of illustration we report baseline and reactivity in Table 2.

[Insert Table 2 about here]

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3.3 Justification for separate regression analyses for the five and 12 year follow-ups.

In order to justify the separate analyses for the two follow-ups, we tested the time x HR reactivity interaction in a fully adjusted linear mixed model. The interaction was significant for both AH-4 scores, t (914) = 2.06, p = .04, and CRT, t (1005) = 2.40, p = .02.

3.4. Cardiovascular reactivity and future AH-4 performance scores and CRT five years later

In the first model, with no adjustment, HR reactivity was associated with future AH-4 performance scores, β = .200, p < 001, ΔR^2 = .040; individuals with lower HR reactivity had poorer AH-4 scores five years later. SBP (p= .33) and DBP (p = .95) reactivity did not significantly predict future AH-4 scores. In regression analyses that adjusted for age cohort, sex, household occupational group, disability status, HADS depression, BMI, and baseline cardiovascular levels, HR reactivity continued to be associated with AH-4 scores, β = .107, p = <.001, ΔR^2 = .010, with the association in the same direction. The final regression is shown in Table 3. SBP and DBP reactivity did not predict cognitive ability at the fourth follow-up in this fully adjusted model, p = .25 and .67, respectively. The unadjusted association with HR reactivity are illustrated by plotting AH-4 scores against tertiles of reactivity (Figure 1a). AH-4 scores varied significantly with tertiles of HR reactivity, F (2,1167) = 27.27, p < .001, η^2 = .045. The relationship between SBP and DBP and AH-4 scores were again non-significant. In the unadjusted model, HR reactivity was negatively associated with CRT at the fourth follow-up, β = -.194, p < .001, ΔR^2 = .038. SBP (p = .35) and DBP (p = .89) did not significantly associated with future choice reaction time; individuals with lower HRreactivity had longer CRTs five years later. In the model that adjusted for age cohort, sex, household occupational group, disability status, HADS depression, BMI, and baseline cardiovascular levels, HR reactivity was still negatively associated with CRT, β = -.056, p =

.018, $\Delta R^2 = .003$. The final regression is shown in Table 4. SBP reactivity was also negatively associated with CRT in this fully adjusted model, $\beta = -.055$, $p = .016$, $\Delta R^2 = .003$. DBP reactivity was not associated with future choice reaction time ($p = .78$). The unadjusted association between HR reactivity and CRT are illustrated by plotting CRT scores against tertiles of reactivity (Figure 2a). CRT varied among the tertiles of HR reactivity, F (2,1284) = 27.63, $p < .001$, $\eta^2 = .042$.

3.5. Cardiovascular reactivity and future AH-4 performance scores and CRT 12 years later

In the unadjusted model, HR reactivity was associated with AH-4 performance scores at the fifth follow-up, $\beta = .21$, $p < 001$, $\Delta R^2 = .046$; lower HR reactivity was again associated with poorer cognitive ability 12 years later. SBP ($p = .99$) and DBP ($p = .35$) was not significantly associated with future AH-4 scores. In the fully adjusted model, HR reactivity was still positively associated with AH-4 scores, $\beta = .130$, $p = <.001$, $\Delta R^2 = .015$. The final regression is shown in Table 3. Neither SBP ($p = .14$) nor DBP ($p = .41$) reactivity were associated with future AH-4 scores in this model. The unadjusted association with HR reactivity is again illustrated by plotting AH-4 scores against tertiles of reactivity (Figure 1b). AH-4 scores varied significantly with tertiles of HR reactivity, F (2,1145) = 27.73, $p < .001$, $\eta^2 = .046$. HR reactivity was negatively associated with CRT 12 years later in the unadjusted model, $\beta = -.177$, $p < .001$, $\Delta R^2 = .031$. SBP ($p = .25$) and DBP ($p = .86$) were not. In the fully adjusted model, HR reactivity was still associated with CRT, $\beta = -.078$, $p = .002$, $\Delta R^2 = .005$. The associations between SBP ($p = .74$) and DBP ($p = .50$) and future CRT were still not significant. The final regression is shown in Table 4. The unadjusted association between HR reactivity and CRT at the fifth follow-up is illustrated in Figure 2b. CRT varied significantly between the tertiles of HR reactivity, F (2,1186) = 24.93, $p < .001$, $\eta^2 = .040$.

[Insert Figure 1 and 2 and Tables 3 and 4 about here]

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3.6. Cardiac reactivity and future numerical and verbal reasoning ability

In the fully adjusted model, HR reactivity was positively associated with both AH-4 numerical and AH-4 verbal reasoning scores at the fourth follow-up, β = .107, $p < .001$, $\Delta R^2 = .010$, and β = .076, $p = .006$, $\Delta R^2 = .005$, and the fifth follow-up, β = .150, $p < .001$, $\Delta R^2 = .020$, and β = .096, $p < .001$, $\Delta R^2 = .008$, respectively.

3.7. Cardiovascular reactivity predicting future change in cognitive ability

In order to examine the association between reactivity and individual differences in change in cognitive ability over time, models were tested with AH-4 score or CRT at the fifth follow-up as the dependent variables and cardiovascular reactivity as the independent variable, with the earlier, fourth follow-up, AH-4 score or CRT, respectively, entered as a covariate. HR reactivity was associated with change in AH-4 score from the fourth to the fifth follow-ups, β = .110, $p < .001$, $\Delta R^2 = .012$. There were no associations for either SBP (p =.74) or DBP ($p = .98$). In the model that additionally adjusted for all the other covariates, HR reactivity was still associated with change in AH-4 scores, β = .042, $p = .01$, $\Delta R^2 = .002$. HR reactivity was also associated with CRT at the fifth follow-up after adjusting for CRT at the fourth follow-up, β = -.065, $p = .004$, $\Delta R^2 = .004$. Again, there were no analogous associations for SBP ($p = .51$) and DBP ($p = .72$). The association between HR reactivity and CRT change was still significant in the fully adjusted model, β = -.057, $p = .01$, $\Delta R^2 = .003$. Change in AH-4 score and CRT between the fourth and fifth follow-up was calculated by simple subtraction. Incidentally, the same results as those reported above emerge from fully adjusted regression models for HR reactivity when the dependent variables were the AH-4 (p = .01) and CRT ($p = .01$) change scores. To illustrate the HR reactivity associations, change scores for AH-4 and CRT were compared for tertiles of HR reactivity. Whereas change in AH-4 between the two follow-ups was not significant ($p = .35$), change in CRT was, F(2,

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1035) = 6.88, p = .001., η^2 = .013, the highest tertile of HR reactors showed less decline in CRT over time. The summary data are presented in Figure 3a and 3b. Finally, in a supplementary analyses using ANCOVA, we analysed the effect of the interaction between tertiles of HR reactivity and age cohort on change in cognitive ability between the two follow-ups: these analyses were fully adjusted. For CRT, but not AH-4 scores, there was a significant reactivity x cohort interaction, F (4, 1000) = 2.44, p = .04, η^2 = .010. This is illustrated in Figure 4 which plots the change in CRT for tertiles of HR reactivity separately for the three age cohorts. As can be seen, the effect of tertiles of reactivity on CRT change is concentrated in the older cohort.

[Insert Figure 3 and 4 about here]

4. Discussion

This study examined the association between cardiovascular reactivity and future cognitive ability, as indexed by scores on the AH-4 test of verbal and future numerical reasoning and by CRT. Both are accepted measures of cognitive ability (Deary et al., 2001; Rabbit & Goward, 1994). The two measures were strongly, but imperfectly correlated at both follow-ups. Low, not high, HR reactions to acute stress were associated with low AH-4 test scores and longer CRTs five and 12 years later. Blood pressure reactivity was not associated with cognitive ability at either time point. Post hoc analyses of tertiles of HR reactivity indicated a dose-response relationship between cardiac reactivity and AH-4 scores and CRT at both follow-ups; blunted HR reactivity was associated with poorer future cognitive ability. HR reactivity was positively associated with both the numerical and verbal reasoning components of the AH-4. These associations between HR reactivity and cognitive ability remained statistically significant in regression models that adjusted for age cohort, sex, household occupational group, disability status, depressive symptomatology, BMI, and baseline HR.

Additionally, HR reactivity was associated with change in cognitive ability over time, i.e., low HR reactivity was associated with poorer AH-4 scores and slower CRTs at the fifth follow-up even after statistical adjustment for cognitive ability at the fourth follow-up, seven years earlier. This suggests that low HR reactivity may be a marker of cognitive aging. Cognitive aging refers to age-related decrements in cognitive function. It would appear that inflammatory markers, such as c-reactive protein (Deary et al., 2009; Weaver et al, 2002; Yaffe et al., 2003) and IL-6 (Deary et al., 2009; Rafnsson et al., 2007; Yaffee et al., 2003), are not only associated with cognitive ability but predict cognitive aging. Increased systemic oxidative stress has also been reported to amplify cognitive aging (Berr et al., 2000; Coyle & Puttafarcken, 2993; Whalley et al., 2004). The present study is the first we know of to find that HR reactivity may also be a predictor of cognitive aging. However, it should be conceded that general intelligence measures are fairly stable over time (Conley, 1984) and, accordingly, may afford less than optimal measures of short term cognitive aging. Further, it has been argued that cognitive aging is mainly accounted for by a decline in inspection time and CRT (Nettelbeck & Rabbitt, 1992). In the present study, the mean AH-4 scores were virtually identical at the two follow-ups, whereas CRT lengthened by 2% between the fourth and fifth follow-ups. Thus, we would expect that if HR reactivity is a marker of cognitive aging, associations would be stronger with CRT as the outcome. Our supplementary analyses were supportive. High HR reactors showed less of a lengthening in CRT over seven years than the rest of the sample; the analogous effect for AH-4 scores was not statistically significant. Finally, the effects of tertiles of reactivity on change in CRT was concentrated in

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the oldest cohort. This is perhaps hardly surprising, given that it is in this cohort that cognitive aging should be most evident.

The observed negative association between cognitive ability and reactivity is in line with that observed in two earlier studies, which found that lower cardiovascular reactivity was associated with poorer performance on the mental stress task (DeGangi et al., 1991; Duschek et al., 2009). However, it should be conceded that two other studies including a sizable study in older adults failed to find an association between reactivity and cognitive ability as revealed by performance on the stress task (Backs & Seljos, 1994; Wright et al., 2005). Nevertheless, the present study is the largest study by some considerable margin to address this issue. In addition, the negative association observed in the present study is consistent with a recent analysis of the oldest cohort in this sample revealing a positive retrospective association between AH-4 scores and HR reactivity seven years later (Ginty et al., 2011). However, this is the first study we know of that links HR reactivity to future cognitive ability. Taken together, our analyses indicate an intimate association between HR reactivity and cognitive ability across the life course. Nevertheless, problems of causation and the direction of causation remain. What the present analyses indicate is that a causal pathway from poor cognitive ability to low reactivity is not the only possibility, but that the link between cognition and reactivity may be bi-directional. Deliberations on causality would have undoubtedly been helped had reactivity been measured at more than one time point and cognitive ability at all time points in the full sample. Unfortunately, as with all the large scale epidemiological studies which measure reactivity, this was not feasible. However, it is worth noting that cardiovascular reactivity has been found to be reasonably stable over time, even across periods of 18 years (Hassellund et al., 2010). Determining causality even in prospective studies is fraught with pitfalls even when a substantial number of variables have been statistically controlled for (Christenfeld et al., 2004). It is possible that some third factor contributes to both cognitive ability and reactivity across the lifecourse. A candidate here may be central motivational dysregulation. By central motivational dysregulation we mean the suboptimal functioning of those systems in the brain, converging at the striatum and ventromedial prefrontal cortex, which appears to shape the motivation of our behaviour.

Our results are certainly consistent with the contention that relatively low cardiovascular reactions to acute stress may be a peripheral marker of central motivational dysregulation (Carroll et al., 2009a; Carroll, Phillips et al., in press). The circuits converging in the striatum and the ventromedial prefrontal cortex may be precisely those that support physiological reactivity (Carroll et al., 2009a; Carroll, et al., in press). As cognitive performance requires the integrity of such motivational systems (Busato et al., 2000; Dweck, 1986; McClelland et al., 1953; Pintrich & Schunk, 1986), it would be expected that lower rather than higher cardiovascular reactivity would be associated with poorer subsequent cognitive ability, which is precisely what was observed for HR reactivity. Although speculative, it is possible that age-related functional deterioration of central motivational systems, to an extent, underpins the link between HR reactivity and cognitive aging.

Our observations are also consistent with a growing body of cross-sectional and prospective evidence that low, not high, cardiovascular reactivity, including HR reactivity, is associated with a range of adverse health and behavioural outcomes, such as obesity (Carroll et al., 2008; de Rooij, et al., in preparation), symptoms of depression (Carroll et al., 2007; de Rooij et al., 2010; Phillips et al., 2011; York et al., 2007), tobacco and alcohol dependence, as well as risk of dependence (al' Absi, 2006; al'Absi et al., 2005; Girdler et al., 1997; Lovallo et al., 2000; Pankin, Dickensheets, Nixon, & Lovallo, 2002; Phillips et al., 2009; Roy et al., 1994), and exercise dependence (Heaney et al., 2011). Thus, it would appear that for health

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outcomes such as high blood pressure, hypertension, and atherosclerosis cardiovascular reactivity is a positive predictor, whereas other outcomes are negatively associated with cardiovascular reactivity. This suggests that there might be an inverted U-shaped relationship such that very high and very low reactivity are maladaptive (Carroll et al., 2009a).

The present study is not without limitations. First, it should be acknowledged that the observed effect sizes are small. However, our effects are of the same order as the positive associations between cardiovascular reactivity and future resting blood pressure in this sample (Carroll et al., 2003), as well as those observed in other prospective studies of reactivity and subsequent blood pressure status (Carroll et al., 1995; Carroll, et al., 2001; Markovitz et al., 1998; Matthews et al., 1993; Newman et al., 1999) and revealed by a recent meta-analysis (Chida & Steptoe, 2010). Second, given the oral response mode in the PASAT, cardiovascular perturbations could be attributed to speech. However, similar levels of HR reaction to mental arithmetic with and without a speech component have been reported (Sloan et al., 1991) and we have reported substantial cardiovascular reactions to the PASAT when the mode of response was manual rather than oral (Carroll et al., 2009b; Balanos et al., 2010). Third, only blood pressure and HR reactivity were measured. It could have proved instructive to have a more comprehensive assessment of haemodynamics, such as that afforded by impedance cardiography. Further, a continuous rather than an intermittent of blood pressure and HR would have allowed us to chart the time course of acute stress reactivity, allowing us to represent cardiac reactivity as interbeat interval rather than HR. However, the decision to test participants in their own home and the size of the sample precluded more sophisticated measurement. An important distinction is made between cardiac and vascular reactivity in terms of both task and individual specificity (Kamarck et al., 1994). It is important to concede that it was only cardiac reactivity that was consistently

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linked to AH-4 scores and CRT in the present study. There were no consistent associations between blood pressure reactivity and future cognitive ability. Cardiac reactivity would appear to reflect both β-adrenergic and parasympathetic influences (Balanos et al., 2010; Sloan et al., 1991). Thus, low cardiac reactivity could reflect reduced β-adrenergic drive or less of a reduction in vagal tone during the stress task. Regrettably, in the present study we cannot determine which of these was the predominant mechanism for low cardiac reactivity. However, β-adrenergic blockade has been observed to attenuate cardiac reactivity, but not blood pressure reactivity (Winzer et al., 1999). Thus, reduced β-adrenergic drive would certainly accord with the present pattern of associations. Fourth, the absence of measures of subjective stress and task engagement constitute another limitation, as it means we cannot fully rule out, as an explanation of the current results, the possibility that those with lower cognitive ability tended to disengage from what it is a cognitively challenging stress task. However, it seems to us equally possible that those with lower cognitive ability would have experienced more subjective stress when confronted with a difficult and challenging task.

In conclusion, we observed a positive association between HR reactivity and cognitive ability measured five and 12 years later. Reactivity was also associated with the relative change in cognitive ability over time; those with high HR reactivity were less likely to show relative cognitive decline. Our results are consistent with the notion that high cardiovascular stress reactivity may not necessarily be maladaptive and that low or blunted reactivity may also have negative corollaries.

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References

al'Absi, M., 2006. Hypothalamic-pituitary-adrenocortical responses to psychological stress and risk for smoking relapse. Int. J. Psychophysiol. 59, 218-227.

al'Absi, M., Hatsukami, D., Davis, G.L., 2005. Attenuated adrenocorticotropic responses to psychological stress are associated with early smoking relapse. Psychopharmacology. 181, 107-117.

Backs, R.W., Seljos, K.A., 1994. Metabolic and cardiorespiratory measures of mental effort: The effects of level of difficulty on working memory task. Int. J. Psychophysiol. 16, 57-68.

Balanos, G.M., Phillips, A.C., Frenneaux, M.P., McIntyre, D., Lykidis, C., Griffin, H.S., Carroll, D., 2010. Metabolically exaggerated cardiac reactions to acute psychological stress: The effects of resting blood pressure status and possible underlying mechanisms. Biol. Psychol. 85, 104-111.

Barnett, P.A., Spence, J.D., Manuck, S.B., Jennings, J.R.,1997. Psychological stress and the progression of carotid artery disease. J. Hypertens. 15, 49-55.

Berr, C., Balansard, B., Arnaud, J., Roussel, A.M., Alperovitch, A., 2000. Cognitive decline is associated with systemic oxidative stress: The EVA study. JAGS 48, 1285-1291.

Busato, V.V., Prins, F.J., Elshout, J.J., Hanmaker, C., 2000. Intellectual ability, learning style, personality, achievement motivation, and academic success of psychology students in higher education. Pers. Indiv. Differ. 29, 1057-1068.

Carroll, D. Harrison, L.K., Johnston, D.W., Ford, G., Hunt, K., Der, G., et al., 2000. Cardiovascular reactions to psychological stress: the influence of demographic variables. J. Epidemiol. Commun. H. 54, 876-877.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

(a) Carroll, D., Lovallo, W.R., Phillips, A.C., 2009. Are large physiological reactions to acute psychological stress always bad for health? Soc. Pers. Psychol. Compass 3, 725-743.

(b) Carroll, D., Phillips, A.C., Balanos, G.M., 2009. Metabolically exaggerated cardiac reactions to acute psychological stress revisted. Psychophysiology 46, 270-275.

Carroll, D., Phillips, A.C., Der, G., 2008 Body mass index, abdominal adiposity, obesity, and cardiovascular reactions to psychological stress in a large community sample.Psychosom. Med. 70, 653-660.

Carroll, D., Phillips, A.C., Hunt, Der, G., 2007. Symptoms of depression and cardiovascular reactions to acute psychological stress: Evidence from a population study. Biol. Psychol. 75, 68-74.

Carroll, D., Phillips, A.C., Lovallo, W.R. in press. The behavioural and health corollaries of blunted physiological reactions to acute psychological stress: Revising the reactivity hypothesis. In Wright, R.A., and Gendolla, G.H.E. (Eds.). Motivation perspectives on cardiovascular response. APA Press. Washington, D.C.

Carroll, D., Ring, C., Hunt, K., Ford, G., Macintyre, S., 2003. Blood pressure reactions to stress and the prediction of future blood pressure: Effects of sex, age, and socioeconomic position. Psychosom. Med. 70, 653-660.

Carroll, D., Smith, G.D., Sheffield, D., Shipley, M.J., Marmot, M.G., 1995. Pressor reactions to psychological stress and prediction of future blood pressure: Data from the Whitehall II Study. BMJ 310, 771-776.

Carroll, D., Smith, G.D., Shipley, M.J., Steptoe, A., Brunner, E.J., Marmot, M.G., 2001. Blood pressure reactions to acute psychological stress and future blood pressure status: A 10-year follow-up of men in the Whitehall II Study. Psychosom. Med. 63, 737-743.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology,* 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Chida, Y. & Steptoe, A. (2010). Greater cardiovascular response to laboratory mental stress are associated with poor subsequent cardiovascular risk status: A meta-analysis of prospective evidence. Hypertension 55, 1026-1032.

Christenfeld, N.J., Sloan, R.P., Carroll, D., Greenland, S., 2004. Risk factors, confounding and the illusion of statistical control. Psychosom. Med. 66, 737-743.

Cox, B.D., Blaxter, M., Buckle, A.L.J., Fenner, N.P., Golding, J.F., Gore, M., et al., 1987. The health and lifestyle survey: Preliminary report of a nationwide survey of the physical and mental health, attitudes and lifestyle of a random sample of 9003 British adults. London: Health Promotion Research Trust.

Conley, J.J., 1984. The hierarchy of consistency: A review and model of longitudinal findings on adult individual differences in intelligence, personality and self-opinion, Pers. Indiv. Differ. 5, 11-25.

Coyle, J.T., Puttfarcken, P., 1993. Oxidative stress, glutamate, and neurodenerative disorders. Science 262, 689-695.

Damasio, A., 2000. The Feeling of What Happens: Body and Emotion in the Making of Consciousness. Harvest Books.

Deary, I.J., 2000. Looking down on human intelligence: From psychometrics to the brain. Oxford: Oxford University Press.

Deary, I.J., Corley, J., Gow, A.J., Harris, S.E., Houlihan, L.M., Marioni, R.E., Penke, L., Rafnsson, S.B., Starr, J.M., 2009. Age-associated cognitive decline. Brit. Med. Bull. 92, 135-152.

Deary, I.J., Der, G., Ford, G., 2001. Reaction times and intelligence differences in a population-based cohort study. Intelligence 29, 389-399.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

DeGangi, G.A., DiPietro, J.A., Greenspan, S.I., Porges, S.W., 1991. Psychophysiological characteristics of the regulatory disordered infant. Infant. Behav. Dev. 14, 37-50.

deRooij, S.R., Phillips, A.C., Carroll, D., Roseboom, T.J. (under review). Cardiovascular and cortisol reactions to acute psychological stress and adiposity: Cross-sectional and prospective associations in the Dutch Famine Birth Cohort Study.

deRooij, S.R., Schene, A.H., Phillips, D.I., Roseboom, T.J., 2010. Depression and anxiety: Associations with biological and perceived stress reactivity to a psychological stress protocol in a middle-aged population. Psychoneuroen. 35, 866-877.

Duschek, S., Muckenthaler, M., Werner, N., Reyes del Paso, G.A., 2009. Relationships between features of autonomic cardiovascular control and cognitive performance. Biol.Psychol. 81, 110-117.

Dweck, C.S., 1986. Motivational processes affecting learning. Am. Psychol. 41, 1040-1048.

Ecob, R., 1987. The sample scheme, frame and procedures for the cohort studies (Working paper No. 6). MRC Medical Sociology Unit, Glasgow.

Elias, M.F., Wolf, P.A., D'Agostino, R.B., Cobb, J., White, L.R., 1993. Untreated blood pressure level is inversely related to cognitive functioning: The Framingham Study. Am. J. Epidemiol. 138, 353-364.

Everson, S.A., Lynch, J.W., Chesney, M.A., Kaplan,G.A., Goldberg, D.E., Shade, S.B., Cohen, R.D., Salonen, R., Salonen, J.T., 1997. Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study. BMJ 314, 553-558.

Ford, G., Ecob, R., Hunt, K., Macintyre, S., West, P., 1994. Patterns of class inequality in health through the lifespan: Class gradients at 15, 35, and 55 years in the west of Scotland. Social Sci Med 39, 1037-1050.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology,* 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Georgiades, A., Lemne, C., De Faire, U., Lindvall, K., Fredrikson, M., 1997. Stress-induced blood pressure measurements predict left ventricular mass over three years among borderline hypertensive men. Eur. J. Clin. Invest. 27, 733-739.

Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., Carroll, D., (in press). Cognitive ability and simple reaction time predict cardiac reactivity in the West of Scotland Twenty-07 Study. Psychophysiology.

Girdler, S.S., Jammer, L.D., Jarvik, M., Soles, J.R., Shapiro, D., 1997. Smoking status and nicotine administration differentially modify hemodynamic stress reactivity in men and women. Psychosom. Med. 59, 294-306.

Heaney, J.L.J., Ginty, A. T., Carroll, D., Phillips, A.C., 2011. Preliminary evidence that exercise dependence is associated with blunted cardiac and cortisol reactions to acute psychological stress. Int. J. of Psychophysiol. 79, 323-329.

Heim, A.W., 1970. Manual for the AH4 group test of general intelligence. Windsor: NFER.

Kamarck, T.W., Jennings, J.R., Pogue-Geile, M., Manuck, S.B., 1994. A multidimensional measurement model for cardiovascular reactivity: Stability and cross-validation in two adult samples. Health Psychol. 13, 471-478.

Kapuku, G.K., Treiber, F.A., Davis, H.C., Harshfield, G.A., Cook, B.B., Mensah, G.A., 1999. Hemodynamic function at rest, during acute stress, and in the field: Predictors of cardiac structure and function 2 years later in youth. Hypertension 34, 1026-1031.

Karlsson, H., Ahlborg, B., Dalman, C., Hemmingsson, T., 2010. Association between erythrocyte sedimentation rate and IQ in Swedish males aged 18-20. Brain Behav. Immun. 24, 868-873.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology,* 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Kuo, H.K., Yen, C.J., Chang, C.H., Kuo, C.K., Chen, J.H., Sorond, F., 2005. Relation of C-reactive protein to stroke, cognitive disorders, and depression in the general population: systematic review and meta-analysis. Lancet Neurol. 4, 371-380.

Launer, L.J., Masaki, K., Petrovich, H., Foley, D., Havlik, R.J., 1995. The association between mid-life blood pressure levels and late-life cognitive function: the Honolulu-Asia Aging Study. JAMA 274, 1846-1851.

Laurin, D., David Curb, J., Masaki, K.H., White, L.R., Launer, L.J., 2009. Midlife C-reactive protein and risk of cognitive decline: A 31-year follow-up. Neurobiol. Aging 30, 1724-1727.

Lovallo, W.R., 2006. Cortisol secretion patterns in addiction and addiction risk. Int. J. Psychophysiol. 59, 195-202.

Lovallo, W.R., 2007. Individual differences in response to stress and risk for addiction. In M. al'Absi, M. (Ed). Stress and Addiction: Biological and Psychological Mechanisms. Academic Press. New York.

Lovallo, W.R., Dickensheets, S.L., Myers, D.A., Thomas, T.L., Nixon, S.J., 2000. Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. Alcohol. Clin. Exp. Res. 24, 651-658.

Lynch, J.W., Everson, S.A., Kaplan, G.A., Salonen, R., Salonen, J.T., 1998. Does low socioeconomic status potentiate the effects of heightened cardiovascular responses to stress on the progression of carotid atherosclerosis? Am. J. Public Health 88, 389-394.

Macintyre, S., 1987. West of Scotland Twenty-07: Health in the community. The survey's background and rationale (Working paper No. 7). MRC Medical Sociology Unit, Glasgow.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Markovitz, J.H., Raczynski, J.M., Wallace, D., Chettur, V.,Chesney, M.A.,1998. Cardiovascular reactivity to video game predicts subsequent blood pressure increases in young men: The CARDIA study. Psychosom. Med. 60, 186-191.

Matthews, K. A., Owens, J. F., Kuller, L. H., Sutton-Tyrrell, K., Lassila, H. C., Wolfson, S.K., 1998. Stress-induced pulse pressure change predicts women's carotid atherosclerosis. Stroke 29, 1525-1530.

Matthews, K.A. Woodall, K.L., Allen, M.T., 1993. Cardiovascular reactivity to stress predicts future blood pressure status. Hypertension 22, 479-485.

McClelland, D.C., Atkinson, J.W., Clark, R.A., Lowell, F.L., 1953. The achievement motive, New York- Appleton-Century- Crofts.

Murdison, K. A., Treiber, F. A., Mensah, G., Davis, H., Thompson, W., Strong, W. B, 1998. Prediction of left ventricular mass in youth with family histories of essential hypertension. Am. J. Med. Sci. 315**,** 118-23.

Nettelbeck, T., Rabbitt, P.M., 1992. Aging, cognitive performance, and mental speed. Intelligence 16, 189-205.

Newman, J.D., McGarvey, S.T., Steele, M.S., 1999. Longitudinal association of cardiovascular reactivity and blood pressure in Samoan adolescents. Psychosom. Med. 61, 243-249.

O'Brien, E., Waeber, B., Parati, G., Staessen, J., Myers, M.G., 2001. Blood pressure measuring devices: recommendations of the European Society of Hypertension. BMJ 322, 531-536.

Panknin, T.L., Dickensheets, S.L., Nixon, S.J., Lovallo, W.R., 2002. Attenuated heart rate responses to public speaking in individuals with alcohol dependence. Alcohol. Clin. Exp. Res. 26, 841-847.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Phillips, A.C., 2011. Blunted cardiovascular reactivity relates to depression, obesity, and self-reported health. Biol. Psychol. 86, 106-113.

Phillips, A.C., Der, G., Carroll, D., 2009. Self-reported health and cardiovascular reactions to psychological stress in a large community sample: cross-sectional and prospective associations. Psychophysiology, 46, 1020-1027.

Phillips, A.C., Hunt, K., Der, G., & Carroll, D., 2011. Blunted cardiac reactions to acute psychological stress predict symptoms of depression five years later: evidence from a large community sample, Psychophysiology, 48, 142-148.

Phillips, A.C., Der, G., Hunt, K., Carroll, D., 2009. Haemodynamic reactions to acute psychological stress and smoking status in a large community sample. Int. J. Psychophysiol. 73, 273-278.

Pintrich, P.H., Schunk, D.H., 1986. Motivation in education theory, research, and applications. Englewood Cliffs, NJ- Prentice Hall.

Rabbitt, P., Diggle, P., Smith, D., Holland, F., McInnes, L., 2001. Identifying and separating the effects of practice and of cognitive ageing during a large longitudinal study of elderly community residents. Neuropsychologia 39, 532-543.

Rabbitt, P., Goward, L., 1994. Age, information processing speed, and intelligence. Q. J. Exp. Psychol. 47, 741-760.

Rafnsson, S.B., Deary, I.J., Smith, F.B., Whiteman, M.C., Rumley, A., Lowe, G.D.O., Fowkes, G.R. Cognitive decline and markers of inflammation and hemostasis: The Edinburgh Artery Study. JAGS 55, 700-707.

Registrar General, 1980. Classification of Occupations. HMSO: London, UK.

Ring, C., Burns, V.E., Caroll, D., 2002. Shifting hemodynamics of blood pressure control during prolonged mental stress. Psychophysiology 39, 585-590.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Roy, M.P., Steptoe, A., Kirschbaum, C., 1994. Association between smoking status and cardiovascular and cortisol stress responsivity in healthy young men. Int. J. Beahv. Med. 1 264-283.

Schram, M.T., Euser, S.M., de Craen, A.J., Witteman, J.C., Frolich, M., Hoffman, A., Jolles, J., Breteler, M.M., Westendorp, R.G., 2007. Systematic markers of inflammation and cognitive decline in old age. JAGS 55, 708-716.

Singh-Manoux, A., Ferrie, J.E., Lynch, J.W., Marmot, M., 2005. The role of cognitive ability (intelligence) in explaining the association between socioeconomic position and health: Evidence from Whitehall II prospective cohort study. Am. J. Epidemiol. 161, 831-839.

Singh-Manoux, A. Marmot, M., 2005. High blood pressure was associated with cognitive function in middle-age in the Whitehall II study. J. Clin. Empidemiol. 58, 1308-1315.

Sloan, R.P., Korten, J.B., Myers, M.M., 1991. Components of heart rate reactivity during mental arithmetic with and without speaking. Physiol. Behav. 50, 1039-1045.

Waldstein, S.R., 2003. The relation of hypertension to cognitive function. Curr. Dir. Psychol. Sci. 12, 9-12.

Weaver, J.D., Huang, M.H., Albert, M., Harris, T., Rowe, J.W. Seeman, T.E., 2002. Interleukin-6 and risk of cognitive decline. Neurology 59, 371-378.

Whalley, L.J., Deary, I.J., Aplleton, C.L., & Starr, J.M. (2004). Cognitive reserve and the neurobiology of cognitive aging. Ageing Research Reviews, 3, 369-382.

Willemsen, G., Ring, C., Carroll, D., Evans, P., Clow, A., & Hucklebridge, F. (1998). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and cold pressor. Psychophysiology, 35, 252-259.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Winzer, A., Ring, C., Carroll, D., Willemsen, G., Drayson, M., Kendall, M., 1999. Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of beta-adrenergic blockade. Psychophysiology 36, 591-601.

Wright, C.E., Kunz-Ebrecht, S.R., Iliffe, S., Foese, O., & Steptoe, A., 2005. Physiological correlates of cognitive functioning in an elderly population. Psychoneuroendocrino. 30, 826-838.

Yaffe, K., Lindquist, K.., Penninx, B.M., Simonsick, E.M., Pahor, M., Kritchevsky, S., Launer, L., Kuller, L., Rubin, S., Harris, T., 2003. Inflammatory markers and cognition in well-functioing African-American and white elders. Neurology 61, 76-80.

York, K. M., Hassan, M., Li, Q., Li, H., Fillingim, R. B., Sheps, D. S., 2007. Coronary artery disease and depression: Patients with more depressive symptoms have lower cardiovascular reactivity during laboratory-induced mental stress. Psychosom. Med. 69, 521–528.

Zigmond, A.S., Snaith, R.P., 1983. The Hospital Anxiety and Depression Scale. Acta Psychiatr. Scand. 67, 361-370.

Post-print, not final published version. Cite this article as: Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, 82, 167-174. http://dx.doi.org/10.1016/j.ijpsycho.2011.08.004

Table 1. Mean (SD) AH-4 scores and CRT by age cohort, sex, occupational group and disability status at the fourth and fifth follow-ups.

	AH-4 scores				CRT			
	N		Mean (SD)		N		Mean (SD)	
	4th	5th	4th	5th	4th	5th	4th	5th
Age cohort								
Youngest	396	429	38.9 (9.70)	39.8 (9.73)	429	433	538.7 (72.51)	535.0 (63.18)
Middle	478	485	36.2 (11.27)	35.6 (10.84)	496	501	621.1 (86.8)	629.3 (94.9)
Eldest	296	234	29.0 (10.92)	26.7 (10.04)	326	255	724.5 (111.5)	790.2 (210.40)
Sex								
Male	529	530	36.0 (11.37)	35.7 (11.11)	574	541	616.2 (110.49)	626.0 (163.85)
Female	641	618	34.7 (11.41)	35.0 (11.48)	677	648	622.8 (118.00)	632.4 (143.97)
Occupational group								
Manual	507	495	30.4 (11.10)	31.44 (10.95)	562	525	642.0 (124.20)	648.9 (178.22)
Non-manual	658	649	39.1 (10.17)	38.4 (10.63)	684	660	601.7 (102.93)	613.8 (128.21)
Disability status								
No disability	1136	1119	35.6 (11.32)	35.6 (11.22)	1212	1156	615.9 (110.77)	624.7 (148.68)

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Disability	34	29	26.2 (10.63)	24.3 (9.43)	39	33	740.0 (160.62)	796.0 (213.54)

Table 2. Mean (SD) values of SBP, DBP, and HR baseline and reactivity by age cohort, sex, and occupational status.

	SBP		DBP		HR	
	Baseline	Reactivity	Baseline	Reactivity	Baseline	Reactivity
Age cohort						
Yongest (n = 592)	120.0 (15.07)	10.1 (10.24)	73.4 (10.08)	6.8 (9.04)	67.5 (11.00)	10.0 (10.56)
Middle (n = 624)	127.1 (18.08)	12.3 (11.44)	80.6 (11.13)	7.1 (8.03)	66.7 (11.17)	7.7 (10.00)
Eldest (n = 431)	144.4 (21.68)	12.3 (13.92)	83.8 (11.17)	7.0 (8.92)	65.7 (9.92)	6.1 (7.74)
Sex						
Male (n = 757)	134.7 (18.25)	12.8 (11.77)	81.2 (11.18)	7.2 (8.43)	64.7 (10.43)	8.7 (9.73)
Female (n = 890)	124.3 (21.07)	10.4 (11.70)	76.8 (11.56)	6.8 (8.81)	68.4 (10.84)	7.6 (9.83)
Occupational group						
Manual (n = 722)	130.5 (21.44)	11.1 (12.22)	79.3 (11.93)	6.5 (9.07)	67.0 (11.26)	6.9 (9.53)

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Non-manual (n =872)	127.8 (19.58)	11.8 (11.39)	78.4 (11.29)	7.3 (8.24)	66.5 (10.40)	9.1 (9.90)

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Table 3. Predictors of AH-4 score at the fourth and fifth follow-up in the fully adjusted heart rate reactivity regression model.

	AH-4 scores 4th follow-up			AH-4 scores 5th follow-up		
	β	*p*	ΔR^2	β	*p*	ΔR^2
Age cohort	-.263	<.001		-.361	<.001	
Sex	-.051	.050		-.031	.226	
Occupational group	-.352	<.001		-.282	<.001	
Disability status	-.061	.019		-.084	.001	
HADS depression	-.083	.001		-.122	<.001	
BMI	-.021	.438		-.006	.804	
Baseline heart rate	-.006	.814	.254	.013	.621	.284
Heart rate reactivity	.107	<.001	.010	.130	<.001	.015

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Table 4. Predictors of CRT at the fourth and fifth follow-up in the fully adjusted heart rate reactivity regression model.

	CRT 4th follow-up			CRT 5th follow-up		
	β	*p*	ΔR^2	β	*p*	ΔR^2
Age cohort	.584	<.001		.561	<.001	
Sex	.021	.336		.026	.271	
Occupational group	.124	<.001		.084	<.001	
Disability status	.077	.001		.083	<.001	
HADS depression	.135	<.001		.104	<.001	
BMI	-.010	.656		-.012	.600	
Baseline heart rate	.019	.422	.438	-.045	.064	.389
Heart rate reactivity	-.056	.018	.003	-.078	.002	.005

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Figure Captions

Figure 1. a) AH-4 scores at the fourth follow-up by tertiles of heart rate reactivity, b) AH-4 scores at the fifth follow-up by tertiles of heart rate reactivity

Figure 2. a) CRTs at the fourth follow-up by tertiles of heart rate reactivity, b) CRTs at the fifth follow-up by tertiles of heart rate reactivity

Figure 3. a) CRT change between fourth and fifth follow-up by tertiles of heart rate reactivity, b) AH-4 change score between fourth and fifth follow-up by tertiles of heart rate reactivity

Figure 4. CRT change between fourth and fifth follow-up for tertiles of HR reactivity separately for the three age cohorts

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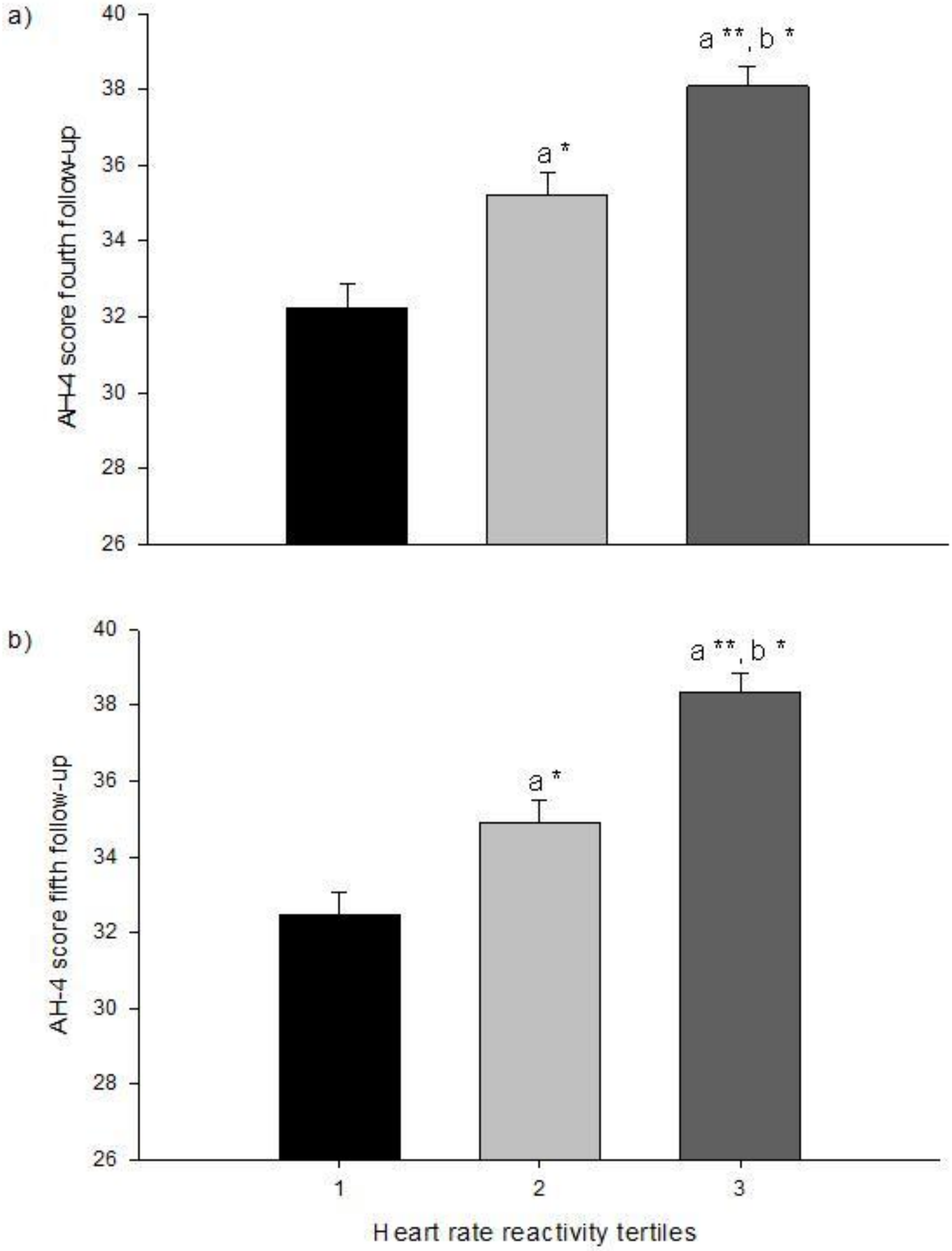

Note: a = significantly different from 1st, b = significantly different from 2nd. * = p < .01, ** = p < .001

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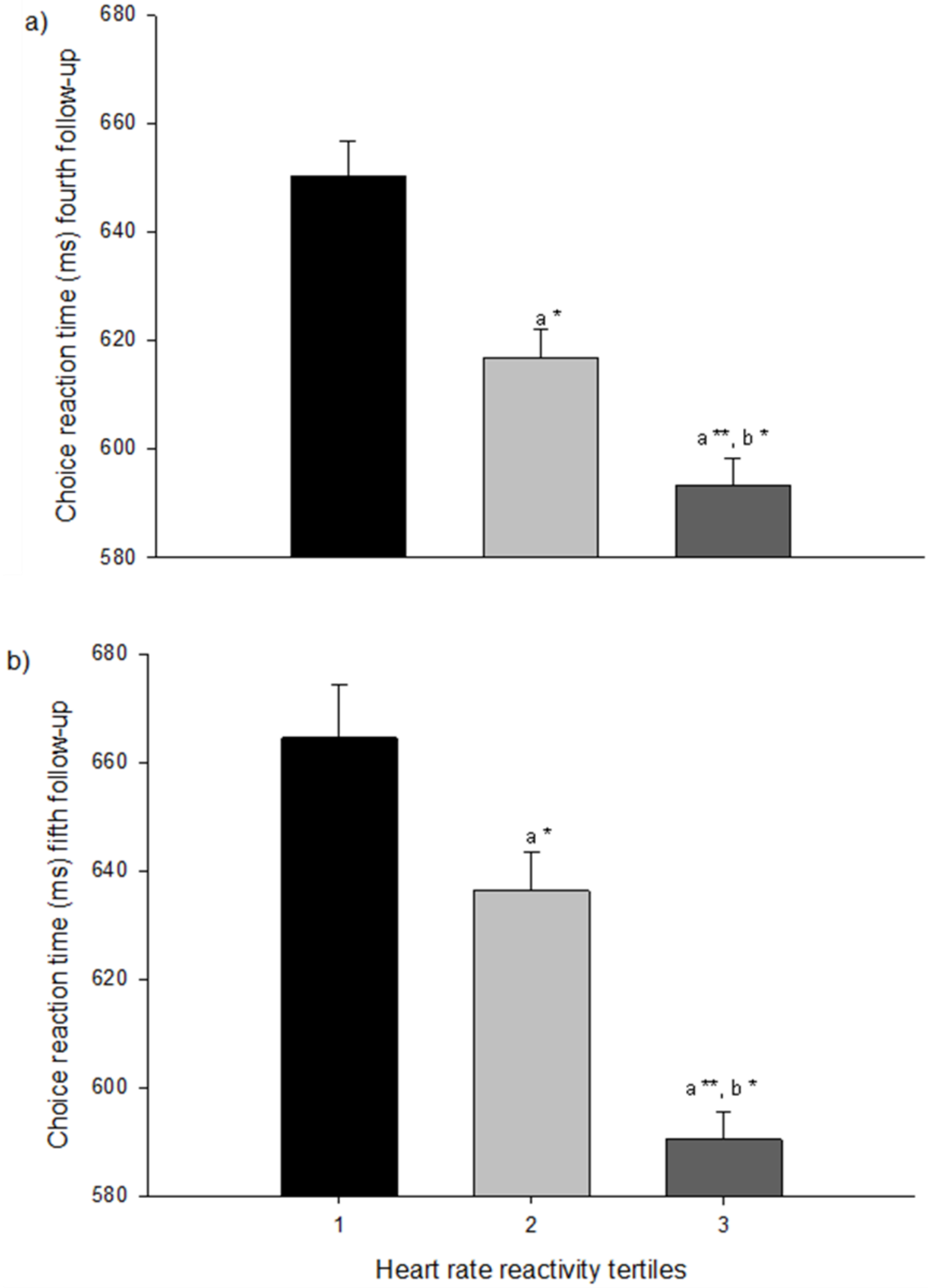

Note: a = significantly different from 1st, b = significantly different from 2nd.
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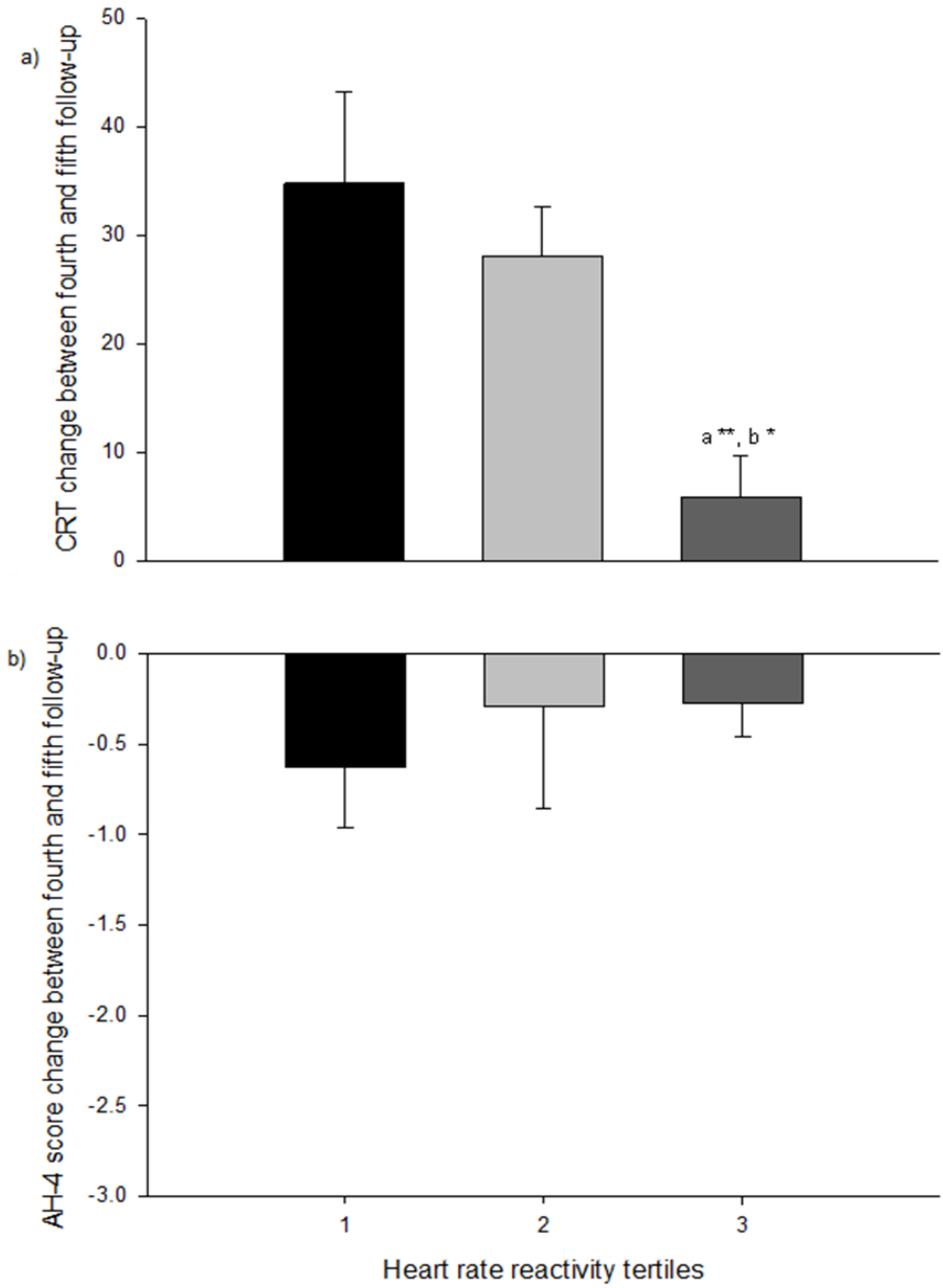

Note: a = significantly different from 1st, b = significantly different from 2nd.
*= p < .05, ** = p < .001

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