Systolic blood pressure reactions to acute stress are associated with future hypertension status in the Dutch Famine Birth Cohort Study

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Abstract

These analyses examined the association between blood pressure reactions to acute psychological stress and subsequent hypertension status in a substantial Dutch cohort. Blood pressure was recorded during a resting baseline and during three acute stress tasks, Stroop colour word, mirror tracing and speech. Five years later, diagnosed hypertension status was determined by questionnaire. Participants were 453 (237 women) members of the Dutch Famine Birth Cohort. In analysis adjusting for a number of potential confounders, systolic blood pressure reactivity was positively related to future hypertension. This was the case irrespective of whether reactivity was calculated as the peak or the average response to the stress tasks. The association was strongest for reactions to the speech and Stroop tasks. Diastolic blood pressure reactivity was not significantly associated with hypertension. The results provide support for the reactivity hypothesis.

Descriptors: systolic blood pressure, diastolic blood pressure, reactivity, acute stress, hypertension, prospective study.
1. **Introduction**


In the present analyses of data from the Dutch Famine Birth Cohort Study (Roseboom, de Rooij, Painter, 2006), we re-visited the issue of the role of cardiovascular stress reactivity in cardiovascular pathology, by examining the relationship between blood pressure reactions to a battery of standard stress tasks and prospectively determined diagnosed hypertension. Hypertension is a disease that is multiply determined (Beever & Macgregor, 1995); accordingly, the case for a role for stress reactivity in its aetiology is less likely to rest on the size
of its association with hypertension, but more on the consistency of that association across different populations, genders, and ages (Carroll et al., 2011). Further, such is the richness of the current data set that it permits adjustment for a range of potential confounding variables, far more than previous studies. In addition, blood pressure was measured continuously during stress exposure, in contrast to most other prospective studies of reactivity and hypertension where it was measured intermittently.

2. Methods

2.1. Participants

Participants were members of the Dutch Famine Birth Cohort, which comprises men and women who were born in Amsterdam, between November 1943 and February 1947. The study was designed to investigate the potential consequences of prenatal exposure to famine (the Famine occurred in the winter of 1944–45) on health in later life. It might, therefore, be suggested that population characteristics could hamper generalization of the present study results. However, this is very unlikely, as deleterious health effects have mainly been found for those exposed to famine in early gestation (Roseboom, Painter, van Abeelen, Veenendaal, & de Rooij, 2011). Only 42 (9%) of the present study sample were exposed to the famine in early gestation; a further 146 (32%) were exposed mid to late gestation. Participants were considered to be prenatally exposed to the famine if the average daily ration during any 13 week period of gestation was less than 1000 calories; information about gestation period was obtained from hospital obstetric records (Roseboom, van der Meulen, Osmond, Barker, Ravelli, & Bleker, 2001). The selection procedures and subsequent loss to follow up have been described
elsewhere (Painter et al., 2005). In 2002-2004, 725 members of the cohort provided data at a clinic assessment conducted by a research nurse. This included exposure to stress testing. In 2008-2009, 453 of those who had attended the clinic returned a completed questionnaire package, which among other things, asked about diagnosed illness. The study was approved by the local Medical Ethics Committee; the participants provided written consent.

2.2. Apparatus and Procedure

In 2002-2004, socio-demographics, life style, and anthropometrics were assessed. Socio-economic status (SES) was measured using the ISEI (International Socio-Economic Index)-92, which is based on the participant’s or partner’s occupation, whichever was higher (Bakker & Sieben, 1992). Measured values on the ISEI-92 scale ranged from 16 (low status, e.g. a cleaning person) to 87 (high status, e.g. a lawyer). Height was measured twice using a stadiometer and weight twice using Seca and portable Tefal scales. Body mass index was computed in kg/m² from the averages of the two height and weight measurements.

The stress session started in the afternoon with a baseline period after which three psychological stress tasks were performed, Stroop, mirror tracing task and a speech. The baseline consisted of a 20-min period during which the participant sat quietly. Each stress task lasted 5 minutes with 6 minutes of rest in between. The Stroop task was a computerized version of the classical colour-word conflict challenge. After a short introduction, participants were allowed to practise until they fully understood the task’s requirements. Errors and exceeding the response time limit of 5 seconds triggered a short auditory beep. For the mirror-tracing task, a star had to be traced that could only be seen in mirror image (Lafayette Instruments Corp,
Lafayette, IN, USA). Every divergence from the line triggered an auditory stimulus. The participants were allowed a practice. Participants were instructed to prioritize accuracy over speed and were told that most people could perform 5 circuits of the star without divergence from the line within the given 5 minutes. Following this, participants listened to an audio-taped instruction in which they were told to imagine that they were falsely accused of pick-pocketing (Steptoe, Kearsley, & Walters, 1993). They were then given 2 minutes to prepare a 3-minute speech to defend themselves against the accusation. The speech was videotaped and participants were told that the number of repetitions, eloquence, and persuasiveness of their performance would be marked by a team of communication experts. Continuous blood pressure recordings were made using a Finometer or a Portapres Model-2 (Finapres Medical Systems, Amsterdam, Netherlands). Four periods of 5 minutes were designated as the key measurement periods: resting baseline (15 minutes into the baseline period), and 5 minutes of Stroop, mirror-tracing, and speech task (including preparation time). A questionnaire was completed after each of the stress tasks. It included the question, ‘did you feel committed to the task?’ Answers were given on a 7-point scale with scores ranging from 1 (not at all) to 7 (very much); thus, overall commitment scores could range from 3 to 21. Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) was calculated for each measuring period by averaging over all blood pressure wave forms measured during the 5 minutes of each period. The highest average SBP and DBP value from the $3 \times 5$ minute stress periods was designated the peak response. Stress reactivity was defined as the increase from average baseline to that peak value.
The questionnaire administered in 2008-2009 asked participants whether or not they had ever received a diagnosis of hypertension from a physician. The mean (SD) temporal lag between this assessment and the stress session was 5.5 (0.6) years.

### 2.3. Statistical Analyses

Repeated measures ANOVAs (baseline, peak value) were undertaken to check whether the stress exposure perturbed SBP and DBP. The main analyses were by logistic regression with diagnosed hypertension status as the dependent variable and peak SBP and DBP reactivity as the independent variables in separate models. We first tested the unadjusted association between reactivity and hypertension and then tested models that adjusted for the following variables measured at the clinic visit: age, sex, socio-economic status, body mass index, antihypertensive medication, baseline blood pressure, smoking status, and stress task commitment, all measured at the clinic visit in 2002 - 2004. In subsequent analyses, we additionally adjusted for whether or not participants were exposed to the Dutch Famine. In sensitivity analyses, we re-ran this fully adjusted model but represented reactivity as the average SBP and DBP level across the three stress tasks, rather than the peak, minus the baseline. Finally, we also ran this adjusted model for reactivity to each stress three stress tasks separately.

### 3. Results

Table 1 presents the characteristics of the sample at the time of the clinic visit. Two hundred and eighteen participants (48%) reported a diagnosis of hypertension at the subsequent follow-up. Stress exposure perturbed both SBP, $F(1,451) = 2245.79, p < .001$, and DBP, $F(1,451) =$
2297.06, \( p < .001 \). The mean (SD) baseline and peak stress values for SBP were 127.89 (19.73) and 174.72 (28.69) and for DBP were 67.17 (11.82) and 88.39 (14.78). Peak SBP reactivity was positively associated with future hypertension in the unadjusted regression model, \( \text{OR} = 1.011, 95\% \text{CI} 1.001 – 1.021, p = .02 \). Figure 1 plots the percentage of participants with a diagnosis of hypertension by tertiles of peak SBP reactivity to illustrate this association. No such relationship was evident for peak DBP reactivity, \( p = .12 \). In the model that adjusted for the covariates listed above, high peak SBP reactivity was still associated with increased risk for hypertension, \( \text{OR} = 1.014, 95\% \text{CI} 1.002 – 1.026, p = .02 \). Risk of hypertension was also higher in men, those with elevated baseline SBP prior to stress task exposure, those with a higher body mass index, and those taking antihypertensive medication at the clinic visit. Again, there was no significant relationship between peak DBP reactivity and hypertension, \( p = .15 \). Finally, we tested a model in which, in addition to the covariates above, we adjusted for whether participants were exposed \textit{in utero} to the Dutch Famine. In all, 188 (42\%) were exposed. The outcome of these regression models were identical to those reported above; peak SBP reactivity was positively associated with hypertension, \( \text{OR} = 1.014, 95\% \text{CI} 1.002 – 1.026, p = .02 \), whereas peak DBP reactivity was not, \( p = .15 \). Table 2 presents the full results of this regression model. The famine variable was also computed as a binary variable that contrasted early exposure with the rest of the sample. Substitution of the overall exposure variable with this early exposure variable in the fully adjusted regression models left the outcomes unchanged. Peak SBP reactivity was still significantly associated with hypertension, \( \text{OR} = 1.014, 95\% \text{CI} 1.002 – 1.026, p = .02 \), whether DBP reactivity was not, \( p = .29 \). In this model, early famine exposure was not related to future hypertension status, \( p = .80 \). We also examined whether there were any interaction effects of sex...
and peak SBP reactivity and age and peak SBP reactivity using mean centred versions of the continuous variables; neither interaction was significant, $p = .59$ and $p = .63$, respectively.

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

As sensitivity analyses, we re-ran the fully adjusted, including famine exposure, models where SBP and DBP reactivity were represented as the average SBP and DBP level across the three stress tasks minus the baseline. The same outcomes emerged. Average SBP reactivity was positively related to hypertension status, $\text{OR} = 1.019$, 95%CI $1.003 - 1.035$, $p = .02$, but average DBP reactivity was not, $p = .15$. Regarding individual stress tasks, mean (SD) SBP reactivity values in mmHg were 19.77 (16.27), 30.41 (18.48), and 45.32 (21.87) for Stroop, mirror tracing, and speech, respectively. Analogous values for DBP reactivity were 9.12 (6.21), 15.75 (9.47), and 19.88 (10.29). High SBP reactions to the speech and Stroop tasks were significantly associated with an increased risk of hypertension, $\text{OR} = 1.014$, 95%CI $1.002 - 1.026$, $p = .02$, and $\text{OR} = 1.017$, 95%CI $1.001 - 1.033$, $p = .04$, respectively. This was not the case for mirror tracing, $\text{OR} = 1.011$, 95%CI $0.997 - 1.024$, $p = .12$. DBP reactivity to none of the three tasks was linked to hypertension status, $p = .15 - .39$.

4. Discussion

There was a positive bivariate association between SBP stress reactivity and diagnosed hypertension status five years later. This association was still evident after adjustment for a range of potentially confounding variables. It was also independent of whether SBP reactivity was characterised as the peak or average SBP response to the stress tasks. Analyses of the individual stress tasks indicated that larger SBP reactions to the speech and Stroop tasks, but not
mirror tracing, were associated with an increased likelihood of having a diagnosis of hypertension. There were no sex × SBP reactivity and age × SBP reactivity interactions. This is consistent with what was recently found in the West of Scotland Twenty-07 Study (Carroll et al., 2011). DBP stress reactivity was not significantly related to hypertension in any of the models tested. That SBP reactivity was a more compelling predictor of future blood pressure status then DBP reactivity is consistent with findings from both the Whitehall II (Carroll et al., 1995; Carroll et al., 2001) and West of Scotland (Carroll et al., 2011; Carroll et al., 2003) Studies and reflects a general trend (Chida & Steptoe, 2010). This would suggest that the association is largely a predominant function of the β-adrenergic activation (Carroll et al., 2011).

This study has limitations. First, the effect sizes are small. However, this is invariably the case (Chida & Steptoe, 2011). Second, 244 (35%) of participants were lost to questionnaire follow-up. This was due to cohort members having died, moved away, or no longer wanting to participate in the study. However, those lost to follow-up did not differ from those who remained in the study either in terms of baseline SBP, \( p = .78 \), or peak SBP reactivity, \( p = .23 \). Third, a substantial number of the hypertensive participants were already hypertensive at the time of stress testing and thus what might be driving the observed association is in fact a cross-sectional relationship between cardiovascular stress reactivity and hypertension, a well-documented finding. However, our findings survived adjustment for both baseline SBP level and antihypertensive medication status at the earlier time point, suggesting they were not simply an epiphenomenon of a cross-sectional relationship. Fourth, determining causality from even prospective observational studies is fraught with pitfalls and we cannot completely dismiss the possibility of residual confounding as a result of poorly measured or unmeasured variables.
However, we adjusted for a broad range of potential confounders, more than previous studies. Fourth, our outcome measure comprised self-reported diagnoses of hypertension; blood pressure was not measured at follow-up. However, given that 48% of the sample indicated that they had received a diagnosis of hypertension, the likelihood of false negatives is low.

In conclusion, greater SBP stress reactivity was associated with increased risk of having a diagnosis of hypertension five years later. The effect was small but robust, emerging in multivariate analyses for different representations of SBP reactivity. Thus, the present study lends further weight to the original reactivity hypothesis, which argues that exaggerated cardiovascular reactions to acute psychological stress will, over the life course, contribute to the development of hypertension.
Acknowledgements

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REFERENCES


Table 1. Characteristics of final sample at clinic assessment ($n = 453$)

<table>
<thead>
<tr>
<th>Variable</th>
<th>M/n</th>
<th>SD/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.23</td>
<td>0.92</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>237</td>
<td>52.3</td>
</tr>
<tr>
<td>Socio-economic status (ISEI-92)</td>
<td>50.32</td>
<td>13.73</td>
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<tr>
<td>Body mass index (kg/m$^2$)</td>
<td>28.69</td>
<td>4.79</td>
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<tr>
<td>Anti-hypertensive medication</td>
<td>108</td>
<td>23.8</td>
</tr>
<tr>
<td>Current smoker</td>
<td>104</td>
<td>23.0</td>
</tr>
<tr>
<td>Commitment to stress tasks</td>
<td>14.87</td>
<td>3.91</td>
</tr>
<tr>
<td><strong>Famine exposure (yes)</strong></td>
<td><strong>188</strong></td>
<td><strong>41.5</strong></td>
</tr>
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</table>

Table 2. Fully adjusted, including famine exposure, logistic regression model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.828</td>
<td>0.634 – 1.081</td>
<td>.83</td>
</tr>
<tr>
<td>Sex</td>
<td>1.696</td>
<td>1.052 – 2.734</td>
<td>.03</td>
</tr>
<tr>
<td>Socio-economic status</td>
<td>0.997</td>
<td>0.979 – 1.014</td>
<td>.70</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.150</td>
<td>1.085 – 1.219</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline SBP</td>
<td>1.034</td>
<td>1.020 – 1.048</td>
<td>&lt;.001</td>
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<tr>
<td>Task involvement</td>
<td>1.006</td>
<td>0.948 – 1.067</td>
<td>.85</td>
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<tr>
<td>Hypertensive medication</td>
<td>10.939</td>
<td>5.576 – 21.460</td>
<td>&lt;.001</td>
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<tr>
<td>Famine exposure</td>
<td>1.046</td>
<td>0.836 – 1.310</td>
<td>.69</td>
</tr>
<tr>
<td>Peak SBP reactivity</td>
<td>1.014</td>
<td>1.002 – 1.026</td>
<td>.02</td>
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</tbody>
</table>
http://dx.doi.org/10.1016/j.ijpsycho.2012.04.001

Figure 1. Percentage with diagnosed hypertension by tertiles of peak systolic blood pressure (SBP) reactivity
http://dx.doi.org/10.1016/j.ijpsycho.2012.04.001