Pulse rate reactivity in childhood as a risk factor for adult hypertension: the 1970 Birth Cohort Study

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Abstract

Purpose: Cardiovascular reactivity to mental stress has been used as a tool to predict short-term hypertension risk in adults but the impact of cardiovascular reactivity in childhood on hypertension in adulthood is unknown. Using the 1970 British Cohort study, we examined the association between pulse rate reactivity in childhood and risk of hypertension in adulthood.

Methods: A total of 6,507 participants (51.6% female) underwent clinical examination at 10 years of age that involved measurement of blood pressure, body mass index, and pulse rate pre- and post-examination. Hypertension was ascertained by self-reported doctor diagnosis 32 years later at age 42.

Results: On average, there was a reduction in pulse rate after the medical examination (-1.2±8.2 bpm), although nearly a third of the sample recorded an increase in pulse rate of ≥3bpm. A total of 488 (7.5%) study members developed hypertension at follow-up. After adjustment for a range of covariates including resting blood pressure and body mass index in childhood, a heightened pulse rate response to the examination (≥3bpm) was associated with greater risk of hypertension in adulthood (odds ratio = 1.30, 95% CI, 1.02, 1.67). The association persisted whether we modelled pulse rate as an absolute measure (post examination) or a change score.

Conclusion: These observational data suggest that elevated childhood cardiovascular reactivity could increase risk for hypertension in adulthood.

Key words: psychophysiology; pulse rate; stress; epidemiology; birth cohort

Introduction

Cardiovascular response to experimentally induced laboratory stressors index the way in which people may respond to stress in their everyday life.[1,2] There is robust evidence demonstrating that individuals with greater cardiovascular responses to laboratory induced mental stressors (also known as stress reactivity) subsequently have an increased risk of elevated blood pressure (BP), hypertension, left ventricular mass, subclinical atherosclerosis, and clinical cardiac events.[3,4] However, the majority of stress reactivity studies have been performed in middle- and older-aged adults in whom data interpretation is complicated by the problem of reverse causation. As such, it is unclear whether elevated reactivity indeed raises the risk of cardiovascular disease and its markers, or if heightened reactivity is simply a reflection of underlying disease pathophysiology.[5]

While investigators have attempted to address this issue by sampling apparently healthy or low-risk populations, or controlled for existing illness in their analyses, subclinical (undetected) morbidity will still be in adults present. An alternative and more powerful but little-utilised approach to minimising such reverse causation bias is to perform stress reactivity testing in pre-adult populations in whom morbidity is very rare, then follow study members over many years for the occurrence of important clinical events. Such studies are, unsurprisingly, very rare. In a small prospective study conducted on male military personal, higher norepinephrine responses to mental stress at the baseline examination (aged 19) was associated with higher BP measurements two decades later.[6]

We conducted a large, population-based study on cardiovascular reactivity with extended follow up from childhood into adulthood to examine the association of pulse rate reactivity at age 10 years with risk of hypertension in adulthood (age 42 years). Heightened pulse rate responses to a medical examination (the stressor) were used in this study as a marker of a highly reactive psychological

disposition, which we hypothesized would be representative of the way that individuals respond to stressors presented to them throughout their life course. To the best of our knowledge, this is the first such stress reactivity study in a childhood population followed into middle age for hypertension.

Methods

The 1970 British Cohort Study (BCS70) is an on-going, longitudinal study of 17,284 people born in England, Scotland and Wales in a single week of 1970 when data were collected about the births and social circumstances of babies.[7] The original study aimed to examine the social and biological characteristics of the mother in relation to neonatal morbidity but is now a multi-purpose study which has collected detailed information from cohort members on many different aspects into their adulthood. In the survey at 10 years of age study members' mother provided informed consent. At age 42 years study members provided written consent and full ethical approval was granted by the London Central Research Ethics Committee.

Data collection at 10 years of age

The age 10 survey, conducted in 1980 by a health visitor, consisted of a medical examination of the participant and a structured interview with the mother or carer. Study member's mother or carer provided information regarding how often their child watched television and played sports (categorised as: never/sometimes/often). Parents provided information on their occupation, which was categorised using the 1970 and 1980 Office of Population Censuses and Surveys Classification of Occupations (Managerial/Professional/ Intermediate [skilled & non-skilled]/ Routine and manual), and smoking habits.

The medical examination incorporated measurement of height, weight, tests of vision, hearing, and co-ordination. Systolic and diastolic BP was measured towards the end of the medical examination using a sphygmomanometer.[8] An appropriate cuff size was selected to sufficiently encircle the upper arm completely and cover two thirds of its length. Diastolic pressure was recorded at the fourth Korotkoff sound. Pulse rate was recorded at the radial artery by palpation over one minute at the beginning and end of the examination after the child had been left to settle for two minutes. Repeat assessments of pulse rate were gathered in a sub-sample (n=3600) of participants at the 16 years old follow-up. We observed moderate correlations (r's=0.25 – 0.28) between age 10 and age 16 pulse rate (Supplementary Table 1).

Data collection at 42 years of age

At age 42 years (2012/13), study members were re-surveyed. Data collection comprised a 60 minute face-to-face computer-assisted-personal-interview, which included a self-completion section. Of the 12,918 cohort members who participated in the medical examination at age 10 years, 9,842 (76.2%) took part in the age 42 survey. Hypertension was ascertained from self-reported physician diagnosis. In this sample, resting systolic BP at age 10 was predictive of self-reported hypertension at age 42 (sex adjusted OR per SD increase = 1.24, 95% CI, 1.15, 1.34, p<0.001), suggesting these self-reported data have validity.

Statistical analyses

We examined associations between pulse rate reactivity to the medical examination at age 10 with risk of hypertension at age 42 using logistic regression models. Pulse rate reactivity was modelled in several ways. Firstly, we used the post-examination pulse rate adjusting for pre-examination measure. Secondly, we calculated a change score by subtracting the post examination pulse rate

from pre-examination value. Thus, positive values represented a pulse increase in response to medical examination. For both approaches the pulse rate exposure variable was categorised into three equal groups. We calculated odds ratios (OR) and 95% confidence intervals (CI) for the risk of hypertension according to pulse rate category. Initially, ORs were adjusted for sex and resting pulse rate (model 1). They were then further adjusted (Model 2) for the child's resting systolic BP and BMI age 10, child TV viewing and sports participation age 10, father's occupation, and parents' smoking habit. All analyses were conducted using SPSS version 22.

Results

The final analytic sample comprised 6,507 participants. Reasons for missing data included loss to follow-up (n=1,939), and missing outcome (n= 1,770) or covariate data (n=2,702). On comparing the age 10 key clinical characteristics in those included and excluded from analyses, there were no differences in child BMI (p=0.36), systolic BP (p=0.75), or resting pulse rate (p=0.86). There was considerable variation in change in pulse rate following the medical examination. On average, there was a reduction in pulse rate after the examination (-1.2± 8.2 bpm), although nearly a third of the sample recorded an increase in pulse rate of ≥3bpm.

Hypertension was reported in 7.5% (n=488) of the sample at age 42. As shown in table 1, adults reporting hypertension in adulthood had slightly higher resting pulse rate, BP, and BMI at age 10 years. In addition, hypertensive adults were more likely to come from families of lower social background and have parents who smoked.

In table 2 we show that a higher pulse rate response to medical examination was associated with greater risk of hypertension in adulthood (OR = 1.30, 95% CI, 1.02, 1.67), and there was very little attenuation after adjustment for covariates, including resting BP. The association persisted whether we modelled pulse rate as an absolute measure (post examination) or a change score.

Discussion

The aim of this study was to examine the association between pulse rate reactivity at age 10 with risk of hypertension in adulthood (age 42) in a large British birth cohort study. To our knowledge, this is the first study to explore the stress reactivity hypothesis prospectively in a large population cohort with cardiovascular reactivity measures from childhood. Our findings show that a higher pulse rate response to a stressor (a medical examination) in childhood was associated with a 30% increased risk of hypertension in adulthood three decades later. This association persisted after adjusting for resting BP and other risk factors of hypertension in childhood.

Prior studies

Although heightened pulse rate response to a stressor at age 10 is not meaningful in itself, it was used as a marker of a highly reactive psychological disposition, which we hypothesized to be representative of the way that individuals respond to stressors presented to them throughout their life course. The "stress reactivity hypothesis" posits that a highly reactive psychological disposition or physiological constitution could increase the risk of future cardiovascular disease,[5] although one of the key challenges in this field has been resolving if elevated reactivity is a cause or consequence of disease. Other prospective studies examining stress reactivity and incident hypertension[9-15] have been limited to a maximum of 12 years follow-up with baseline assessment conducted in adulthood. In the present study baseline measures were conducted in childhood and outcome was measured 32 years later. Thus, it is reasonable to assume that a hyper-reactive disposition preceded the development of hypertension in the present study.

Confounding factors that influence stress responses and contribute to disease pathology may still be at play early in life. In addition, the frequency of exposure to situations that elicit stress responses is important. In order to control for these factors, we adjusted our effect estimates for childhood

adiposity, behaviours such as physical activity, exposure to parents smoking, and socioeconomic circumstances. Nevertheless, residual confounding from unmeasured variables cannot be discounted. For example, we lacked data on family history of hypertension that has been suggested to modify the association between heightened cardiovascular reactivity and risk of hypertension.[16]

The lack of a standardized psychophysiological stress paradigm was a limitation although the medical examination has relevance to real life situations. Indeed, repeated episodes of hyper-reactivity and disturbed hemodynamics in everyday life might over the life course increase tonic BP, eventually leading to incident hypertension. Previous evidence has suggested that stressors involving cognitive tasks are most strongly associated with disease outcomes,[3] although studies in this field have tended to use a wide variety of stressors.

A hyper-reactive disposition in childhood may be a marker for other underlying psychobiological processes across the life course relevant to disease. For example, acute stressors elicit transient endothelial dysfunction,[17] greater fibrinogen and interleukin 6 responses that are positively associated with increased ambulatory BP,[18] and increased cortisol responses that have been related to coronary artery calcification[19] and incident hypertension.[13]

Study strengths and limitations

The present study has some limitations. Since ratings of stress were not administered, we could not verify if changes in pulse were fully attributed to the clinical examination conducted in childhood. However, the white coat effect is well documented in pediatric populations,[20] suggesting that clinical visits are often perceived as a stressful experience. Hypertension was self-reported at age 42 years, and in the absence of direct measurement, we were unable to identify undiagnosed hypertension cases. To the best of our knowledge, however, there is no reason to expect that childhood

cardiovascular reactivity would be systematically related to failure to detect hypertension. Also, self-reported hypertension has been well validated against gold standard measures in other population studies,[21,22] and, as expected, our measure of resting BP in childhood was robustly associated with hypertension in adulthood that partly validates the outcome. Blood pressure and pulse measurements in childhood were not automated and were therefore subject to observer variation. We observed modest reproducibility of pulse rate measures between the ages of 10 and 16, thus possible visit-to visit variability is a limitation. The strengths of this study include the large sample size and ability to undertake reactivity measures in childhood with prolonged follow-up period.

Conclusion

Repeated episodes of hyper-reactivity and disturbed hemodynamics in everyday life might over the life course contribute to disease pathology, and partly explain the link between psychosocial stress and risk of cardiovascular diseases. In the present study higher pulse rate reactivity during a single visit in childhood was associated with a greater risk of hypertension in adulthood after 32 years follow up. Our data support the notion that a highly reactive psychological disposition could increase risk for hypertension in later life. These data suggest that the origins of hypertension may begin early in life, which have clinical implications for prevention.

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Author contributions

MH had full access to the data, and takes responsibility for the integrity and accuracy of the results. All authors contributed to the concept and design of study, drafting and critical revision of the manuscript.

Conflict of interest

None of the authors have any competing interests to declare.

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Table 1: Childhood characteristics according to hypertension in adulthood (n=6,507)

Childhood variables (age 10)	**Status at Age 42 follow-up**	
	Normotensive	**Hypertensive**
Sex (% male)	47.8	54.7
Body mass index (kg/m^2)†	16.9± 2.0	17.2± 2.4
Resting pulse (bpm) †	81.3± 11.2	81.5± 11.1
Resting systolic BP (mmHg) †	97.9± 10.9	100.5±10.9
Resting diastolic BP (mmHg) †	62.2± 9.2	64.1 ± 9.4
TV viewing (%)		
Never/ sometimes	21.4	18.4
Often	78.6	81.6
Sports participation (%)		
Never/ sometimes	45.7	47.1
Often	54.3	52.9
Fathers' socio-occupational class		
Managerial	6.9	6.8
Professional	26.6	22.3
Intermediate (skilled & non-skilled)	52.3	51.8
Routine/manual	14.2	19.1
Parental smoking habit		
Non-smoker	63.5	59.8
Smoker	36.5	40.2

† Mean (SD)

Table 2. Association between pulse rate reactivity in childhood with risk of adult hypertension.

Post examination pulse (bpm)	**Cases /Number at risk**	**Model 1** **OR (95% CI)**	**Model 2** **OR (95% CI)**
Low (<=76)	172/2581	1.0 (ref)	1.0
Medium (77 to 84)	162/2039	1.30 (1.02, 1.66)	1.27 (1.00, 1.62)
High (>= 85)	154/1887	1.44 (1.08, 1.94)	1.42 (1.06, 1.91)
Pulse change score (bpm)			
Reduction (<=-4)	168/2406	1.0 (ref)	1.0
Stable (-3 to 2)	164/2290	1.04 (0.83, 1.29)	1.07 (0.85, 1.36)
Increase (>= 3)	156/1811	1.35 (1.06, 1.72)	1.30 (1.02, 1.67)

Model 1: Odds ratio (OR) adjusted for sex and resting pulse rate

Model 2: OR adjusted for sex, resting pulse, systolic BP, BMI, TV viewing and sports participation aged 10, father's SES, parental smoking.

Supplementary Table 1. Reproducibility of pulse rate at age 10 and 16 (n=3,600)

	Pre-examination pulse rate at age 16	**Post-examination pulse rate age 16**
Pre-examination pulse rate at age 10	r=0.25**	r=0.25**
Post-examination pulse rate age 10	r=0.25**	r=0.28**

****p<0.001**