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Prenatal and early childhood blood lead levels and cardiovascular functioning in 9½ year old children

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Abstract

A number of studies have found that increasing lead exposure is associated with increases in blood pressure in humans. Studies with animals suggest that lead-induced increases in vascular resistance account for these increases in blood pressure. The present study assessed cardiovascular functioning at rest and in response to acute stress for 9½ year old children ($N=122$) having relatively low prenatal (cord) blood lead levels ($M=1.98$ μg/dL, $SD=1.75$) and low postnatal (early childhood) blood lead levels ($M=4.62$ μg/dL, $SD=2.51$). Higher cord blood levels were associated with higher baseline systolic blood pressure (SBP), and higher early childhood lead levels were associated with greater total peripheral (vascular) resistance (TPR) responses to acute stress. In addition, a negative association between blood lead levels and stroke volume (SV) suggests that lead-induced increases in vascular resistance were sufficient to produce cardiac afterload, a situation arising when blood pressure in the aorta makes it difficult for the left ventricle to eject blood. These effects were not mediated by differences in task performance or emotional responses to the acute stress tasks. Finally, these effects were significant for lead levels considered low, notably, below the 10 μg/dL threshold currently adopted by the CDC for deleterious effects.

Keywords: Cardiovascular; Children; Lead; Stress; Blood pressure; Vascular

1. Introduction

The association of blood lead concentration with blood pressure has been studied extensively. Although a number of studies have shown a positive association between lead and blood pressure [16,37], other studies have not shown this association [47,46]. Despite these inconsistencies, however, systematic reviews of the literature [44,14] tend to support a small positive association between blood lead levels and blood pressure. Furthermore, a lead–blood pressure association in humans is biologically plausible and is supported by research with animals [55].

It remains to be determined whether the lead-blood pressure association is causal and, if so, by what mechanism. One possibility is that increasing lead levels produce greater cardiovascular responses to acute stressors. Heightened cardiovascular reactivity has been shown to prospectively predict higher baseline blood pressure

Abbreviations: BMI, body mass index; CO, cardiac output; CVD, cardiovascular diseases; DBP, diastolic blood pressure; DDE, 1,1-dichloro-2,2-*bis*(*p*-chlorophenyl)ethylene; ECG, electrocardiogram; HCB, hexachlorobenzene; HOME, home observation for measurement of the environment; HR, heart rate; PCB, polychlorinated biphenyl; SBP, systolic blood pressure; SES, socioeconomic status; SV, stroke volume; TPR, total peripheral resistance.

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[26,58,52] and increased left ventricular mass [30] in children, as well as to predict future hypertension [28,27] and carotid atherosclerosis [5] in adults. The presumption is that chronically heightened blood pressure responses lead to hypertension either indirectly through the development of atherosclerosis, or directly, through structural remodeling of resistance vessels, as well as through vascular wall thickening that produces heightened blood pressure [11]. Therefore, heightened blood pressure responses to acute stressors represent one possible mechanism by which lead could affect resting blood pressure. Because increases in blood pressure occur either because of increases in cardiac output (CO) or total peripheral vascular resistance (TPR), blood lead levels could affect either CO or TPR, and thereby increase blood pressure responses to acute stressors.

Do heightened blood lead levels predict greater blood pressure responses to acute stressors either through underlying increases in CO or through increases in TPR? We are not aware of any studies in humans that have addressed this question. However, a number of studies with animals exposed to lead suggest increases in cardiovascular responses to chemical pressors, specifically norephinephrine and angiotensin II [17,57]. Moreover, this response appears to be a function of underlying lead-induced changes in vascular reactivity [8,56], possibly through alterations in cellular calcium metabolism [50,36,10].

The present study considered cardiovascular functioning at rest and in response to acute stress, in 9½ year old children with varying levels of prenatal and postnatal blood lead. Our cohort was drawn from those children enrolled in the Oswego Children's Study, a project designed to study the developmental effects of prenatal exposure to polychlorinated biphenyls (PCBs). Although the Oswego Children's Study is not a lead study per se, the assessment of pre-and postnatal blood lead levels as a covariate control in the Oswego cohort provided us with a serendipitous opportunity to investigate the effects of lead on cardiovascular responses to acute stress. Based on previous findings in adults, we hypothesized that increasing prenatal and postnatal blood lead levels are associated with increasing baseline blood pressure. However, because the mechanism by which lead is associated with heightened baseline blood pressure is unknown, this association may require time to develop. Based on previous findings in animals, we hypothesized that increasing postnatal blood lead levels are associated with significantly increased TPR responses to acute stress, and that this vascular resistance might, in turn, produce heightened blood pressure reactivity. We did not predict significant gender differences in lead effects, because the lead-blood pressure association has been shown in women [31] as well as men, and because the magnitude of the lead effect does not appear to vary as a function of gender [24].

2. Methods

2.1. Participants

Participants were recruited in the context of an ongoing longitudinal study of the effects of environmental toxicants on development [49,23]. Of the 202 children currently enrolled in the Oswego Children's Study, we included 122 children (66 females and 56 males) in the present analyses. Children were not included because they were either not tested ($N=25$) or had missing postnatal blood lead levels ($N=55$). Reasons for not being tested included inability to schedule within the testing window ($N=16$), technical problems ($N=4$), and refusal ($N=5$). Children were tested within 2 weeks of becoming 9½ years old, and their families were paid US$60 for participation in the current visit.

2.2. Physiological recording apparatus

Impedance cardiography and the electrocardiogram (ECG) were used for the measurement of stroke volume (SV) and heart rate (HR). An Impedance Cardiograph (Model HIC-2000, Bio-Impedance Technology, Chapel Hill, NC) was used for the generation of the impedance waveforms using a Tetrapolar band electrode configuration [21]. The ECG signal was transduced using two disposable silver/silver chloride electrodes (Meditrace 533), placed on each side of the abdomen below the impedance electrode bands, as well as a ground electrode beside the navel.

Processing of the impedance signals and ECG carried out using the Cardiac Output Program (COP_WIN, Version 5.04), an on-line computerized videographics system for impedance cardiography analysis developed by Bio-Impedance Technology (distributed by Microtronics Corporation, Chapel Hill, NC). Basal impedance, the first derivative of the pulsatile impedance signal (dZ/dt) and the ECG were sampled by a microcomputer hosting a Microstar analogue-to-digital converter board (Model 820/103). The output of the COP program included SV, HR, and cardiac output (CO; calculated as the product of mean SV and HR for a given period). The COP program calculates SV using the Kubicek equation [20] and ensemble-averaged waveforms for 30-s time periods (28-s ensemble average period, plus 2 s allowed for storage of data). Details of the calculation of the various physiological measures from impedance cardiography can be found in the guidelines by Sherwood, Allen, Fahrenberg, Kelsey, Lovallo, and van Doornen [45].

Customized software extracted continuous interbeat intervals (IBIs) from the COP program output. The IBI values were screened and edited for artifactual values. For each data series (i.e., 28-s period), the mean successive difference statistic (MSD) was computed. This statistic reflects the mean of the difference between successive IBIs. MSD filters out low-frequency sources of variability in IBI series and has been validated against pharmacologically