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Research article

Linking systemic arterial stiffness among adolescents to adverse childhood experiences

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ABSTRACT

Adverse childhood experiences (ACEs) have been linked with cardiovascular disease and early mortality among adults. Most research examines this relationship retrospectively. Examining the association between ACEs and children's cardiovascular health is required to understand the time course of this association. We examined the relationship between ACEs exposure and ECG-to-toe pulse wave velocity (PWV), a measure of systemic arterial stiffness that is strongly related to cardiovascular mortality among adults. PWV (distance/transit time; m/s) was calculated using transit times from the ECG R-wave to the pulse wave contour at the toe. Transit times were collected over 15 heartbeats and the distance from the sternal notch to the left middle toe was used. A total of 221 children (119 females) aged 10–14 years participated in data collection of PWV, hemodynamic and anthropometric variables. Parents of these children completed a modified inventory of ACEs taken from the Childhood Trust Events Survey. Multivariable regression assessed the relationship between ACEs group (<4 ACEs versus ≥4 ACEs) and PWV. Analyses yielded an ACEs group by sex interaction, with males who experienced four or more ACEs having higher PWV ($p < 0.01$). This association was independent of hemodynamic, anthropometric and sociodemographic variables ($R^2 = 0.346$; $p < 0.01$). Four or more ACEs is associated with greater arterial stiffness in male children aged 10–14 years. Addressing stress and trauma exposure in childhood is an important target for public health interventions to reduce early cardiovascular risk.

Background

Adverse childhood experiences (ACEs), a collection of traumatic early-life events during childhood such as abuse, neglect, or household dysfunction, predispose an individual to a greater risk of health problems in adulthood including cancer and heart disease (Felitti, 2002; Felitti et al., 1998). Recent national data from the U.S. indicate that approximately 679,000 children experienced one or more forms of maltreatment in 2013 (U.S. Department of Health and Human Services, Administration for Children and Families Administration on Children, Youth and Families, & Children's Bureau, 2015). This figure may underestimate the prevalence and severity of ACEs as these estimates often under-report severe exposures, such as child

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maltreatment, owing to mandatory disclosure issues associated with child protection laws (Gilbert et al., 2009a). Some speculate that only 10% of child physical or psychological abuse is reported (Gilbert et al., 2009b). In fact, data on both U.S. and Canadian adults provides evidence that approximately 31–32% of individuals reported being exposed to some form of abuse as a child (Afifi, 2011; Afifi et al., 2014).

One mechanism linking ACEs to adult health outcomes may be via disease-promoting behaviors and risk factors such as smoking, alcohol and drug abuse, physical inactivity, obesity, diabetes, and hypertension (Afifi, Mota, MacMillan, & Sareen, 2013; Alastalo et al., 2009; Dong et al., 2004; Felitti et al., 1998; Kestilä et al., 2014; Stein et al., 2010). Others have speculated that exposure to adverse experiences during child development affects the biological systems (e.g., hypothalamic–pituitary–adrenal axis; HPA axis) responsible for adapting to both external and internal stressors (i.e., allostatic dysfunction). Pathological remodeling of these systems modulates the body's response to stress, resulting in altered baseline functioning or modified stress response (Danese & McEwen, 2012; De Bellis & Zisk, 2014). For example, chronic activation of the HPA axis in children results in elevated baseline cortisol production, which may promote arterial stiffness as it suppresses nitric oxide (a potent vasodilator) synthesis (Kelly, Mangos, Williamson, & Whitworth, 1998). Pathological changes to the vasculature stemming from chronic HPA axis activation may increase a child's risk for diseases later in life including cardiovascular disease (CVD).

Arterial stiffness, which refers to the relative rigidity of the arteries, is associated with both hypertension (HTN) and CVD among adults. Adverse changes in arterial health are associated with a greater likelihood of CVD outcomes (e.g., coronary heart disease; CHD) and mortality (Hansen et al., 2006). Moreover, arterial stiffness may precede the development of HTN (Dernellis & Panaretou, 2005), a preventable risk factor of CVD (Chobanian et al., 2003). It is unclear if ACEs are associated with arterial stiffness in children or when this relationship begins, as research examining this relationship in children is scarce. In a study by Su et al. (2014), young adults (aged 13–29 years; average 21 years) who experienced two or more ACEs (e.g., abuse or neglect) had greater peripheral arterial stiffness than those who did not experience ACEs. Similarly, Loucks et al. (2014) found that middle-aged adults who experienced a poor family environment prior to the age of 18 years were more likely to have increased carotid artery intima media thickness (IMT), a measure of sub-clinical atherosclerosis. These data provide evidence that ACEs may be responsible for increased arterial stiffness in young adults; however, if cardiovascular remodeling appears in children remains unclear. The majority of studies exploring ACEs and adult health outcomes perform retrospective inquiries of early life adversity using adult samples (Afifi et al., 2013; Felitti et al., 1998). However, retrospective studies are subject to recall bias which may lead to over or underestimation of the ACEs–disease relationship and do not provide insight to the time course of this relationship. In fact, recent findings indicate that the onset of cardiovascular risk factors (e.g., clinical obesity, elevated heart rate; HR, increased waist circumference) may occur in children as young as 11 who have experienced more than four ACEs (Pretty, O'Leary, Cairney, & Wade, 2013). Beyond this, $\geq$4 ACEs is associated with a higher prevalence of learning/behavior problems (Burke, Hellman, Scott, Weems, & Carrion, 2011) as well as almost three times greater odds of poor health and serious illness (Flaherty et al., 2006) in young children, compared to children who had not been exposed to ACEs.

Finally, some studies have investigated whether an individual's sex influences exposure to ACEs or the health outcomes related to early life adversity (Afifi et al., 2014, 2013; Almeida et al., 2010; Cunningham et al., 2014). For example, Afifi and colleagues found that females were more likely to report sexual abuse and exposure to intimate partner violence as children, while males were more likely to report any type of abuse and physical abuse as children (Afifi et al., 2014). They also found that chronic diseases (e.g., CVD, HTN or diabetes) were more prevalent among males who experienced harsh physical punishment (e.g., hit, slapped, shoved), while the same chronic diseases were more prevalent among females who experienced maltreatment including abuse or neglect (Afifi et al., 2013). Other studies suggest that early life adversity is associated with coronary heart disease (CHD) in females but not males (Almeida et al., 2010). Conversely, among children, Pretty et al. (2013) found sex to be a non-significant covariate in the relationship between ACEs and HR, BMI as well as waist circumference. Beyond this small body of work, research on sex differences in the ACEs–disease relationship is sparse. As a result, it is not known if the impact of ACEs exposure on arterial stiffness varies by sex in children or adults.

Researchers often employ pulse wave velocity (PWV) as a non-invasive measure of arterial stiffness due to its inherent simplicity and reproducibility (Laurent et al., 2006). PWV refers to the speed at which an arterial pulse wave travels through the vasculature. The force of the blood ejected from the left ventricle is transmitted into a pulse wave, which travels to distal sites of the body through the arterial wall. The speed at which a pulse wave travels provides an index of arterial stiffness, as stiffer arteries transmit pulse waves faster than arteries that are more elastic (London & Pannier, 2010). Therefore, PWV's are greater in stiffer arteries. Aortic PWV (Vlachopoulos, Aznaouridis, & Stefanadis, 2010) as well as systemic PWV (Ankle Brachial Index Collaboration, 2008) are predictive of cardiovascular mortality and all-cause mortality.

The two main objectives of this study were to examine the relationship between ACEs and arterial stiffness in children and to explore potential sex differences in this relationship. Using pulse wave velocity (PWV) as a measure of systemic arterial stiffness, following previous research (Felitti et al., 1998), we hypothesized that individuals exposed to four or more ACEs would have greater arterial stiffness (higher PWV) compared to those who experienced fewer than four ACEs. Given previous findings that sex did not impact the relationship between ACEs and cardiovascular risk factors (e.g., HR, BMI) (Pretty et al., 2013), we also hypothesized that there will be no sex differences in the relationship between ACEs and PWV.