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Adult cognitive ability and socioeconomic status as mediators of the effects of childhood disadvantage on salivary cortisol in aging adults

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Summary In this longitudinal study we investigate the influence of childhood disadvantage on midlife hypothalamic-pituitary-adrenal (HPA) axis regulation. Two mechanisms by which early life stress may affect later pathophysiology are through its influence on cognitive functioning or later socioeconomic (SES) disadvantage. We predicted that individual differences in young adult cognitive ability and midlife SES would mediate the influence of childhood disadvantage on midlife cortisol. On each of three nonconsecutive days, participants provided five salivary cortisol samples corresponding to their diurnal rhythm ($N = 727$ men; mean age 55, SD = 2.6). We calculated three measures of cortisol regulation (area-under-the curve cortisol reflecting total

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daytime cortisol output; cortisol-awakening-response; and wake-to-bed slope), averaging scores for each measure across multiple days. Childhood disadvantage combined four dichotomous indicators used previously by Rutter (1985): father low SES; mother education less than 12th grade; major family disruption/separation before age 18; and large family size (more than 5 siblings). The two mediators were a measure of general cognitive ability assessed at age 20 and highest achieved midlife SES. Men from more disadvantaged childhoods were significantly more likely to have dysregulated cortisol at midlife, with higher daytime cortisol levels decades after their childhood experience. Effects of childhood disadvantage were both direct and indirect. Cognitive ability and adult SES, however, only partially mediated the associations between early life stress and midlife cortisol. Specific indirect effects accounted for 33.8% of the total effect of childhood disadvantage [$\beta = 0.12$ (0.05; 0.18)] on total daytime cortisol. Associations remained significant after accounting for ethnicity, smoking status, and self-reported depressive symptoms.

1. Introduction

A number of studies find that children from disadvantaged backgrounds are more likely to exhibit immediate and long-term dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis—the primary neuroendocrine system initiating the stress response. Forms of childhood disadvantage that disrupt the HPA axis include sociodemographic (parental low SES, maternal low education), environmental (housing, crowding), and psychological risks (family disruptions, separations from parents, trauma, parental psychiatric illness) (Chen et al., 2010; Decker, 2000; Evans, 2003; Evans and Kim, 2007; Gustafsson et al., 2010a; Hunter et al., 2011; Luecken, 1998; Luecken and Appelhans, 2006; Nicolson, 2004; Pesonen et al., 2010). Furthermore, in response to subsequent stress, children subjected to trauma and other severe early life stress develop anxiety and depression, as well as persistent sensitization of corticotropin releasing factor receptor-mediated HPA responses (Hauger et al., 2006). Researchers find that accumulation of multiple childhood hardships, rather than the impact of individual risks, is particularly pathogenic (Evans, 2004; Rutter and Quinton, 1977; Rutter et al., 1976).

The long-term influence of early life exposure to stress on the HPA axis may have potential implications for healthy aging (Hunter et al., 2011; Seeman et al., 2010; Taylor et al., 2011). The HPA axis has crucial regulatory links with multiple biological systems associated with allostatic load as well as with sleep, mood, and brain; thus functioning of the HPA axis at midlife may be part of a path ultimately linking childhood disadvantage with later pathophysiology (McEwen and Gianaros, 2010; Miller et al., 2009). Elevated cortisol in older adults predicts poorer cognitive function as well as higher prevalence of chronic medical illnesses and psychiatric disorders (Franz et al., 2011a; Lupien et al., 2009). Previous research also shows that, in adults, childhood adversity predicts higher levels of stress, lower educational attainment, later marital and occupational difficulties, higher prevalence and incidence of diseases, premature mortality, poorer health habits, poor mental health, and higher use of health care services (Anda et al., 2010; Centers for Disease Control, 2013; Rutter et al., 1976). Given these findings, understanding links between childhood environmental influences and neuroendocrine functioning at midlife has important public health implications.

Two possible mechanisms by which childhood adversity might affect HPA axis functioning in older adults are through its influences on cognitive ability and level of adult socioeconomic success. A sizable literature shows that, within a normal range of experiences, the effects of childhood environment on cognitive development are modest; in childhood environments marked by high levels of disadvantage, however, the effects of environment on cognitive development are substantial (Kremen et al., 2005; Rowe et al., 1999; Rutter, 1985; Turkheimer et al., 2003). A number of paths by which childhood environment potentially influences cognitive ability and subsequent HPA axis functioning have been proposed. It may be that pre- and post- natal experiences in a disadvantaged family environment influence both physical and brain development; the compromised physical and brain development of the child likely affect stress responsivity, cognitive development, and neuroendocrine system functioning. Animal and human studies have shown that early stress and HPA axis dysregulation has deleterious effects on the brain and cognitive functioning (McEwen and Gianaros, 2010, 2011). Children from disadvantaged environments are more likely to develop problematic health behaviors (such as smoking, low exercise or poor diet) that affect HPA axis functioning. Lower cognitive ability is also associated with poorer educational and occupational adult outcomes that are likely to affect the HPA axis through increased stress and health risks (Franz et al., 2010a, 2011a; Hart et al., 2003; Kremen et al., 2007). Low SES adult occupations tend to be more dangerous, physically onerous, and lacking in personal control than higher SES occupations; across the life course, having lower cognitive ability may thus result in more exposure to stressors and less access to resources that enable individuals to cope with stress (Evans and Kim, 2007; Evans et al., 2008). Thus the effects of childhood disadvantage on HPA axis functioning may be indirect, through its influence on cognitive ability and/or through the effects of cognitive ability on adult SES (Bertrand et al., 2004; Hart et al., 2003; Hayward and Gorman, 2004). Alternatively the influence may be direct, and not mediated by accumulated adult disadvantages. Although there are some studies that examine associations between childhood adversity and/or adult SES in relation to adult cortisol regulation, little attention has been paid to the mediating role of cognitive ability. These associations are understudied, primarily because few longitudinal studies have data on indicators of familial disadvantage, early life cognitive ability and later life HPA axis functioning. In two separate longitudinal studies, cognitive ability in early life (childhood/late adolescence) predicted HPA axis dysregulation in middle age (Franz et al., 2011a; Power et al.,