



# Socioeconomic status in children is associated with hair cortisol levels as a biological measure of chronic stress



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## ABSTRACT

**Introduction:** Low socioeconomic status (SES) may be associated with a high risk of lifestyle-related diseases such as cardiovascular diseases. There is a strong association between parental SES, stress and indicators of child health and adult health outcome. The exact mechanisms underlying this association have not yet been fully clarified. Low SES may be associated with chronic stress, which may lead to activation of the hypothalamic-pituitary-adrenal (HPA)-axis, resulting in a higher circulating level of the stress hormone cortisol. Therefore, chronic stress may mediate the association between low SES and elevated cortisol levels and its adverse outcomes.

**Aim:** We investigated whether SES was associated with a chronic measure of cortisol exposure in a child population.

**Methods:** Cortisol and cortisone were measured in scalp hair in 270 children and adolescents, aged 4–18 years, enrolled through school visits. Neighborhood level SES was based on a score developed by the Netherlands Institute for Social Research using postal codes, and this includes neighborhood measures of income education and unemployment. Maternal and paternal education level were used as indicators of family SES.

**Results:** Neighborhood level socioeconomic status score was significantly associated with hair cortisol ( $\beta = -0.103$ ,  $p = 0.007$ , 95%CI [-0.179, -0.028]) and hair cortisone ( $\beta = -0.091$ ,  $p = 0.023$ , 95%CI [-0.167, -0.015]), adjusted for age and sex. Additionally, hair cortisol was significantly correlated with maternal education level and hair cortisone was significantly correlated with paternal education level.

**Conclusion:** The results of our study suggest that the widely shown association between low family SES and adverse child health outcomes may be mediated by chronic stress, given the chronically higher levels of cortisol in children and adolescents in families with low SES. It is especially notable that the association between SES and cortisol was already found in children of young age as this can have major consequences, such as increased risk of cardio metabolic diseases in later life.

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## 1. Introduction

There is a strong association between parental socioeconomic status (SES) and indicators of child health (Evans and Kantrowitz,

2002; Evans and Kim, 2010; Clearfield et al., 2014). The association of parental SES is partly driven by environmental exposures, such as nutrition, lifestyle and healthcare. However, these variables do not explain the complete picture as the association exists even in the context of adequate healthcare and nutrition (Adler et al., 1994). Low SES is also associated with increased stress by violence in the neighborhood and at home, disorganization in school environments, environmental toxins, crowding, and noise (Evans and Kantrowitz, 2002; Evans, 2006; Evans and Kim, 2010). Psychological stressors can elicit cortisol activation through the biological stress response, depending on the characteristics of the stressor

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(Dickerson and Kemeny, 2004; Felner, 2014). This involves a physiological response to situations in which the individual experiences stress. The stress response leads to activation of the hypothalamic-pituitary-adrenal (HPA)-axis. Elevated HPA-axis activity results in increased levels of circulating cortisol. In animal studies, where randomization is feasible, intervention trials show that chronic stress exposure leads to activation of the HPA-axis. For example, cortisol concentrations measured in hair of rhesus macaques were found to be elevated in response to a prolonged environmental stressor (being relocated to a newly constructed building) (Davenport et al., 2006). In humans, where randomization trials are not feasible, association studies show a link between low SES, chronic stress and dysregulation of the HPA-axis (Hajat et al., 2010; Sheridan et al., 2013; Vaghri et al., 2013; Clearfield et al., 2014). Van Uum et al., for example, found that hair cortisol contents were significantly greater in chronic pain patients than in controls and that HCC was also increased in patients with major chronic stress (Van Uum et al., 2008). Several studies found an association between lower SES and higher levels of cortisol, many found no association, with some reporting an opposite relationship (Lupien et al., 2000; Dowd et al., 2009; Sheridan et al., 2013; Clearfield et al., 2014).

Lupien et al. measured basal morning salivary cortisol levels in 217 children with different SES levels ranging from 6 to 10 years of age. They found that children with low SES had significantly higher salivary cortisol levels than children with high SES (Lupien et al., 2000). Clearfield et al. compared diurnal salivary cortisol and maternal-infant synchrony in 32 infants, aged 6–12 months and their mothers (with low or high SES). Low-SES infants and mothers exhibited higher average salivary cortisol, compared to high-SES infants (Clearfield et al., 2014). Sheridan et al. (2013) compared maternal self-rated social status and salivary cortisol in 40 children, aged 8–12 years and also found a negative association (Sheridan et al., 2013). However some other studies even found opposite associations e.g. low SES linked to lower cortisol levels (Fuller-Rowell et al., 2012; Sturge-Apple et al., 2012).

Thus, both activation and suppression of the HPA-axis have been found in these studies. SES is associated with dysregulation of the HPA-axis, but literature is inconsistent concerning the nature of this association, varying from a positive association to a negative association, a blunted cortisol response or a flattened daily rhythm (Lupien et al., 2000; Dowd et al., 2009; Hajat et al., 2010; Sheridan et al., 2013; Vaghri et al., 2013; Clearfield et al., 2014).

These inconsistencies may arise from the way the cortisol is measured. Cortisol concentrations in these studies are mainly measured in saliva, urine, or serum. However, due to the circadian rhythm, pulsatile secretion, and the daily variation in the secretion of cortisol, none of these sampling matrices is an optimal measure of chronic cortisol concentrations. A more suitable matrix appears to be scalp hair, because hair samples can provide a historical timeline of cortisol exposure (Manenschijn et al., 2011a; Manenschijn et al., 2012; Stalder and Kirschbaum, 2012). Scalp hair at the posterior vertex displays regular growth at an average rate of 1 cm/month (Hayashi et al., 1991; Sauve et al., 2007) providing a retrospective calendar of mean cortisol exposure and HPA-axis activity of recent months to years. Hair cortisol analysis has previously been applied to investigate different causes of stress, such as shift work, unemployment and chronic pain (Davenport et al., 2006; Dettenborn et al., 2010; Manenschijn et al., 2011b; Staufenbiel et al., 2013).

In addition to cortisol, cortisone might be a useful biomarker for stress research. The biologically inactive hormone cortisone mainly originates from cortisol metabolism by enzymatic activity of 11 $\beta$ -hydroxysteroid dehydrogenase type 2. Cortisone levels in scalp hair of young children experiencing psychosocial stress were found to be elevated (Vanaelst et al., 2013).

Chronic stress can negatively impact health, resulting in an increased incidence of obesity, type 2 diabetes mellitus, and cardiovascular disease (Everson-Rose and Lewis, 2005; Manenschijn et al., 2013). The risk of obesity in young children from lower SES groups is 4 times higher than that in the higher SES groups (Veldhuis et al., 2013). Low SES, in turn, is associated with a high risk of lifestyle-related diseases such as cardiovascular diseases (Shrewsbury and Wardle, 2008). These cardiovascular diseases are partly lifestyle-related, but could also be caused by other factors such as stress or its biological mediator cortisol (Manenschijn et al., 2013).

We hypothesized that children with a lower SES experience more stress, leading to increased activation of the HPA-axis resulting in higher levels of cortisol.

We investigated whether SES was associated with chronic measurements of cortisol and cortisone, measured in scalp hair in children and adolescents from the general population of the Netherlands, aged 4–18 years.

## 2. Methods

We included children from the general population of the Netherlands in a cross-sectional observational study. Children aged 4–18 years were included. Data collection was performed between January 2011 and July 2014. Two elementary schools (one in the city of Amersfoort and one in Rotterdam) and two secondary schools in Rotterdam participated in the study. The schools are located in different districts of the city (difference in SES, income, etc.) and are of different educational levels (low, mid and high) to create the best possible reflection of the general population.

Parents and children of school classes (1 class per grade) were invited to participate in the study. All parents and children above the age of 12 years provided informed consent, children under the age of 12 years provided informed assent. The participation rate approximated 50%.

Exclusion criteria for the children were: suffering from chronic diseases, chronic use of medication, in particular glucocorticoids (both based on a completed questionnaire), or scalp hair length shorter than 2 centimeters. Data were encoded before they were entered in the database. This study was approved by the Medical Ethics Committee of the Erasmus MC (MEC-2012-25).

Anthropometric data were collected in all children, including height (cm) and weight (kg). Standing height was measured in centimeters with the precision of 1 mm, with a wall mounted stadiometer. Body weight was measured in kilograms with the precision of 2 decimal places with a calibrated electric-weight model. The standard deviation scores (SDS) of weight, height and body mass index (BMI: body mass divided by the square of the body height) were calculated based on data from the fourth Dutch nationwide growth study 1997, using Growth Analyser (Fredriks et al., 2000).

### 2.1. Hair cortisol

Hair samples of about 100 hairs were taken from the posterior vertex of the scalp, as close to the scalp as possible, using small surgical scissors. The hair was taped to a piece of paper and the scalp end was marked. The samples were stored in an envelope at room temperature until analysis (Manenschijn et al., 2011a).

The proximal 3 cm of hair, reflecting the most recent 3 months, was cut in 1 cm segments, weighed on an electronic scale and transferred to disposable glass tubes. Subsequently, the hair samples were washed with isopropanol for 2 min, after which the samples were dried for at least 2 days. Deuterated cortisol was added as an internal standard, and steroids were extracted in 1.5 ml of methanol (MeOH) for 18 h at 25 °C. After extraction, the samples

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