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The associations between adolescent sleep, diurnal cortisol patterns and cortisol reactivity to dexamethasone suppression test

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Summary Information on the associations between objectively measured sleep and hypothalamic-pituitary-adrenal axis function in early adolescence is scarce. We examined associations between average sleep duration and quality (sleep efficiency and wake after sleep onset) over 8 days with actigraphs and (1) diurnal cortisol patterns and (2) cortisol reactivity to a low-dose (3 μg/kg) overnight dexamethasone suppression test (DST) in a birth cohort born in 1998 ($N = 265$ participants, mean age 12.3 years, SD = 0.5). We also explored (3) if sleep duration and quality were affected the nights after the DST exposure. Cortisol was measured during 2 days, and participants were exposed to dexamethasone in the evening of first day. In boys, short sleep duration was associated with higher cortisol upon awakening and lower cortisol awakening response (CAR; $P < 0.05$ and $P < 0.01$). Long sleep duration in boys associated with higher CAR ($P < 0.02$). Lower sleep quality in boys associated with lower CAR, but fell slightly short of significance ($P < 0.06$). In girls, no significant associations were detected. Sleep quantity and quality were not associated with responses to the DST. There were no effects of DST on sleep ($P > 0.15$ in between-subject analyses). The average sleep patterns showed associations with diurnal cortisol patterns during early adolescence, but only in boys. Sleep was not associated

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with cortisol reactivity to DST and the exogenous corticosteroid exposure did not affect sleep significantly.

1. Introduction

Adolescence has been associated with alterations in sleep—wake organization. For instance, changes in pubertal maturation have been associated with later circadian phase preference (Carskadon et al., 1993), lower melatonin secretion amplitude (Crowley et al., 2012), and a decline in delta (1—4 Hz) and theta (4—8 Hz) NREM sleep (Campbell et al., 2012). While the need for sleep is argued to remain unchanged through adolescence (Carskadon et al., 1980), greater intrinsic and environmental pressures to later bedtimes, coupled with early school starts, easily lead to daytime sleepiness (Crowley et al., 2007). An estimated 9—42% of adolescents worldwide suffer from insufficient sleep (Gradisar et al., 2011).

Hypothalamic-pituitary-adrenal axis (HPAA), which mediates the reaction to acute physical and psychosocial stress, has a strong diurnal rhythm, with high levels upon awakening, increasing further to a peak, and then decreasing steadily across the day towards lowest level at midnight. This rhythm coincides with sleep—wake cycle, along with the suprachiasmatic nucleus (SCN) that is suggested to regulate the periodicity of corticosteroid activity (Kalsbeek et al., 2012). Sleep patterns are suggested to be in bi-directional regulatory relationship with HPAA activity. Exogenous glucocorticoid exposure (Gillin et al., 1972; Vallance et al., 2010) or environmental stressors (Akerstedt et al., 2007; Petersen et al., 2013) may increase slow wave sleep (SWS) latency, decrease sleep efficiency and increase wake after sleep onset (WASO) time. Inadequate sleep may in turn associate with altered cortisol levels during the day (Kumari et al., 2009; Vgontzas et al., 1999), and impose to adverse health outcomes (Liu et al., 2013).

The connection between altered sleep and HPAA activity characteristics has been detected already before school-age with an objective measurement of sleep (Hatzinger et al., 2008, 2010; Hatzinger et al., 2013). For instance, at 6.4 years, higher WASO time and higher proportions of light and REM-sleep were associated with increased cortisol secretion in the morning (Hatzinger et al., 2013). We have shown among healthy 8-year-old children that those with short sleep duration had higher cortisol awakening response (CAR) and higher cortisol at bedtime, and that those with low sleep efficiency had higher diurnal cortisol levels across the entire day (Räikkönen et al., 2010a). Shorter sleep duration and lower sleep quality have also been associated with higher afternoon cortisol levels at age 9 (El-Sheikh et al., 2008). Impaired sleep has not only been associated with higher diurnal cortisol levels, but also with stress responsiveness induced by the Trier Social Stress Test (TSST). Eight-year-old children with low sleep efficiency displayed higher cortisol reactivity in this test (Räikkönen et al., 2010a).

The shift to adolescence has been associated with significant increase in HPAA activity (Gunnar et al., 2009), with flattening diurnal variation along increasing age (Shirtcliff et al., 2011). However, the interconnections between HPAA function and sleep have rarely been studied among adolescents, and the existing evidence is controversial. One study reported that self-reported chronic fatigue among 15-year-old girls was not associated with CAR (Wolbeek et al., 2007), and another (Rotenberg et al., 2012) showed among 9—19-year-olds that that longer self-reported sleep duration was associated with lower awakening area under the curve (AUC) increment and diurnal AUC. In contrast, in an actigraphy study among 18—20-year-olds, individuals with a longer average sleep duration had higher awakening cortisol level and steeper decline in cortisol across the day (Zeiders et al., 2011). The bi-directionality of the effects was demonstrated in day-to-day within-subject analyses, where longer sleep during the previous night was followed by a steeper cortisol pattern during the day, which again predicted longer sleep and later wake-up time next morning (Zeiders et al., 2011). Finally, experiment of moderate sleep deprivation across three nights among 16-year-old boys did not change the CAR (Klingenberg et al., 2013).

In the current study, we examined the associations between sleep and HPAA function, assuming that poor sleep quality and short sleep duration in early adolescence are related to deviations in diurnal cortisol patterns and in responses to low-dose overnight dexamethasone suppression test (DST). We also examined whether DST affects sleep. Specifically, our first aim was to study the associations between (1) actigraph estimates of average sleep duration and quality and diurnal cortisol patterns in early adolescence. Further, we studied whether (2) average sleep duration and quality were associated with HPAA feedback inhibition as assessed by the DST. Finally, we also explored (3) the effects of the DST on sleep duration and quality on nights after the DST exposure. Since both HPAA function (Shirtcliff et al., 2011) and sleep characteristics (Pesonen et al., 2014) are shown to be dependent on sex in this age, we studied these questions separately in girls and boys.

2. Methods

2.1. Participants

The adolescents came from an urban community-based cohort comprising 1049 infants born between March and November 1998 in Helsinki, Finland (Strandberg et al., 2001). In 2009—2011, initial cohort members who had given permission to be contacted and whose addresses were traceable ($N = 920$, 87.7% of the original cohort in 1998) were invited to a follow-up, of which 692 (75.2%) could be contacted by phone (mothers of the adolescents). Of them, 451 (65.2% of those who could be contacted by phone, 49% of