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Poor sleep as a pathophysiological pathway underlying the association between stressful experiences and the diurnal cortisol profile among children and adolescents



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KEYWORDS

Sleep; Cortisol; Stressful life events; Perceived stress; Child; Adolescent Summary Recent evidence suggests that poor sleep is a potential pathway underlying the association between stressful experiences and the diurnal cortisol profile. However, existing findings are largely limited to adults. The present study examines whether poor sleep (duration, quality) mediates the relation between stressful experiences and the diurnal cortisol profile in children and adolescents. Children and adolescents (N=220, $M_{\rm age}=12.62$) provided six saliva samples over two days to derive cortisol indices (bedtime, AUC_{AG} , AUC_{TG} , slope_{MAX}). Perceived stress, stressful life events, self-reported sleep duration, and sleep quality were measured. Using bootstrapping analyses, sleep quality mediated the relation between perceived stress and AUC_{TG} ($R^2=0.10$, F(7,212)=3.55, p=.001; 95% BCI[0.09, 1.15]), as well as the relation between stressful life events and AUC_{TG} ($R^2=0.11$, F(7,212)=3.69, p=.001; 95% BCI[0.40, 3.82]). These mediation models remained significant after adjusting for sleep duration, suggesting that poor sleep quality underlies the association between stressful experiences and the diurnal cortisol profile in children and adolescents. Longitudinal data combined with objectively-measured sleep is essential to further disentangle the complex association between sleep and stress. © 2015 Elsevier Ltd. All rights reserved.

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Stress is known to alter cortisol secretion. Exposure to acute laboratory-induced stressors elicits transient increases in cortisol level (Dickerson and Kemeny, 2004). Naturally occurring stressful experiences, including perceived stress

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and stressful life events, have also been associated with a disrupted diurnal cortisol profile. Adults who report greater perceived stress (i.e., nonspecific, subjective appraised stress, Cohen et al., 1995) have higher cortisol awakening response, total cortisol level, and flatter diurnal slopes (Miller et al., 2007; Pruessner et al., 1999; Schulz et al., 1998). Greater stressful life events (e.g., unemployment, divorce) are associated with higher morning and evening cortisol levels and flatter diurnal slopes (Miller et al., 2007). Similar findings have been established in both children and adolescents (hereafter referred to as "youth" for parsimony). Youth who report greater stressful life events (e.g., family conflict, academic stress) have a higher cortisol awakening response and elevated afternoon cortisol levels than their less stressed counterparts (Gustafsson et al., 2010; Wolf et al., 2008). While there is convincing evidence that stressful experiences disrupt the diurnal cortisol profile, the potential pathways underlying this association remain unclear.

Sleep is one plausible pathway by which stressful experiences disrupt the diurnal cortisol profile. The sleep-wake cycle has a close, temporal association with diurnal cortisol secretion. Nocturnal sleep onset reliably exerts an inhibitory effect on cortisol secretion (Van Cauter et al., 1991), with the emergence of slow-wave sleep, especially during the first sleep cycle, coinciding with the lowest cortisol level across the 24-h period (Born and Fehm, 1998). Cortisol level then gradually increases over the night, paralleling the upsurge of REM sleep and the decline of slow-wave sleep in later sleep cycles (Somers et al., 1993). Given the modulatory effect of sleep on cortisol secretion, sleep has been proposed as one plausible pathway by which stress exposure "gets under the skin" to affect the diurnal cortisol profile (Vargas and Lopez-Duran, 2014). Moreover, bedtime/evening cortisol is thought to be regulated by the negative feedback loop of the hypothalamic-pituitary adrenal axis, which suppresses the release of corticotropinreleasing-hormone and adrenocorticotropic hormone from the anterior pituitary into the bloodstream, resulting in the reduction of cortisol secretion throughout the day (Sapolsky et al., 1984). As such, poor sleep may be implicated in the association between stressful experiences and the diurnal cortisol profile through alterations at the level of the negative-feedback loop of the hypothalamic-pituitary adrenal axis.

Stressful experiences also have an adverse physiological effect on sleep. Experimental findings based on animal studies show that chronic stress exposure results in adverse sleep architecture changes, including decreased slow-wave sleep, decreased REM sleep latency, and increased REM sleep (Adrien et al., 1991; Cheeta et al., 1997). In adults, greater report of perceived stress over the past month was associated with poorer sleep quality and shorter sleep duration (Kashani et al., 2012; Lund et al., 2010). In youth, cross-sectional findings show that greater exposure to stressful life events over the past year adversely affects both subjectively-reported and objectively-measured sleep. For instance, greater parental conflict, family stress, and high academic stress are related to shorter sleep duration, poorer sleep quality, lower sleep efficiency, and greater sleep problems (El-Sheikh et al., 2006; Roberts et al., 2011). Greater stressful life events are also associated with changes in sleep architecture, including decreased slow-wave sleep, decreased REM sleep latency, and increased REM sleep duration among youth (Williamson et al., 1995). Altogether, there is a clear association between greater stressful experiences and poorer sleep.

Experimental manipulation of the sleep-wake cycle disrupts the diurnal cortisol profile. Adults undergoing partial or total experimental sleep deprivation exhibit flatter diurnal slopes and 37–45% increase in cortisol levels the subsequent evening (i.e., bedtime cortisol level; Balbo et al., 2010; Leproult et al., 1997; Spiegel et al., 1999). Selective deprivation of slow-wave sleep also stimulates increased cortisol levels (Tasali et al., 2008). These experimental findings provide causal evidence suggesting that both poor sleep quality and short sleep duration contribute to disruption of the diurnal cortisol profile. Emerging cross-sectional evidence suggests that the effect of sleep deprivation on cortisol secretion also exists in youth. Greater youthreport sleep fragmentations are associated with higher total cortisol level in children (El-Sheikh et al., 2008). Shorter sleep duration, longer sleep onset latency, lower sleep efficiency, and greater sleep fragmentation based on actigraphy-assessment are associated with higher afternoon and evening cortisol levels, higher total cortisol, and flatter diurnal slopes in children (El-Sheikh et al., 2008; Hatzinger et al., 2012; Pesonen et al., 2012; Räikkönen et al., 2010). As well, adolescent boys, but not girls, with shorter actigraphyderived sleep duration have higher morning cortisol levels and a lower cortisol awakening response (Pesonen et al., 2014). Polysomnography-derived longer sleep onset latency, shorter sleep duration, lower sleep efficiency, and higher sleep fragmentation are related to higher morning and daytime cortisol levels (Hatzinger et al., 2008, 2010). While both poor sleep quality and short sleep duration have been linked to a disrupted diurnal cortisol profile, evidence suggests that sleep quality may be a marker of slow-wave sleep, a sleep stage thought to have important inhibitory effects on cortisol secretion (Jarrin et al., 2013; Kaneita et al., 2007). It is plausible that the quality of sleep may have greater impact on the diurnal cortisol profile than the quantity of sleep.

Based on evidence in the extant literature, there is strong support for the adverse effect of stressful experiences on the diurnal cortisol profile. Findings also suggest that sleep is one plausible pathway mediating this association. Despite emerging adult evidence suggesting poor sleep as a potential mediating pathway, this hypothesis has not been examined in youth. In the present study, the mediating role of sleep in the association between stressful experiences and the diurnal cortisol profile was examined in a cross-sectional sample of youth. It was hypothesized that poor sleep would mediate the relation between stressful experiences and the diurnal cortisol profile in youth.

1. Method

1.1. Participants

Youth aged 8—18 were recruited as part of the Healthy Heart Project at Concordia University, Montreal, Quebec. Participants were recruited using bookmarks distributed in primary

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