Brief Report: The Temporal Relationships Between Sleep, Cortisol, and Lung Functioning in Youth with Asthma

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Objectives This study tested the directionality of the association between sleep and health outcomes in youth with asthma. **Method** Thirty-eight youth with asthma (aged 9–19) completed a daily diary study on sleep, asthma symptoms, peak expiratory flow (PEF) measures, and salivary cortisol samples. **Results** Greater quantity of sleep predicted lower PEF% [$\beta(32) = -.33$, $p = .02$], and lower daily cortisol output [$\beta(33) = -.31$, $p = .07$] the following day. Additionally, poorer self-reported sleep quality predicted more severe symptoms the next day [$\beta(33) = .27$, $p = .05$]. In contrast, PEF%, cortisol, and asthma symptoms did not significantly predict self-reported sleep quantity or quality the next night. **Conclusions** Results suggest that sleep may affect subsequent health outcomes, rather than asthma impacting subsequent sleep, indicating the potential benefits of targeting sleep behaviors in youth with asthma.

Key words asthma; cortisol; sleep; youth.

Asthma is a disease characterized by airway obstruction, airway inflammation, and heightened reactions of the airway to stimuli. It is the most common chronic disease in children within industrialized countries, with mortality rates in adolescence exceeding those of any other age group (Akinbami & Schoendorf, 2002).

Individuals with asthma report poorer sleep than healthy individuals (Janson, Gislason, Boman, Hetta, & Roos, 1990; Vir, Bhagat, & Shah, 1997). Previous research has also demonstrated an association between poorer sleep and increased asthma symptoms and poorer pulmonary function (Chung, Khanna, & Shah, 2006; Janson et al., 1996). However, a recent review suggests that the temporal relationships among sleep and asthma outcomes are not yet understood—that is, it is unclear whether experiencing asthma symptoms disrupts sleep, or whether having poor sleep affects subsequent asthma symptoms (Majde & Krueger, 2005). It is important to understand the directionality of the association between sleep and asthma symptoms to determine how we should focus intervention efforts. For example, if poor sleep results in increased asthma symptoms, sleep could be targeted as one approach to improving asthma morbidity.

While some research supports the hypothesis that asthma symptoms lead to poorer sleep (Stores, Ellis, Wiggs, Crawford, & Thomson, 1998), other studies have found the opposite temporal relationship, reporting that poor sleep leads to asthma symptoms (Bonsignore, 1991; Ising & Ising, 2002). However, as these studies did not use objective markers of lung functioning, such as peak flow monitoring, nor did they measure sleep and asthma symptoms for several consecutive nights, more research is needed to clarify the direction of the relationship. The current study, therefore, is a preliminary attempt to assess the temporal relation between self-reported sleep and asthma during youth by employing a daily diary approach and by gathering objective lung functioning measures.

In addition to understanding the directionality of associations, we also sought to understand the potential mechanisms through which sleep and asthma may be connected. One such mechanism may involve cortisol, a hormone secreted by the hypothalamic-pituitary adrenal axis that provides anti-inflammatory signals to immune cells (Sapolsky, Romero, & Munch, 2000). Youth with asthma have been shown to have lower daily cortisol

output than healthy controls (Landstra, Postma, Boezen, & Can Aalderen, 2002). As well, Capaldi and colleagues (Capaldi Ii, Handwerger, Richardson, & Stroud, 2005) found that earlier bedtimes and fewer sleep problems in youth were associated with more adaptive cortisol responses to acute lab stressors. Low levels of cortisol could lead to poorer regulation of inflammatory processes, resulting in detrimental clinical outcomes for inflammatory conditions such as asthma. However, no previous studies that we are aware of have investigated the impact of sleep on cortisol levels in youth with asthma.

Thus, the present study involved a preliminary investigation of sleep in the context of asthma. We aimed to test the directionality of the relationships between sleep and asthma-related outcomes, including pulmonary function and asthma symptoms, as well as biological pathways, including cortisol, by using a daily diary method. We hypothesized that poorer sleep would be associated with poorer pulmonary function, more severe symptoms, and lower cortisol in youth with asthma.

Method
Participants

Thirty-eight youth with asthma, aged 9–19, were recruited from Vancouver, British Columbia for the current study and were consecutively enrolled as they participated in a larger longitudinal study on the psychosocial determinants of asthma morbidity. The University of British Columbia IRB approved the study protocol, and parents and youth signed consent/assent forms. The sample was 39.7% female, and 64% European descent, 16% Asian, and 21% ''other'' (e.g., 2.7% Aboriginal/First Nations). Youth were eligible for the study if they had been diagnosed with asthma by a doctor, were 9- to 18-years old at the time of their first visit, were English speaking, were free of any other chronic illnesses, and had not had a respiratory illness in the previous 4 weeks (if participants had a respiratory illness their visit was rescheduled).

Measures
Sleep

Youth recorded the time they went to sleep and the time they woke up every day for 2 weeks on diary cards. They rated the quality of their sleep every day on a four-point scale, from 1 (great) to 4 (terrible). This item was based on items from the Pittsburgh Sleep Quality Index, a measure that has demonstrated adequate ability to distinguish between good and poor sleepers (Buysse, Reynolds, Monk,

Berman, & Kupfer, 1989). Sleep quantity and quality values were averaged across the monitoring days to create a summary score.

Asthma Symptoms

Youth recorded the severity of their asthma symptoms during the night and day (i.e., coughing, wheezing, shortness of breath, or chest tightness) on a scale from 0 (none) to 4 (really bad). Our measure was based on the four-item CAPS scale (Chen, Oliver-Welker, Rodgers, & Strunk, 2007), which demonstrates high internal consistency ($\alpha = .85$) and predictive validity ($r = -.43$). We created a summary score by averaging ratings across the monitoring period. In the lagged analyses we assessed severity of daytime symptoms only.[1]

Lung Function

Youth completed lung function assessments in the morning and at night every day for 2 weeks using an electronic Peak Flow Meter (AM1, Jaeger, Germany). Youth were instructed to blow through the meter quickly and powerfully for at least 1 s. The Meter measures peak expiratory flow (PEF), a marker of maximum airflow during a forced expiratory maneuver beginning with the lungs fully inflated. PEF% values were calculated as a percent of each child's best PEF value (based on the youths' best value across all lab visits). Average PEF% was calculated by averaging the morning and evening percent values for each day, and then averaging values across days.[2]

Cortisol

Youth collected salivary cortisol samples using Salivettes (Sarstedt, Nuembrecht, Germany). Samples were collected four times per day over two consecutive days at 1, 4, 9, and 11 hr after waking to capture the diurnal rhythm of cortisol secretion. To determine whether youth were compliant with the sampling schedule, youths' Salivettes were stored in a bottle sealed by a MEMS 6 TrackCap Monitor (Medication Event Monitoring System, Aardex Ltd, Switzerland). Caps recorded the date and time of each opening. This methodology has been used previously (Adam, Hawkley, Kudielka, & Cacioppo, 2006). Saliva samples were mailed back to the lab and

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[1]Analyses were performed separately for night and day symptoms. Severity of night symptoms did not significantly predict any outcome variables. Therefore, only daytime symptoms were included in subsequent analyses.

[2]Analyses were also performed separately for morning and evening PEF% values. Patterns of results did not change for either cross sectional or lagged analyses.

Table I. Sample characteristics

Variable	%	Min	Max	M	SD
Age		9	19	13.85	2.72
Gender (% Male)	60.3				
Ethnicity (% White)	63.5				
Sleep (hours)		6.75	12.43	9.31	1.03
Sleep (quality)		1	2.64	1.72	0.48
PEF% best		66%	114%	87%	8%
Cortisol AUC (nmol/L)		3.33	20.32	12.47	4.33
Asthma symptoms		0	2.25	0.39	0.55

Sleep quality ratings ranged from $1 =$ Great to $4 =$ Terrible. Asthma symptom ratings range from $0 =$ none to $4 =$ really bad.

centrifuged at 1000g for 5 min, transferred to deep-well plates, and stored at $-30°C$ until assayed. Free cortisol levels in saliva were measured in duplicates using a commercially available chemiluminescence assay (IBL, Hamburg, Germany). We log transformed the data to reduce substantial skewness and calculated daily output via an area-under-the-curve (AUC) statistic using the trapezoidal rule (Pruessner, Kirshbaum, Meinlschmid, & Hellhammer, 2003).

Procedure

Families came in for a laboratory assessment as part of a larger study described elsewhere (Chen et al., 2006). After the visit, youth recorded sleep quantity, sleep quality, and asthma symptoms via daily diaries. As well, youth completed lung functioning measures and cortisol samples at home. Families received an honorarium for their participation.

Results
Associations with Demographic and Descriptive Variables

Information on demographics, other descriptives, and study variables is presented in Table I. We first tested whether any demographic or descriptive variables were associated with study outcome variables. We found that age was significantly associated with both cortisol and sleep quality ($r = .38$, $p = .03$, and $r = -.28$, $p = .04$, respectively). No other correlations were statistically significant.[3] Age was controlled in subsequent analyses.

[3]More specifically, the potential confounds of gender, ethnicity, maternal education, chronic stress, BMI, smoke exposure, inhaled corticosteroid use, beta agonist use, and asthma severity were not significantly correlated with any measures of sleep, PEF%, cortisol values, or asthma symptom severity.

Cross-sectional Associations of Sleep with Asthma Outcomes and Biological Markers

We assessed the association between sleep and study outcomes, including PEF%, cortisol, and self-reported asthma symptom severity via hierarchical linear regression analysis, with age entered into the first step and dependent variables entered into the second step. As well, we calculated effect sizes for each analysis. Cohen (1988) suggests that values close to .2 are considered small, .5 considered medium, and .8 considered large. In our cross sectional analyses, we found that greater reported quantity of sleep was associated with lower PEF% [$\beta(32) = -.33$; $b = -33.67$; CI: -60.50 to -6.85; $p = .02$, $d = .72$], and marginally lower daily cortisol output ($\beta(33) = -.31$; $b = -1.21$; CI: -2.54 $-.12$; $p = .07$, $d = .50$), but was not associated with symptom severity. In addition, youth who reported poorer sleep quality also reported more severe asthma symptoms [$\beta(33) = .27$; $b = .19$; CI: $.001$ $-.38$; $p = .05$, $d = .51$], although associations with PEF% and cortisol were not significant. Age accounted for 14% of the variance in the sleep quantity-PEF% relationship, 45.8% in the sleep quantity-cortisol relationship; and for 20.8% of the relationship between sleep quality and asthma symptoms.

Day-to-day Associations

We next sought to test whether sleep on one night would predict asthma outcomes or biological markers the next day, or alternatively, whether asthma or biological markers on one day would impact sleep the next night. The data used for these analyses were collected on days 1–3. All associations were tested using linear regression analyses, controlling for age. Our analyses demonstrated that, in general, reported sleep predicted health outcomes, but not the reverse. Reported sleep quantity on one night predicted PEF% [Night1-Day2: $\beta(32) = -.24$; $b = -18.16$; CI: -37.75 to -1.42; $p = .05$, $d = .56$; Night2-Day3: $\beta(31) = -.29$, $b = -16.64$; CI: -35.19 – 1.90; $p = .06$, $d = .52$] and cortisol [Night1-Day2: $\beta(31) = -.29$, $b = -.87$; CI: -1.98 $-.25$; $p = .11$, $d = .59$; Night2-Day3: $\beta(32) = -.38$, $b = -1.46$; CI: -2.80 $-.11$; $p = .04$, $d = 1.01$] the next day, although sleep quantity did not predict asthma symptom severity. Poorer reported sleep quality at night predicted more severe asthma symptoms the next day [Night1-Day2: $\beta(31) = .46$, $b = .33$; CI: $.15$ $-.52$; $p < .01$, $d = .72$; Night2-Day3: $\beta(31) = .27$, $b = .23$; CI: $-.05$ $-.50$; $p = .06$, $d = .57$], but did not predict PEF% or cortisol. Effect sizes were generally in the moderate range. There were no significant associations between

PEF%, asthma symptoms, or cortisol values and subsequent sleep quantity or quality the next night (all p's >.11).

Discussion

In this study, we sought to determine the temporal relationships between self-reported sleep and asthma and biological outcomes in youth with asthma. We found that greater reported sleep quantity predicted lower cortisol output and lower PEF% the following day. As well, poorer reported sleep quality predicted more severe asthma symptoms the next day. In contrast, asthma and biological measures did not predict self-reported sleep the following night. Effect sizes were in the moderate range, suggesting that these findings are both statistically and clinically meaningful. Greater sleep quantity is generally thought of as a desirable health behavior, thus it was surprising that more sleep was related to poorer health the next day. It is possible that youth who report greater sleep quantity may actually have less efficient sleep (i.e., spend more of their time in bed awake) and hence may have sleep that appears long but is actually not restorative. However, we did not have information on sleep disruptions through the night, and hence future research is needed to empirically test this possible explanation.

As well, our study found that poorer reported sleep quality predicted more severe asthma symptoms the next day. Our findings add a temporal dimension to previous research, documenting that poor sleep quality precedes increased symptom severity, and suggest that it may be beneficial to target sleep quality as one component of interventions aimed at minimizing symptoms in youth with asthma. Longer sleep duration may also be an early warning sign for worsening symptoms, and with more research, could be used as a tool for asthma management.

It is interesting that, in our results, self-reported sleep quantity, presumably a biological process, predicted biological outcomes (PEF%, cortisol), whereas sleep quality, a subjective measure, predicted self-reported severity of asthma symptoms, a subjective outcome. There may be specificity, whereby certain aspects of sleep are more strongly related to certain types of health measures. Alternatively, it may be that the subjective measures were related to one another due to similar reporting styles.

Note that age accounted for a significant proportion of the variance in the associations of self-reported sleep with lung functioning and cortisol. This may be in part because sleep requirements increase as youth enter adolescence (Dahl & Lewin, 2002), as well as because cortisol secretion increases with age (Seeman, Singer,

Wilkinson, & McEwen, 2001). Future studies should consider the impact of sleep on cortisol across the lifespan in order to determine whether sleep affects cortisol differently in various age groups.

Limitations

There are several important limitations of the study. Our sample size is small and sleep and asthma symptom variables were gathered via self-report. Future studies that utilize objective measures of sleep would help clarify relationships between quantity and quality of sleep. In addition, although we did not find asthma severity categorization or recent medication use to be confounding variables, we did not have more detailed information about youths' history of asthma. However, because our sample spanned the range of asthma severity, from mild intermittent to severe persistent, we believe that the results would be generalizable to other asthma populations. Finally, we do not know whether the influence of sleep on pulmonary functioning is unique to youth with asthma due to the lack of a healthy comparison group with these measures.

Despite these limitations, results from this study suggest that sleep may be an important health behavior for youth with asthma. In particular, both poor quality and greater sleep quantity may be risk factors for more severe asthma symptoms, poorer pulmonary function, and lower cortisol. Clinicians involved in the care of youth with asthma should be aware of these effects of sleep and consider incorporating good sleep routines into current asthma management plans. To the extent that families can work to maximize high sleep quality within children's daily routines (e.g., by instituting consistent bed times, minimizing noise and light in youths' bedroom), this may represent one behavioral approach to help youth who experience difficulties with their asthma.

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