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Poor sleep moderates the relationship between daytime napping and inflammation in Black and White men

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ABSTRACT

Objectives: To test whether napping was associated with 2 inflammatory markers with known relationships to cardiovascular disease: high-sensitivity C-reactive protein (hsCRP) and interleukin-6 (IL-6). Because IL-6 is known to impact central inflammatory processes that relate to sleep regulation, including subjective fatigue, we tested whether this relationship was moderated by sleep duration, sleep efficiency, and self-reported sleep quality.
Design: Cross-sectional.
Participants: A community sample of Black and White men (N = 253) completed a week of actigraphy and diary measures of sleep and napping and provided a fasting blood sample.
Measurements/analysis: Napping was measured as the proportion of days with at least 30 minutes napped and the average minutes napped per day. Linear regressions adjusted for race, socioeconomic status, employment, body mass index, smoking, medications that affect sleep or inflammation, working the nightshift, and day-sleeping status, followed by interaction terms between napping and sleep duration, efficiency, and quality, respectively.
Results: There were no significant main effects of actigraphy- or diary-measured napping on IL-6 or hsCRP. Moderation analyses indicated elevated IL-6 values among men who napped more days (by actigraphy) and demonstrated short sleep duration ($P = .03$). Moderation analyses also indicated elevated IL-6 among men who demonstrated greater average minutes napped (by actigraphy) and short sleep duration ($P < .001$), low efficiency ($P = .03$), and poor quality ($P = .03$). Moderation analyses involving diary napping or hsCRP were not significant.
Conclusions: Actigraphy-assessed daytime napping is related to higher IL-6 in men who demonstrate worse sleep characteristics. Daytime napping may pose additional risk for inflammation beyond the known risk conferred by short sleep.

Introduction

Sleep characteristics are associated with cardiovascular morbidity and mortality in epidemiological studies of adults. Meta-analyses support associations between self-reported short sleep and increased risk for morbidity and mortality from coronary heart disease (CHD) and stroke,[1] as well as all-cause mortality.[2,3] Additionally, meta-analytic evidence demonstrates positive associations between self-reported daily daytime napping and increased risk of all-cause mortality[4–6] and risk of cardiovascular disease (CVD).[4]

Inflammation is an important process in the etiology and pathogenesis of CVD.[7,8] Common markers of inflammation include C-reactive protein (CRP), an acute phase reactant marker of inflammation synthesized in hepatocytes,[9] and interleukin (IL)-6, a pro-inflammatory cytokine that plays a role in coordinating local and systemic inflammatory responses.[10] Circulating concentrations of CRP[11] and IL-6[12] are associated with atherosclerosis, a disease process involving the accumulation of plaque within artery walls and resulting obstruction of blood flow, which may result in clinical CVD events (eg, heart attack, stroke).[13] High-sensitivity CRP

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(hsCRP) prospectively predicts cardiovascular events in both healthy subjects and those with coronary disease,[14] whereas IL-6 is associated with risk of CHD, particularly nonfatal myocardial infarction and fatal CHD.[15]

Moreover, inflammation is increasingly studied in relation to nocturnal sleep in community samples. A recent meta-analysis found associations between continuous measures of actigraphy- or polysomnography (PSG)-assessed short sleep with elevated IL-6 but not with CRP.[16] However, comparisons of short sleep duration (<7 hours) versus a "normal" (as defined by the study authors) sleep reference (7 to 8 hours) showed no association with IL-6 or CRP.[16] In contrast, long sleep duration (>8 hours) compared with normal sleep was associated with higher CRP and IL-6.[16] Overall, the extant literature suggests associations between both short and long sleep duration with inflammatory markers, although results depend on how sleep duration is measured. Taken together, these associations mirror the literature on sleep and other indicators of poor health, such as diabetes[17] and depressive symptoms.[18]

One behavioral response to short sleep is daytime napping. However, there is limited evidence concerning associations between napping and inflammation. In older adults, one study reported a positive association between self-reported daily napping and CRP, particularly among those who reported spending either the fewest or the most hours in bed at night[19]; however, a second study reported no association between self-reported napping and circulating levels of IL-6.[20] In young adults (mean age = 29 years), evidence suggested a positive association between self-reported nap frequency across the past week and CRP, particularly among those who napped every day *and* slept short (<5 hours) at night.[21] Finally, in a sample of healthy high school students, more actigraphy-assessed proportion of days napped across a weeklong study period was associated with elevated serum IL-6 but not CRP, although, notably, almost all students in this study had short nocturnal sleep.[22] In summary, the available evidence largely suggests a positive relationship between napping and inflammation, and the possibility that short sleep may potentiate the effects of napping on inflammatory outcomes. However, there are few studies in this area, and current evidence is clearly limited by a lack of objective measurement of napping.

The current study investigated the association between napping and inflammation in a sample of Black and White men in their early 30s. There were 2 main objectives. First, we assessed associations between napping frequency and duration with CRP and IL-6, two widely examined markers of inflammation that are associated with the development of CVD. Second, because IL-6 is known to impact central inflammatory processes that relate to sleep regulation, including subjective fatigue,[10] we tested whether the relationship between napping and inflammation was stronger among men who reported poorer subjective sleep quality and experienced shorter or less efficient nocturnal sleep. We hypothesized that (1) greater napping would be associated with elevated inflammatory markers and (2) associations between napping and inflammatory markers, particularly IL-6, would be stronger among those with shorter sleep duration, lower sleep efficiency, and poorer subjective sleep quality. Finally, given meta-analytic evidence that Blacks demonstrate shorter and more fragmented sleep using both PSG and self-report measures,[23] we conducted exploratory analyses to examine whether relationships between napping and inflammation varied by race.

Methods

Participants

Data for the current study came from the population-based Pittsburgh Youth Study (PYS). Initiated in 1987, PYS is an ongoing study of Black and White men originally recruited from Pittsburgh public schools when they were in either first or seventh grade. Approximately half the sample was recruited based on a screen for risk for antisocial behavior. Further information about the PYS is available elsewhere.[24]

A subsample from the original PYS study was recruited to participate in the Pathways to Healthy Hearts Study. Men were ineligible if they were incarcerated, lived more than 75 miles away from Pittsburgh and were not planning to return, were severely mentally disabled, had withdrawn from the original PYS study, or were deceased. Recruitment began with the younger cohort. Of the 322 eligible men in the younger cohort, 272 participated in all or some portion of the study. Because the target sample size was 300 men for the measurement of cardiovascular risk, we recruited 40 additional participants from potentially eligible men in the older cohort. Overall, 307 men provided a fasting blood draw and completed a health behavior interview, and of those, 285 participated in the sleep protocol (n = 37 were from the older cohort). This study was approved by the Institutional Review Board at the University of Pittsburgh, and all participants provided informed consent. The analytic sample was similar to both the younger cohort and the potentially eligible men from the older cohort in proportion of Blacks and high-risk screening group (*P*s > .17).

Overview of procedure

Participants were scheduled to complete a laboratory visit and a 7-day sleep and daily diary protocol. Participants had a venous blood draw in a recumbent position. The blood draw was performed in the morning by trained personnel after verifying that participants had been fasting for at least 8 hours, had not used tobacco products or engaged in strenuous physical activity for at least 3 hours, and had not taken medications for infectious disease or used any illicit drugs (ie, marijuana) for at least 24 hours. Participants who reported having a cold, flu, or allergies within 3 days of the blood draw were rescheduled. For the sleep assessment, participants wore an actigraph continuously for 7 days and nights. They completed handwritten diaries each morning and evening to report sleep duration and napping. Days on which the participants reported feeling ill during the sleep assessment were removed from analyses (<1% of total study days across all participants). The blood draw occurred for 93.2% of the sample on the first day of the sleep protocol and for 3.6% during the week of the sleep protocol. The remaining 3.2% (n = 8) of the sample completed the blood draw more than 1 week before the sleep protocol (range = 9-46 days prior) because of actigraph malfunction or participant noncompliance, and subsequent participant agreement to redo the sleep protocol.

Measures

Actigraphy

Actigraph devices are worn on the nondominant wrist and record movements/accelerations; using activity counts and diary records of bedtime and wake time, periods of sleep and wake can be estimated. The Mini-mitter actiwatch models AW-16, AW-64, and Actiwatch 2 (Phillips Respironics, Bend, OR) were used to collect actigraphy data continuously over 7 days and nights. Stored data were downloaded into the Actiware software program (version 5.61) for processing and analysis. The watches were configured to collect data over a 1-minute epoch. The medium threshold (default) was selected to detect one major sleep period of at least 3 hours in duration, and as many minor sleep periods as occurred, based upon sleep onset and offset using the 10-minute criterion. Sleep periods occurring within 30 minutes of the major (generally nocturnal) sleep interval (either 30 minutes prior to sleeping or after waking) were combined with the major sleep interval. All subsequent sleep variables were then

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