Insomnia as a Cardiometabolic Risk Factor

Commentary on Strand et al. Insomnia symptoms and cardiorespiratory fitness in healthy individuals: the Nord-Trøndelag Health Study (HUNT). *SLEEP* 2013;36:99-108.

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Over the past two decades, many studies have challenged the conceptualization of insomnia as a primary or secondary disorder. Empirical studies show that insomnia tends to be a risk factor for, and a prodrome of new-onset illness and a risk factor for poor treatment response and illness recurrence.^{1,2} Theoretical papers suggest that it is difficult to establish that most cases of insomnia exhibit the temporal contiguity and variability needed to be classified as “secondary.”^{3,4} Accordingly, insomnia may be better conceptualized as a comorbid condition when it occurs concurrently with other disorders. This shift in perspective has been sufficiently persuasive that the next edition of the APA Diagnostic and Statistical Manual of Mental Disorders will abandon the primary/secondary distinction in favor of the diagnostic entity of “Insomnia Disorder.” The net effect of this change is to suggest that, as a disorder (as opposed to a symptom), more research is needed regarding the causes and consequences of insomnia.

To date, there is a relatively large literature on the association between insomnia and mental illness, particularly major depression. This literature is primarily epidemiologic in nature and focused on insomnia as a risk factor. The literature on insomnia as a risk factor for medical illnesses is substantially more recent and sparse.⁵⁻⁷ The study by Strand and colleagues⁸ in this issue of *SLEEP* is important in that it represents a critical next step in the evaluation of how insomnia disorder may serve to predispose, precipitate, and/or perpetuate medical illness. The study presented by Strand et al. is exceptionally valuable because it adds to the nascent literature on a relationship between insomnia and cardiorespiratory function.

Strand and colleagues utilized the HUNT-3 cohort to assess the relationship between (1) insomnia in terms of frequency of difficulty initiating sleep (initial insomnia), repeated awakenings (middle insomnia), and early morning awakenings (late insomnia), as well as with a global measure that summed these domains; and (2) cardiometabolic function in terms of peak oxygen uptake under heavy exercise conditions. They found that $\text{VO}_{2\text{peak}}$ (mL/kg/min) was negatively associated with insomnia

severity. For example, values were 40.4 mL/kg/min in those with no insomnia and 35.1 mL/kg/min in those with initial, middle, and late insomnia. When specific symptoms/subtypes were explored, there was a linear trend for reduced $\text{VO}_{2\text{peak}}$ to be associated with the severity of middle insomnia, and to a lesser extent with initial insomnia. These effects persisted even after adjustment for a number of potential confounders.

The study of Strand et al. has a number of important strengths. First is its large sample size ($n = 3,489$). Second, the sample is community-based (not self-selected for insomnia). Third, the use of an objective measure of cardiorespiratory fitness is exceptionally unusual to have such data on such a large sample. Fourth, the implementation of a challenge paradigm (assessing VO_2 peak) essentially adopts a “testing the limits” approach that may be needed for insomnia, given the lack of findings in studies that fail to use such an approach when evaluating insomnia.⁹ Fifth, the authors attend to insomnia subtype (initial, middle, and late insomnia)—distinctions often ignored in favor of the broader categorization of primary or chronic insomnia. Clearly, this effort was fruitful, given that middle insomnia in particular was found to be associated with reduced respiratory fitness.

The finding that middle insomnia was primarily responsible for the association of insomnia and respiratory fitness may be rationalized from a number of perspectives. One possibility is that middle insomnia describes a condition that captures the majority of the sleep state (i.e., a period ranging from 4 to 6 hours of sleep). Another possibility is that middle insomnia occurs after the initial sleep homeostatic response in the first few hours of sleep, and therefore it is, putatively, not as confounded by sleep homeostasis considerations, and thus allows for a “cleaner” assessment of the effects of sleep continuity disturbance. Yet another possibility is that compromised cardiometabolic function may be more disruptive to middle-of-the-night sleep, or, alternatively, middle insomnia is more disruptive to the processes that occur within sleep that serve to facilitate cardiometabolic function.

Although novel and important, the report by Strand et al.⁸ has a few limitations that suggest possible avenues for future research. First, the authors did not (along with many studies before them) discern whether the present findings map on to the established ICSD-2 insomnia types (e.g., idiopathic, psychophysiologic, and paradoxical insomnia types). Second, although the authors did account for smoking, a more in-depth treatment of smoking (amount, chronicity, and timing) may be

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needed. Third, the current analysis focused on insomnia as a risk factor, but analyses did not adequately address the issue of a potential overlap between insomnia and short sleep duration. There is a growing literature documenting habitual short sleep duration as an independent cardiometabolic risk factor^{10,11} and an emerging literature showing that insomnia confers the greatest degree of health risks when it is accompanied by short sleep duration.^{6,12-14} Future studies should assess both domains (insomnia and sleep duration) to discern the unique and interactive effects of these two aspects of sleep. Future studies also need to build upon the present findings by incorporating longitudinal analyses to gain insights into the following questions: Are long periods of inactivity (stemming from insomnia) leading to reduced fitness? Does insomnia (or sleep continuity disturbance or reduced sleep time) disrupt physiologic processes that confer risk for reduced fitness? Further, it is unclear from the present study⁸ whether the decreased cardiorespiratory fitness associated with insomnia would translate to increased cardiometabolic disease.

Finally, it should also be noted that VO_2 measures have been used to characterize insomnia and to support the hyperarousal hypothesis.¹⁵ Bonnet and Arand found tonic elevations in VO_2 in the context of insomnia across the 24-hour day. In contrast, Strand et al.⁸ found that individuals with insomnia, when assessed within the context of a challenge paradigm, exhibited lower peak VO_2 . This represents diminished cardiometabolic function under physical stress, as opposed to tonically elevated metabolic tone (and/or the tendency toward reduced daily physical activity¹⁶).

In conclusion, the report from Strand et al.⁸ represents an important contribution to the literature suggesting that there are not only psychological/behavioral consequences, but also medical consequences of insomnia.

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