ORIGINAL RESEARCH

Sleep cognitions associated with anxiety and depression in the elderly

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¹Department of Psychology, Université du Québec à Trois-Rivières, Trois-Rivières, QC, Canada; ²Department of Mathematics, Université du Québec à Montréal, Montréal, QC, Canada **Purpose:** The objective of this study was to identify the maladaptive sleep-related cognitions most often maintained by the elderly, according to the presence or absence of anxiety and mood disorders. The presence of dysfunctional sleep-related beliefs and attitudes at bedtime in asymptomatic, depressive, and anxious seniors was thus compared. The second objective was to verify the relationships between various dysfunctional cognitions and mental disorders.

Method: The sample in this study consisted of 2,759 participants aged 65 years and over, with a mean age of 73.8 years. They were recruited through a method of random generation of telephone numbers according to a sampling strategy based on geographic location. After the goal of the study was explained to them, the participants agreed to have health professionals visit their home and to answer questions in a 1.5-hour-long structured interview (after signing a consent form).

Results: Depressive and anxious seniors adopt dysfunctional sleep-related cognitions in higher proportions than asymptomatic older persons. Once we had controlled for the other factors, we were able to specifically link two sleep-related beliefs and all the sleep-related attitudes studied to the probability of being anxious or depressive.

Conclusion: The clarifications obtained will make it possible to improve detection, assessment, and intervention processes regarding anxiety or mood disorders, by pinpointing the most direct link between each of the dysfunctional cognitions and the two types of mental disorders, and not just the link to sleep problems.

Keywords: beliefs, worries, attitudes, thoughts, insomnia, mental health

Introduction

Among the elderly, the prevalence of anxiety and mood disorders is fairly significant. In Québec, Canada, 12% of seniors exhibit symptoms of this type.¹ In France, in any given month, the prevalence of depression and anxiety in older individuals varies from 8% to 11%.² Older persons affected by a mental disorder frequently suffer from insomnia.^{3,4} In this regard, we know that the elderly often experience sleep disturbances or poor quality sleep. In the US^{5,6} as well as in Québec, Canada,⁷ half of the seniors questioned encountered such sleep problems. One-third of the elderly questioned in Brazil also experience these problems.⁸

Included in the factors known to help to maintain sleep difficulties are dysfunctional beliefs and attitudes about sleep. These cognitions involved erroneous conceptions about the causes and consequences of insomnia, or unrealistic expectations in terms of what one's nights should be like.⁹ Attitudes related to sleep also include too many thoughts and worries at bedtime; these invasive thoughts that are difficult to suppress constitute an intrusive mental activity.¹⁰ As well, attempts to control such thoughts produce the opposite effect, and delay sleep.¹¹

Correspondence: Sophie Desjardins Département de Psychologie, Université du Québec à Trois-Rivières, C.P. 500, Trois-Rivières, QC, Canada Tel +1 819 376 5011 Fax +1 819 376 5195 Email sophie.desjardins@uqtr.ca

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© 2015 Leblanc et al. This work is published by Dove Medical Press Limited, and licensed under Creative Commons Attribution — Non Commercial (unported, v3.0) permission from Dove Medical Press Limited, provided the work is properly attributed. Permissions by Pond 2.0/. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. Permissions by Pond the scope of the License are administered by Dove Medical Press Limited, Information on how to request permission may be found at: http://www.dovepress.com/permissions.php Adults struggling with psychiatric disorders have more dysfunctional beliefs about sleep than people without psychiatric illness.¹² Dysfunctional beliefs about sleep have been linked to anxiety and depression in particular.^{13–16} We also know that seniors who sleep poorly have more dysfunctional beliefs about sleep than those who sleep well.¹⁷

A recent study, performed with adult participants, examined the presence of dysfunctional beliefs about sleep in five groups of people: good sleepers, primary insomnia patients, insomnia patients with anxiety, insomnia patients with depression, and insomnia patients with anxiety and depression. Patients suffering from insomnia with comorbidity exhibited more severe pathological sleep beliefs than patients presenting primary insomnia. The latter group of patients also had more dysfunctional beliefs about sleep than good sleepers.¹⁶

In turn, dysfunctional sleep-related attitudes such as thinking too much or worrying, which have been associated with sleep problems,^{17,18} have also been linked to anxiety in the elderly^{19–23} and to depression.^{20–24} Ruminations and worrying are seen as part of a single variable, termed "repetitive thoughts", which has been associated with anxiety and mood disorders in an adult population.²⁵ Another study, this time involving seniors, instead found that these two processes were distinct from one another,²⁶ but they did not specifically concern sleep. So it would appear relevant to verify the links between an elderly clientele and cognitions directly related to sleep, in the study of these two categories of mental disorders, so as to provide some interesting specifications in the areas of both detection and intervention.

Earlier studies have involved small groups or an adult clientele, and beliefs were grouped into more general areas or separated out according to their short- or long-term consequences. Dysfunctional sleep-related attitudes have also been studied in small or very old (individuals aged 85 years and older) samples, most often by examining the overall scores for worries or the most frequent types of worries, which were not, however, related to sleep.

The first objective of this study is to identify the maladaptive sleep-related cognitions most often maintained by the elderly, according to the presence or absence of anxiety and mood disorders. The presence of dysfunctional sleep-related beliefs and attitudes at bedtime in asymptomatic, depressive, and anxious seniors will thus be compared. The second objective is to verify the relationships between the various dysfunctional cognitions and mental disorders. A few studies on the beliefs of the elderly have analyzed associations involving these cognitions; however, the predictive aspect of dysfunctional sleep-related beliefs and attitudes in terms of mental disorders has not yet, to our knowledge, been evaluated for each of them. When these various beliefs and attitudes have been analyzed, it has usually been a matter of verifying the internal coherence or validity of a particular tool as such.

The clarifications thus obtained will make it possible to improve detection, assessment, and intervention processes regarding anxiety or mood disorders, by pinpointing the most direct link between each of the dysfunctional cognitions and the two types of mental disorders, and not just the link to sleep problems.

Method Participants

Data for this cross-sectional study were obtained from the longitudinal Québec Survey on Seniors' Health (Enquête sur la santé des aînés [ESA]) conducted in 2005–2008.27 The aim of the ESA study was to assess the physical and mental health of the French-speaking community-dwelling population aged over 65 years in the province of Québec, Canada. A sampling strategy based on geographic location and the random generation of telephone numbers was used to recruit the participants (N=2,759) in this study. The response rate was 76.5%. The responses obtained came from 90-minutelong interviews administered by health professionals at the participant's home. These health professionals had earlier been given 2 days of training on the computer-assisted questionnaire, which is similar to the Diagnostic Interview Schedule, with its proven validity and reliability,²⁸ and which was adapted for older persons.^{1,29} The interview also included items on sociodemographic data and sleep. Some of the questions verified sleep-related behavior and cognitions, and these items were derived from the Dysfunctional Beliefs and Attitudes About Sleep Scale developed by Morin et al.¹⁸ The goal of the study was explained to the participants, who then signed a consent form and received financial compensation of CAD \$30. Participants with a score of less than 22 on the mini-mental state examination³⁰ were excluded from the sample. The participants were living in 16 different regions of Québec, Canada; they were all at least 65 years of age, and their mean age was 73.8 years. Women represented 59.0% of the participants, and 58.1% of the seniors were under 75 years of age. Nearly 54% of the participants reported that they had no spouse, and more than 35% had a postsecondary level of schooling. Close to half of the participants had an annual household income of under \$25,000. Finally, the participants' sleep efficiency (that is, the ratio of time spent sleeping to the time spent in bed) was found to be over 80% for 71.6% of the seniors selected for this study. Sleep efficiency was evaluated based on the participant's bedtime, the time taken to fall

asleep, the number and duration of awakenings, etc, and was calculated based on the total sleep time divided by the time spent in bed, multiplied by 100.

Variables

The variables under study are dysfunctional beliefs and attitudes about sleep. The former are connected with the following statements: "I need eight hours of sleep to feel refreshed and function well during the day", "Since I'm getting older, I should go to bed earlier at night", "When I find it hard to fall asleep, I should stay in bed and keep trying to sleep", "It's normal not to sleep as well when we get older", and "When I've had a bad night, I should stay in bed longer in the morning to try to recover". The possible answers were: "totally disagree", "agree a bit", "generally agree", "very much agree", and "totally agree". For the purposes of the statistical analyses, these answers were then divided into two categories: that is, "totally disagree, agree a bit or generally agree" and "very much agree or totally agree". The dysfunctional attitudes were also identified as: "Having a lot of worries in my mind before going to bed at night", "Having a lot of thoughts in my head before going to bed at night", and "Being worried about the idea of sleeping when I go to bed at night". The possible answers were: "not at all", "a bit", "moderately", "a lot", and "extremely". These answers were divided into two categories: that is, "not at all or a bit" and "moderately, a lot, or extremely". The covariables under study are sex, age (over or under 75 years), marital situation (living as a couple or not), annual household income (over or under \$25,000), schooling (postsecondary schooling or not), and sleep efficiency (evaluated at over 80% or not). In terms of anxiety and mood disorders, the participants were divided into three groups based on Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-Text Revision (TR) diagnostic criteria. The 161 participants in the depressive group presented major depression, minor depression, or mania. The 103 participants in the anxious group met the diagnostic criteria for obsessive-compulsive disorder, generalized anxiety disorder, panic disorder, or a specific or social phobia. The 2,495 participants in the asymptomatic group did not suffer from a mood or anxiety disorder. The 28 participants presenting both an anxiety and mood disorder were excluded because they were too few in number.

Statistical analysis

First of all, chi-squared tests including all of the variables and covariables were conducted to obtain an overall profile of the three groups under study, and to identify the differences between them. A multinomial regression analysis was then performed with all of the variables and covariables. Next, a fully adjusted model was used to evaluate the distinct probability of suffering from an anxiety or mood disorder according to the sleep-related cognitions adopted or not adopted. The statistical analysis thus enables us to take the contribution of the other variables investigated into account and to determine the distinct significant associations. The statistical analyses were performed using PASW Statistics (v18.0), and the threshold of significance was set at P < 0.05.

Results

The descriptive statistics according to the presence or absence of an anxiety or mood disorder are presented in Table 1, which shows the prevalence of the sleep-related cognitions. The belief "I need eight hours of sleep to feel rested and to function properly the next day" is by far the most popular of the beliefs, followed by "It's normal not to sleep as well when we get older". These two beliefs are shared equally among all the groups, including the seniors not suffering from any mental disorder. The same is true for the belief "I should go to bed earlier at night". More anxious seniors adopt the belief "When I find it hard to fall asleep, I should stay in bed and keep trying to sleep" than depressive or asymptomatic older persons. Finally, the elderly persons experiencing anxiety or depression agree with "When I've had a bad night, I should stay in bed longer in the morning to try to recover" in higher proportions than asymptomatic older individuals, but this is the least frequent problematic belief.

With regard to the three dysfunctional sleep-related attitudes, when we calculate the average proportion of seniors without a mental disorder reporting these attitudes, we find that less than one-third of the people in this group adopt such attitudes. More specifically, however, the dysfunctional attitude "Having a lot of thoughts in my head before going to bed at night" is the most frequent in the asymptomatic seniors. This attitude ("Having a lot of thoughts in my head before going to bed at night") is the most frequent of the three attitudes, and occurs in 73% of the older persons with a mental disorder. Finally, anxious individuals more often have the attitude "Being worried about the idea of sleeping when I go to bed at night" than asymptomatic persons. With regard to "Having a lot of worries in my mind before going to bed at night", more than half of the depressive individuals adopt this attitude, compared with only nearly one-quarter of the asymptomatic or anxious individuals.

The results of the regression analysis (Table 2) show that, all things being equal, moreover, the beliefs "I need eight

Table I Descriptive statistics for the sociodem	ographic variables according to th	ne presence or absence of an anxiety or mood
disorder		

	Asympto	matic	Depressive		Anxious		χ²
	n	%	n	%	n	%	
I need eight hours of sleep to feel rested							
"Totally disagree" or "agree a bit"	1,113	44.6	60	37.3	43	42.4	
"Generally", "very much", or "totally agree"	1,381	55.4	101	62.7	59	57.8	
l should go to bed earlier at night							
"Totally disagree" or "agree a bit"	1,994	80.0	124	77.0	78	75.7	
"Generally", "very much", or "totally agree"	499	20.0	37	23.0	25	24.3	
I should stay in bed and keep trying to sleep							*
"Totally disagree" or "agree a bit"	1,779	72.1	119	73.9	57	55.3	
"Generally", "very much", or "totally agree"	689	27.9	42	26.1	46	44.7	
Normal not to sleep as well when we get older							
"Totally disagree" or "agree a bit"	1,572	63.3	93	59.1	68	66.7	
"Generally", "very much", or "totally agree"	911	36.7	67	41.9	34	33.3	
I should stay in bed longer in the morning							*
"Totally disagree" or "agree a bit"	2,141	86.0	129	80.1	82	80.4	
"Generally", "very much", or "totally agree"	349	14.0	32	19.9	20	19.6	
Having a lot of worries in my mind							*
"Not at all" or "a bit"	1,867	71.8	75	46.6	35	75.0	
"Moderately", "a lot", or "extremely"	621	28.2	86	54.3	68	25.0	
Having a lot of thoughts in my head							*
"Not at all" or "a bit"	1,288	51.7	43	26.7	29	28.2	
"Moderately", "a lot", or "extremely"	1,204	48.3	118	73.3	74	71.8	
Being worried about the idea of sleeping	,						*
"Not at all" or "a bit"	2,224	89.2	133	82.6	75	78.2	
"Moderately", "a lot", or "extremely"	268	10.8	28	17.4	28	27.2	
Age							*
Under 75 years	1,430	57.3	107	66.5	65	63.7	
75 years and over	1,064	42.7	54	33.5	37	36.3	
Sex	,						*
Male	1,057	42.4	46	28.6	29	28.4	
Female	1,438	57.6	115	71.4	73	71.6	
Civil status	,						
Married or living together	1,150	46.3	70	44.0	50	49.5	
Single, separated, divorced, or widowed	1,336	53.7	83	56.0	51	50.5	
Schooling	,						
None to secondary	1,618	64.9	108	67.1	58	56.3	
Postsecondary	876	35.1	53	32.9	45	43.7	
Annual household income							
Under \$25.000	1,229	49.3	77	47.5	51	49.5	
\$25,000 and over	1,264	50.7	85	52.5	52	50.5	
Sleep efficiency	.,=•.						*
80% or more	1,624	72.5	94	65.3	56	61.5	
Less than 80%	617	27.5	50	34.7	35	38.5	

Notes: *P<0.05, **P<0.01.

hours of sleep to feel rested and to function properly the next day", "Since I'm getting older, I should go to bed earlier at night", and "When I've had a bad night, I should stay in bed longer in the morning to try to recover" do not enable one to predict the fact of belonging to one of the three groups. The probability of suffering from anxiety is greater if one holds the belief "When I find it hard to fall asleep, I should stay in bed and keep trying to sleep" and if one worries about the idea of sleeping at bedtime. Moreover, disagreeing with the belief "It's normal not to sleep as well when we get older" is linked to the risk of suffering from an anxiety disorder. In fact, holding this belief is associated with the likelihood of being depressive rather than anxious. Having many worries at bedtime is linked to the probability of suffering from the two types of mental disorders, but not adopting this dysfunctional attitude is associated with the likelihood of being depressive rather than anxious. Finally, having many thoughts at bedtime is associated with the risk of suffering from a mood disorder.

Table 2 ORs and 95% Cls for slee	p-related cognitions predicting t	the presence or absence of an anxiet	y or mood disorder

	Depressiv		Anxious vs		Depressive vs	
	asymptomatic ^a		asymptomatic ^a		anxious ^a OR 95% C	
	OR	95% CI	OR	95% CI	OR	95% CI
I need eight hours of sleep to feel rested	0.70	0.54 1.15	0.02		0.04	0 47 1 52
"Totally disagree" or "agree a bit"	0.79	0.54–1.15	0.93	0.58–1.50	0.84	0.47-1.52
"Generally", "very much", or "totally agree"	1.00		1.00		1.00	
I should go to bed earlier at night						
"Totally disagree" or "agree a bit"	0.81	0.53-1.25	1.14	0.66–1.97	0.72	0.37-1.39
"Generally", "very much", or "totally agree"	1.00		1.00		1.00	
I should stay in bed and keep trying to sleep						
"Totally disagree" or "agree a bit"	1.33	0.88–2.00	0.43**	0.27–0.68	3.07**	1.69–5.58
"Generally", "very much", or "totally agree"	1.00		1.00		1.00	
Normal not to sleep as well when we get older						
"Totally disagree" or "agree a bit"	0.89	0.61-1.28	1.76*	1.08–2.86	0.50*	0.28-0.91
"Generally", "very much", or "totally agree"	1.00		1.00		1.00	
I should stay in bed longer in the morning						
"Totally disagree" or "agree a bit"	0.74	0.47-1.17	0.81	0.45-1.46	0.91	0.45-1.86
"Generally", "very much", or "totally agree"	1.00		1.00		1.00	
Having a lot of worries in my mind						
"Not at all" or "a bit"	0.49**	0.33-0.73	0.21**	0.12-0.36	2.34*	1.22-4.51
"Moderately", "a lot", or "extremely"	1.00		1.00		1.00	
Having a lot of thoughts in my head						
"Not at all" or "a bit"	0.52**	0.34-0.80	1.08	0.62-1.89	0.48*	0.24-0.96
"Moderately", "a lot", or "extremely"	1.00		1.00		1.00	
Being worried about the idea of sleeping						
"Not at all" or "a bit"	0.83	0.51-1.35	0.43**	0.25-0.74	1.94	0.96-3.92
"Moderately", "a lot", or "extremely"	1.00	0.01	1.00	0120 017 1	1.00	0.00 0.02
Age						
Under 75 years	1.61*	1.10-2.36	1.13	0.71-1.79	1.43	0.80-2.55
75 years and over	1.00	1.10-2.50	1.00	0.71-1.77	1.00	0.00-2.55
Sex	1.00		1.00		1.00	
Male	0.54**	0.36-0.82	0.65	0.39-1.07	0.83	0.45-1.57
Female	1.00	0.36-0.62	1.00	0.39-1.07	1.00	0.45-1.57
	1.00		1.00		1.00	
Civil status	0.70		1.20	0.74 1.02	0.45	0.24 1.14
Married or living together	0.79	0.53–1.14	1.20	0.74–1.93	0.65	0.36-1.18
Single, separated, divorced, or widowed	1.00		1.00		1.00	
Schooling						
None to secondary	1.26	0.85-1.88	0.63	0.39–1.01	2.01*	1.11–3.64
Postsecondary	1.00		1.00		1.00	
Annual household income						
Under \$25,000	0.73	0.49-1.08	0.96	0.58–1.57	0.76	0.41-1.40
\$25,000 and over	1.00		1.00		1.00	
Sleep efficiency						
80% or more	0.97	0.64-1.45	1.05	0.62-1.77	0.92	0.49-1.73
Less than 80%	1.00		1.00		1.00	

Notes: ^aReference group. R^2 =0.066 (Cox and Snell), 0.125 (Nagelkerke). Model $\chi^2(28)$ =166.27, P<0.001. *P<0.05, **P<0.01. **Abbreviations:** CI, confidence interval; OR, odds ratios.

The percentage of classification accuracy is 90.5%. Also, no problems of multicollinearity were found, as the statistical tolerance level obtained was higher than 0.20.

Discussion

The first objective of this study was to identify the sleeprelated cognitions that the elderly most often deal with according to the presence or absence of a mental disorder. The beliefs "I need eight hours of sleep to feel rested and to function properly the next day" and "It's normal not to sleep as well when we get older" are the ones most frequently held by the seniors participating in our study. Overall, 56% of the participants said that they generally, very much, or totally agreed with the first belief, and 37% with the second. These beliefs were found just as often in asymptomatic older persons as in those presenting an anxiety or mood disorder.

A meta-analysis published in 2004 pertaining to the sleep of 3,600 individuals from 5–102 years of age has given us normative data on sleep duration and sleep latency for people of various ages.³¹ The average duration of sleep was approximately 6.25 hours at 65 years of age and 5.83 hours at 80 years of age. In the elderly, the average sleep latency was about 18–19 minutes. Studies conducted subsequently have arrived at similar results, but with sleep latencies of approximately 30 minutes for older women.^{32–36} Large individual differences were found for both the duration of sleep and the time taken to fall asleep.

Based on the results that they obtained, the authors of the meta-analysis concluded that, after 60 years of age, only sleep efficiency continued to decline, and that the other sleep parameters did not vary. The time taken to fall asleep increased by an average of 10 minutes between the ages of 20 and 80 years.³¹

Believing that one absolutely must sleep 8 hours to function properly can trigger performance anxiety (especially when an individual is unable to sleep long enough) and may lead to insomnia.¹⁷ Also, the total duration of sleep is not a good indicator for distinguishing between good and poor sleepers in the senior population.³⁷ Geriatric sleep experts claim that it is sleep efficiency, rather than its duration, that should be the primary objective to target in elderly individuals wishing to maintain good health and a good quality of sleep over the years.³⁸

One might be tempted to believe that sleep problems are linked to certain developmental changes affecting the elderly rather than to a mental disorder. Indeed, we know that with advancing age, the time spent in bed tends to increase, without the number of hours of actual sleep changing very much.³⁹ Believing that it is normal to not sleep well as one ages can lead to a feeling of resignation that does not encourage the individual to seek out the causes of and solutions for the sleep problems experienced.

In terms of sleep-related attitudes, having a lot of thoughts in one's head at bedtime proved to be most frequent in seniors presenting a mental disorder, with 73% of them experiencing this situation moderately, a lot, or extremely. The statistical regression that we performed enabled us to more specifically associate this with depression.

The main finding regarding the second objective is that once we have controlled for the other factors, we were able to specifically link two sleep-related beliefs and all the sleeprelated attitudes studied to the probability of being anxious or depressive. Previously conducted studies had shown that adults struggling with psychiatric disorders hold more dysfunctional cognitions about sleep than people without psychiatric illness and that older persons experiencing poor sleep have more dysfunctional cognitions about sleep than seniors who sleep well. The present study offers a significant contribution to the state of knowledge on this subject by revealing that, in general, in the elderly, having dysfunctional sleep cognitions is associated with the presence of anxiety or mood disorders, independently of the quality of sleep.

Insomnia was long considered merely as a symptom of anxiety or mood disorders, without existing by itself. It is now known that insomnia may precede the appearance of a mental disorder, appear at the same time, or appear afterward. This concept is adopted by the new diagnostic criteria of the DSM-5 with insomnia as a primary diagnosis even when comorbid with other mental or medical disorders.

We now see that there are direct links between sleep-related cognitions and anxiety and mood disorders. Longitudinal studies could be performed to more precisely determine the direction and nature of the associations that we found between the variables studied. It will then be possible to further clarify and specify the role of sleep cognitions in explanatory models for insomnia and anxiety and mood disorders.

Conclusion

The results of this study have a number of clinical implications. Since we now know that several dysfunctional cognitions are more often manifested in seniors suffering from a mental disorder, dysfunctional beliefs and attitudes should be the focus of evaluation during interventions concerning sleep.^{3,14,15,40,41} More concretely, it is to the advantage of health professionals who observe that elderly individuals are reporting many thoughts or worries at bedtime, including worries about sleep, to know that these cognitions have been shown to be linked to one or both types of mental disorders. They can then further investigate the possible presence of these disorders. Providing psychoeducation about sleep, in order to counter erroneous beliefs, could also be used as a quick and easy means of prevention. In terms of intervention, cognitive behavioral therapies targeted to dysfunctional cognitions have been shown to have good results in combating sleep problems,¹⁴ which often occur in people dealing with anxiety and mood disorders.3,4

Few studies have explored the relationship of the various sleep-related cognitions to mental disorders, and these few studies have used small, clinical samples or have grouped the various cognitions into different areas or by calculating the total scores for them. The present study stands out positively from the other studies due to its large overall sampling size and randomly selected composition. The characteristics of this sample are comparable to those of the general population, although this is limited to the elderly population of Québec, Canada. Nor is any particular group underrepresented in the present study (whether this be men or individuals over 75 years of age). In our study, 41% of the participants are men; this is quite an interesting proportion, in that it differs from that in many other studies which only include women or a higher percentage of women. As well, assignment of the participants to the groups of anxious or depressive persons was based on the DSM diagnostic criteria.

Despite the strengths of the present study, the results obtained should be interpreted with caution in the light of certain potential limitations. First, this cross-sectional study does not enable one to assign causality to the variables. Second, the participants' sleep efficiency was self-reported information, so may deviate from the real situation. Third, some potentially confounding variables such as physical illnesses or the use of medications were not taken into account.

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Disclosure

The authors report no conflicts of interest in this work.

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