

Genetic and environmental influences on sleep quality in middle-aged men: a twin study

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SUMMARY

Poor sleep quality is a risk factor for a number of cognitive and physiological age-related disorders. Identifying factors underlying sleep quality are important in understanding the etiology of these age-related health disorders. We investigated the extent to which genes and the environment contribute to subjective sleep quality in middle-aged male twins using the classical twin design. We used the Pittsburgh Sleep Quality Index to measure sleep quality in 1218 middle-aged twin men from the Vietnam Era Twin Study of Aging (mean age = 55.4 years; range 51–60; 339 monozygotic twin pairs, 257 dizygotic twin pairs, 26 unpaired twins). The mean PSQI global score was 5.6 [SD = 3.6; range 0–20]. Based on univariate twin models, 34% of variability in the global PSQI score was due to additive genetic effects (heritability) and 66% was attributed to individual-specific environmental factors. Common environment did not contribute to the variability. Similarly, the heritability of poor sleep—a dichotomous measure based on the cut-off of global PSQI > 5—was 31%, with no contribution of the common environment. Heritability of six of the seven PSQI component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, and daytime dysfunction) ranged from 0.15 to 0.31, whereas no genetic influences contributed to the use of sleeping medication. Additive genetic influences contribute to approximately one-third of the variability of global subjective sleep quality. Our results in middle-aged men constitute a first step towards examination of the genetic relationship between sleep and other facets of aging.

INTRODUCTION

Previous studies provide evidence that poor sleep quality is a risk factor for mortality (Hublin *et al.*, 2011), as well as a number of age-related disorders such as cognitive impairments (Potvin *et al.*, 2012) and hypertension (Fang *et al.*, 2012; Gangwisch *et al.*, 2006). Sleep problems increase with age, but are already prevalent in early mid-life (Knutson *et al.*, 2006). A meta-analysis investigating changes in sleep patterns across the lifespan reported that total sleep time and sleep efficiency decreased significantly with age, and sleep

latency and waking after sleep onset increased significantly with age (Ohayon *et al.*, 2004). Cross-sectional studies on healthy participants from early adulthood and mid-life have shown that poor sleep quality, sleep duration and sleep latency are associated positively with biomarkers for poor health outcomes such as telomere length (a marker for cellular aging; Prather *et al.*, 2011), reduced post-waking cortisol secretion (Lasikiewicz *et al.*, 2008) and inflammatory markers (Mills *et al.*, 2007). In addition, longitudinal studies have shown that reduced sleep quality in early adulthood or mid-life increases the risk of poor health later in life. These

poor health outcomes include an inverse relationship between duration of slow wave sleep and blood pressure in older men (Fang *et al.*, 2012), an increased risk for type 2 diabetes with poor sleep characteristics (Cappuccio *et al.*, 2010), an increased risk of cardiovascular and coronary heart disease in individuals with reduced and poor quality sleep (Hoevenaer-Blom *et al.*, 2011). Thus, factors underlying sleep quality are important in understanding the etiology of age-related cognition and a number of age-related health disorders.

Sleep is influenced by both genetic and environmental factors, and genetic factors are thought to play a role in many sleep disorders such as insomnia (Barclay and Gregory, 2012; Hublin *et al.*, 2011; McCarren *et al.*, 1994). One method for investigating the extent to which variation in sleep quality is accounted for by genetic and environmental factors is to conduct twin studies. Twin studies enable the estimation of the relative proportion of genetic (heritability, a^2 ; also referred to as h^2) and environmental influences accounting for the variation in a trait in the population. Using a twin model, environmental factors can be examined further as influences that make both members of a twin pair similar to one another (shared or common environmental factors) and influences that make twins unique (i.e. individual-specific or non-shared environmental factors). In sleep research there have been a number of twin studies investigating the etiology of an array of sleep phenotypes, from subjective measures of sleep quality to objective measures of sleep patterns and disorders. These studies have investigated infants, children, young adults, middle-aged adults and the elderly.

For example, the Finnish Twin Cohort study found the heritability of sleep length and sleep quality to be 0.44 (Partinen *et al.*, 1983). The most recent report on the Finnish Twin Cohort found the heritability of clustering to a good sleeper, average sleeper or poor sleeper group to be 0.46, with genetic and unique environmental factors contributing to the variance (Hublin *et al.*, 2011). Another study of Australian twin pairs aged 17–88 years found that genetic differences accounted for at least 33% of the variance in sleep quality and disturbance and 40% of the variance in sleep pattern; common (or shared) environmental factors contributed no effect to sleep characteristics (Heath *et al.*, 1990). Heritability has also been reported for insomnia-related characteristics using various subjective measures; these estimates range between 28 and 57% (Heath *et al.*, 1990; Hublin *et al.*, 2011; McCarren *et al.*, 1994; Partinen *et al.*, 1983; Watson *et al.*, 2006). As with sleep quality, twin studies on insomnia also found that the variability in insomnia characteristics was explained only by additive genetic and unique (individual-specific) environmental effects, with no contribution of the shared common environment (Heath *et al.*, 1990; McCarren *et al.*, 1994; Watson *et al.*, 2006).

A validated measure of subjective sleep quality, which is becoming a standard instrument in assessing association of sleep quality with health outcomes, is the Pittsburgh Sleep Quality Index (PSQI; Beaudreau *et al.*, 2012). The PSQI is a

self-report measure of sleep quality in the past month which derives an overall global score of 0–21 with seven components: sleep quality, habitual sleep efficiency, sleep duration, sleep disturbance, sleep latency, use of sleeping medication and daytime dysfunction (Buysse *et al.*, 1989). The heritability of the PSQI and its components and the overlap between genes influencing PSQI components was first examined in young male and female adults (age range 18–27 years) consisting of 420 monozygotic (MZ) twins, 773 dizygotic (DZ) twins and 363 sibling pairs assessed at 18–27 years of age (Barclay *et al.*, 2010b). Significant heritability was reported for sleep quality (0.41), sleep disturbance (0.39) and daytime dysfunction (0.47), with the remaining variance attributed to the non-shared environment. Similar to the findings described for other sleep measures, common environmental influence was not significant for the PSQI components, except sleep duration. Although the common environment has been reported to influence sleep behavior at very early life (Brescianini *et al.*, 2011), the effect of the common environment on a number of sleep phenotypes become negligible in adults, due possibly to adults living independent lives from their co-twin as age increases.

Because sleep patterns are observed to change with age, and a number of age-related health outcomes manifest at mid-life, the aim of our study was to employ a classical twin approach to assess the extent to which genes and environment contribute to variance in subjective sleep quality at mid-life. In this study, we investigated the PSQI and the seven components of PSQI sleep quality in a sample of middle-aged (51–60 years) men who are generally representative in socioeconomic and health characteristics of American men in their age range based on Census and Center for Disease Control and Prevention data. This study provides a basis for identifying subjective sleep characteristics for future genetic association studies and studies designed to investigate the overlap of genes contributing to both sleep quality and associated age-related cognitive and health outcomes.

METHODS

Study participants

The present study was part of the Vietnam Era Twin Study of Aging (VETSA), a longitudinal study of cognitive and brain aging. The VETSA project and assessment protocols have been described in detail elsewhere (Kremen *et al.*, 2006). The major goal of the VETSA is to investigate the relative contributions of genes and the environment to cognitive aging and age-related changes in a broad range of biological, psychological and social phenotypes. Baseline data for this study of risk and preventive factors in cognitive aging were collected in assessments conducted from 2003 to 2007. Participants live throughout the United States and were given the option of traveling to San Diego or Boston for a day-long series of assessments. The present study examined 1237 individual twin participants collected during the first wave of

the VETSA. Zygosity was determined using a combination of DNA testing (examination of 25 satellite markers), questionnaire and blood group methods. There was 95% agreement between the DNA and questionnaire methods. Blood-based zygosity was available for 92% of the sample and was used as the gold standard when available.

All participants in VETSA were recruited from the Vietnam Era Twin Registry, a non-clinical, population-based cohort of male–male twin pairs. Ascertainment procedures for the registry have been described previously (Eisen *et al.*, 1987; Henderson *et al.*, 1990). In brief, the Registry consists of 7375 male–male MZ and DZ twins born between 1939 and 1957 who were raised together and served on active duty in the United States military at some point during the Vietnam War Era (1965–1975). The majority of participants did not serve in combat or in Vietnam (Eisen *et al.*, 1987; Henderson *et al.*, 1990). Women were not in the Registry due to the low frequency of women, especially twin pairs, in the military during that era.

In comparison to US census data, participants in the VETSA are similar in socioeconomic and health characteristics to American men in their age range, except that non-Caucasian racial/ethnic minorities are under-represented (Centers for Disease Control, 2003). The VETSA sample consists of 697 MZ twins (347 pairs), 540 DZ twins (267 pairs) and nine unpaired twins. The average age was 55.4 years (range 51–60). Self-reported overall health status was as follows: excellent (12%), very good (36.5%), good (39.1%), fair (10.4%) and poor (1.3%); 9.4% of subjects reported currently having depression and 3.7% of subjects reported currently having an anxiety disorder. Ethnicity was based on self-identification: black or African American ($n = 51$; 4.1%), white ($n = 1110$; 89.7%) and other ($n = 76$; 6.1%; including American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, mixed ethnicity). There were no differences between the MZ and DZ groups with respect to age, education, employment status or ethnicity (Panizzon *et al.*, 2011). The study was approved by local Institutional Review Boards at the University of California, San Diego and Boston University.

Assessments

The Pittsburgh Sleep Quality Index (PSQI)

The PSQI is a widely used and well-validated scale that assesses sleep quality over the preceding month (Buysse *et al.*, 1989). This assessment consists of 19 questions scaled into seven component scores, which are then totaled to provide a global score ranging from 0 to 21. Higher scores represent poorer sleep quality. A global PSQI score greater than five has been found to have a diagnostic sensitivity of 89.6 and specificity of 86.6 in distinguishing individuals with clinically significant sleep problems from those without clinically significant sleep problems (Buysse *et al.*, 1989). The seven component scores range from 0 to 3. Global PSQI

scores could not be computed for 19 individuals with incomplete data due primarily to shift work.

Data analysis

The global PSQI score was treated as a continuous variable in the genetic analyses. Because scores on the PSQI were positively skewed, a square root transformation was applied to the data to achieve a normal distribution. We also examined the genetic and environmental influences on each component score of the PSQI. Each component score was treated as an ordinal variable, with values ranging from 0 to 3.

Genetic analyses were performed utilizing the maximum-likelihood-based structural equation modeling software Mx (Neale *et al.*, 2004). In the classical twin design, the variance of any trait is decomposed into the proportion attributed to additive genetic (A) influences (also referred to as heritability), common or shared environmental (C) influences (i.e. environmental factors that make both members of a twin pair similar to one another) and unique or individual-specific environmental (E) influences (i.e. environmental factors that make members of a twin pair different from one another, including measurement error). Measurement error is included in non-shared environmental variance as it is assumed to be random, i.e. uncorrelated across twins. Models including these three variance components are referred to commonly as ‘ACE’ models (see Fig. 1). In the ACE model A is correlated ($r_{MZ} = 1.0$) in MZ twins because they generally share 100% of their genes. A is assumed to be correlated ($r_{DZ} = 0.5$) in DZ twins because they share, on average, 50% of the segregating genes. It is also assumed that C correlates ($r_{MZ} = r_{DZ} = 1.0$) in both MZ and DZ twins. By definition, E is uncorrelated between members of a twin pair.

Univariate models for continuous or ordinal variables were fitted to the raw data by means of maximum likelihood. For the ordinal variables, we applied a liability (threshold) model,

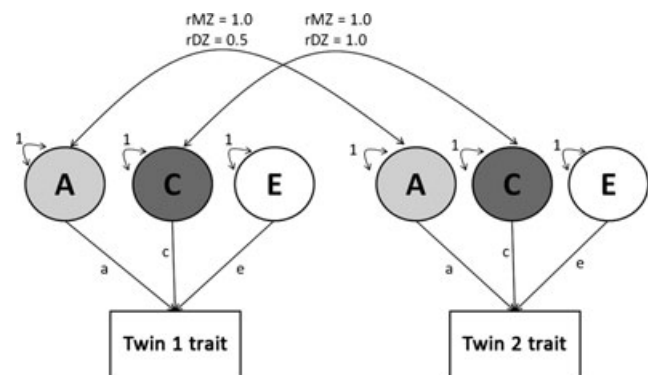


Figure 1. Twin univariate ACE model. A: additive genetic influences; C: common environmental influences; E: unique environmental influences. r_{MZ} : correlation in monozygotic (MZ) twins and r_{DZ} : correlation in dizygotic (DZ) twins. The proportions of phenotypic variance due to A, C and E are a^2 (heritability), c^2 and e^2 , respectively.

which assumed that the ordered categories have an underlying normal distribution with thresholds discriminating the classes (0–3) and phenotypic variance of 1.0 (Neale and Cardon, 1992). For all analyses we first fitted a saturated model, one that captures the observed data perfectly, and then tested whether different theoretical models (e.g. ACE, AE, CE) could account for the data without a significant reduction in fit. The full model (ACE) and reduced models that drop either A or C effects were compared to the saturated model. A chi-square difference test was used to assess the goodness-of-fit for each model. This is obtained by comparing the difference in $-2 \log$ -likelihood ($-2LL$) for each model against that of the saturated model using the likelihood-ratio statistic chi-square test (LRT). If more than one model has non-significant P -values (indicating no significant reduction in fit), the Akaike information criteria (AIC), calculated as $\Delta\chi^2 - 2 \times \Delta df$, was used to identify the model with the best balance of goodness-of-fit and parsimony (indicated by lower AIC values; Akaike, 1987). Significance of individual A, C and E estimates was based on their 95% confidence intervals not including zero.

RESULTS

Of the 1237 twins in the VETSA study, 1218 had complete PSQI data (339 MZ pairs, 257 DZ pairs and 26 singleton twins). Sleep characteristics from the PSQI are presented in Table 1. The mean global PSQI score was 5.6 [standard deviation (SD) = 3.6], with scores ranging from 0 to 20 on a scale of 0–21. There were 491 subjects (40%) classified as having poor sleep based on a global PSQI score >5 . The global PSQI scores were similar in both MZ (5.61) and DZ (5.59) twins.

Heritability of the global PSQI score

The MZ twin correlation for the global PSQI scores was 0.34 and the DZ twin correlation was 0.17. Table 2 shows the parameter estimates of additive genetic (heritability, h^2), common environmental (c^2) and unique environmental contributions (e^2) to variation in global PSQI score from the best-fitting model. Common environment did not contribute to variability in global PSQI. The full ACE model had a good fit relative to the saturated model. Dropping C, which was estimated at 0 in the ACE model, resulted in an improved fit, as indicated by the lower AIC for the AE model. We also analyzed PSQI quality based on a dichotomized score of PSQI greater 5 as poor sleepers and PSQI less than or equal to 5 as good sleepers. This analysis resulted in a similar heritability of 0.31 (Table 2).

In the best-fitting AE model, 34% [95% confidence interval (CI): 0.25, 0.42] of the variability in the global PSQI score was due to additive genetic effects and 66% [Fig. 2, (95% CI: 0.58, 0.75)] was due to unique environmental influences.

Heritability of individual component scores

Table 3 presents the MZ and DZ polychoric correlations and the parameter estimates for the full and best-fitting models for the seven components of PSQI. Best-fitting models are shown in bold type. Based on the AIC values, the AE model provided the best fit for six of the seven component scores of the PSQI: sleep quality, habitual sleep efficiency, sleep duration, sleep disturbance, sleep latency and daytime dysfunction. Although the AE models for sleep quality and sleep disturbance had the lowest AIC values, we showed

Table 1 Sleep characteristics

	Mean	SD		
Time to fall asleep (minutes)	19.2	24.5		
Normal hours of sleep	6.4	1.3		
Sleep efficiency*	88.4%	16.7%		
Subjective sleep quality	Very good	Fairly good	Fairly bad	Very bad
	345 (27.9%)	718 (58.0%)	138 (11.2%)	36 (2.9%)
Cannot fall asleep within 30 min	Not during the past week	Less than once a week	Once or twice a week	Three or more times per week
	562 (45.4%)	388 (31.4%)	147 (11.9%)	139 (11.2%)
Wake up during the night	340 (27.5%)	300 (24.3%)	241 (19.5%)	356 (28.8%)
Have to use to bathroom	359 (29.0%)	284 (23.0%)	227 (18.4%)	366 (29.6%)
Cannot breath comfortably	1087 (87.9%)	71 (5.7%)	33 (2.7%)	41 (3.3%)
Cough or snore loudly	1013 (81.9%)	103 (8.3%)	51 (4.1%)	70 (5.7%)
Feel too cold	1063 (85.9%)	117 (9.5%)	38 (3.1%)	18 (1.5%)
Feel too hot	888 (71.8%)	206 (16.7%)	102 (8.2%)	41 (3.3%)
Had bad dreams	1037 (83.8%)	130 (10.5%)	38 (3.1%)	30 (2.4%)
Have pain	892 (72.1%)	153 (12.4%)	91 (7.4%)	100 (8.1%)
Took medicine to help sleep	1025 (82.9%)	81 (6.5%)	36 (2.9%)	95 (7.7%)
had trouble staying awake during the day	1059 (85.6%)	111 (9.0%)	44 (3.6%)	23 (1.9%)
Lack of enthusiasm for getting things done	683 (55.2%)	389 (31.4%)	135 (10.9%)	29 (2.3%)

* (Total number of hours asleep/total number of hours in bed) \times 100. SD, standard deviation.

Table 2 Model fitting results for global and dichotomized PSQI scores

	Model	Heritability h^2 (95% CI)	Common environment c^2 (95% CI)	Unique environment e^2 (95% CI)	-2LL	df	P	AIC
Global PSQI	Saturated	—	—	—	2689.247	1208	—	273.25
	ACE	0.34 (0.05, 0.42)	0 (0, 0.24)	0.66 (0.57, 0.75)	2691.306	1214	0.914	263.3064
	AE	0.34 (0.25, 0.42)	—	0.66 (0.58, 0.75)	2691.306	1215	0.998	261.3065
	CE	—	0.26 (0.18, 0.34)	0.74 (0.66, 0.81)	2696.490	1215	0.404	266.4875
Poor sleep (dichotomized global PSQI score)	Saturated	—	—	—	1625.90	-798.10	—	-798.10
	ACE	0.31 (0, 0.45)	0 (0, 0.32)	0.69 (0.55, 0.85)	1627.44	-802.57	0.67	-802.57
	AE	0.31 (0.15, 0.45)	—	0.69 (0.55, 0.85)	1627.44	-804.57	0.82	-804.57

P = significance value of the likelihood-ratio chi-square test assessing the reduced model with the full model or nested models with the saturated model. Best-fitting model based on AIC values appears in bold type. All models are tested against the fit of the saturated model. -2LL, negative 2 log-likelihood; df, degrees of freedom; AIC, akaike information criterion; CI, confidence interval. PSQI, Pittsburgh Sleep Quality Index; A, additive genetic influences; C: common environmental influences; E: unique environmental influences.

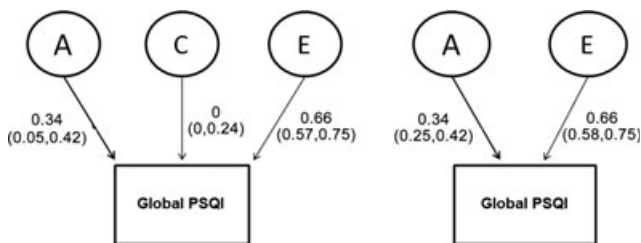


Figure 2. Full model and best-fitting AE model for global Pittsburgh Sleep Quality Index (PSQI). A: additive genetic influences; C: common environmental influences; E: unique environmental influences.

both the ACE and AE models in bold type for each of these components. We did so because dropping the estimated 10 and 7% of variance attributed to common environmental influences in the ACE models and setting it to 0 in the AE models may have somewhat inflated the heritability estimates. Heritability estimates for six of the seven components (excluding use of sleeping medications) ranged from 0.15 to 0.28 in the full ACE model and from 0.23 to 0.34 for the best-fitting reduced models. The CE model provided the best fit for use of sleeping medication, with common environmental influences estimated at 0.31 and unique environmental influences estimated at 0.69.

DISCUSSION

The present study used the classical twin design to determine the extent to which individual differences in sleep quality as measured by the PSQI are due to genetic and environmental influences in a representative population of middle-aged men in the United States. In this study we examine heritability on a widely used and validated instrument of subjective sleep quality, PSQI, in order to facilitate future genetic association studies using this instrument. We also assessed each component score of the PSQI to identify particular characteristics of sleep quality that are influenced

by genetic factors. The best-fitting model indicated that 34% of variability in the global PSQI score was due to additive genetic effects and 66% was attributed to unique environment. The dichotomized PSQI (poor sleepers versus good sleepers) resulted in a similar heritability of 0.31. Heritability of global PSQI was 0.43, in a population of male and female young adult (18–27 years of age) twins and siblings, with unique environmental influences of 0.57 (Barclay *et al.*, 2010a). Similar to our findings, the study on young adults found no common environmental influence on the global PSQI score. Although the heritability estimate was slightly higher in these young adults, the 95% CIs overlap considerably, suggesting that the estimates are not significantly different from one another.

We also investigated the components of PSQI to identify particular characteristics of sleep that may be under genetic influences. The estimates for six of the seven individual components were similar to the estimates for the global PSQI score: modest genetic influences and little or no contribution of the common environment. Our results are similar to the findings of Barclay *et al.* (2010b), in which heritability estimates ranged from 0.21 to 0.47. The one exception was sleep duration, for which heritability was 0.29 in our study, but zero in the Barclay *et al.* (2010b) study. Even for this measure, however, the confidence intervals still overlap considerably.

It may be tempting to speculate that social influences (e.g. peers, co-sleeping) are more influential in childhood to young adulthood, whereas genetic and unique environmental factors (e.g. health differences) may drive sleep patterns later in life. However, findings across studies—except perhaps for infancy and very early childhood—do not provide much support for this notion. Significant common environmental influences have been found in infants and 18-month-olds (Brescianini *et al.*, 2011; Fisher *et al.*, 2012). It seems likely that the times when twin babies are fed and put to bed would be controlled largely by the parents. Patterns are likely to become a little more differentiated in childhood, and findings are mixed with regard to common environmental influences

Table 3 Component score parameter estimates for the full ACE and best-fitting models

correlations	Model	Standardized variance components			Model fit				Cross-twin	
		Heritability a ² (95% CI)	Common environment c ² (95% CI)	Unique environment e ² (95% CI)	df	-2LL	AIC	P	MZ	DZ
Sleep quality	Saturated	–	–	–	1223	2483.29	37.29	–		
	ACE	0.20 (0, 0.41)	0.10 (0, 0.34)	0.70 (0.59, 0.82)	1232	2493.56	29.56	0.33	0.31	0.20
	AE	0.31 (0.20, 0.42)	–	0.69 (0.58, 0.80)	1233	2493.95	27.95	0.38		
Habitual sleep efficiency	Saturated	–	–	–	1209	2241.87	-176.13	–		
	ACE	0.24 (0, 0.39)	0 (0, 0.28)	0.76 (0.61, 0.92)	1218	2254.36	-181.64	0.187	0.24	0.12
	AE	0.24 (0.09, 0.39)	–	0.76 (0.61, 0.91)	1219	2254.36	-183.64	0.253		
Sleep duration	Saturated	–	–	–	1223	3332.43	886.43	–		
	ACE	0.29 (0, 0.39)	0 (0, 0.26)	0.71 (0.61, 0.82)	1232	3334.62	870.62	0.99	0.29	0.13
	AE	0.29 (0.18, 0.39)	–	0.71 (0.61, 0.81)	1233	3334.62	868.62	0.99		
Sleep disturbance	Saturated	–	–	–	1219	1782.66	-655.33	–		
	ACE	0.15 (0, 0.36)	0.07 (0, 0.29)	0.78 (0.64, 0.92)	1228	1790.67	-665.33	0.53	0.21	0.14
	AE	0.23 (0.09, 0.36)	–	0.77 (0.64, 0.91)	1229	1790.79	-667.21	0.62		
Sleep latency	Saturated	–	–	–	1220	2888.04	448.04	–		
	ACE	0.30 (0, 0.44)	0.02 (0, 0.31)	0.68 (0.56, 0.79)	1229	2891.82	433.80	0.93	0.33	0.18
	AE	0.34 (0.23, 0.44)	–	0.66 (0.56, 0.77)	1230	2891.82	431.82	0.96		
Use of sleeping medication	Saturated	–	–	–	1223	1542.84	-903.16	–		
	ACE	0	0.31 (0, 0.45)	0.69 (0.52, 0.84)	1232	1552.78	-911.22	0.35	0.30	0.34
	CE	–	0.31 (0.16, 0.45)	0.69 (0.55, 0.84)	1233	1552.78	-913.22	0.45		
Daytime dysfunction	Saturated	–	–	–	1222	2284.72	-159.28	–		
	ACE	0.28 (0, 0.40)	0 (0, 0.32)	0.71 (0.64, 0.92)	1231	2292.07	-169.93	0.60	0.29	0.15
	AE	0.23 (0.09, 0.36)	–	0.77 (0.68, 0.88)	1232	2292.07	-171.93	0.69		

P = significance value of the likelihood ratio chi-square test assessing the reduced model with the full model or nested models with the saturated model. Best-fitting model based on AIC values appears in bold type. -2LL, negative 2 log-likelihood; df, degrees of freedom; AIC, Akaike information criterion; CI, confidence interval. All models are tested against the fit of the saturated model. A, additive genetic influences; C, common environmental influences; E, unique environmental influences.

on sleep patterns in children (Gregory *et al.*, 2006; Moore *et al.*, 2011). In studies of adults there is generally consistent evidence of negligible common environmental influences on any sleep components (Barclay *et al.*, 2010a,b; Heath *et al.*, 1990; Liu *et al.*, 2012; McCarren *et al.*, 1994; Watson *et al.*, 2006). Ages in these studies ranged from early adulthood to the late 80s, but there was also little or no suggestion of age effects on genetic or environmental variance. All these studies were cross-sectional. Longitudinal assessment of VETSA twins is currently ongoing, and may shed additional light on possible age-related changes in genetic and environmental influences over time.

In contrast to the pattern of environmental and genetic influences on the components of PSQI discussed above, we found that additive genetic effects did not contribute to the use of sleeping medication component. Rather, this was the only item for which a CE model provided the best fit. The common environment accounted for 31% of the variance in sleep medication use, and unique environmental factors accounted for 69% of the variance. Because most medical or psychiatric conditions that are likely to lead to people taking medication have a significant genetic component, we expected to see significant genetic influences underlying variation in this component. We are somewhat more cautious

about the sleep medication finding, because only a small proportion (10.6%) of the cohort used sleeping medications regularly (at least once a week). Conversely, the findings on use of sleeping medication appear to parallel other medication use. We now have preliminary evidence that common environmental, rather than genetic, factors contribute to variability in medication use for other conditions (e.g. hypertension) as well, but this issue will require further systematic study. It has been decades since virtually all twins in the present study were living in the same household, thus indicating that common environmental influences may still be present long after childhood and adolescence. One possibility is that there is a lasting impact of shared aspects of the childhood family environment—such as access to medical care and family attitudes towards medical treatment and medication use.

This study has limitations. PSQI is a subjective self-report questionnaire. Although it has been shown to be a reliable, replicable and valid measure of sleep quality with high diagnostic sensitivity and specificity in distinguishing good and poor sleepers (Buysse *et al.*, 1989), it is not an objective measure of sleep quality or sleep disorders. We did not have data on the stability of PSQI responses in this sample, although there is evidence from a previous report

indicating that PSQI is a stable measure of sleep quality over the course of a year (Knutson *et al.*, 2006). It was also difficult to characterize sleep quality in shift workers using this instrument. Our results may not generalize to women or non-Caucasians. However, in contrast to prior cross-sectional studies, the data provide a good basis for longitudinal studies of the genetic and environmental relationships between sleep quality in mid-life and health outcomes later in life.

In addition, the longitudinal nature of our study will allow us to investigate changes in sleep patterns during later life and the impact of sleep quality on cognitive aging and health outcomes. For example, on average, sleep efficiency of our sample was good (88%), as normal sleep efficiency (total number of hours asleep/total number of hours in bed; Table 1) is reported to be at least 80–85% (Morin, 1993). However, we expect that sleep efficiency in our sample will decrease over time, because sleep efficiency has been found to decline across the full adult lifespan (age 19–102; Ohayon *et al.*, 2004).

The next step may be to identify specific environmental factors and specific genes that influence sleep quality and disorders in order to focus prevention and intervention strategies. For example, an alternative twin design, the MZ twin differences design, could be used to identify specific unique environmental influences on sleep quality while controlling for genetic and common environmental effects. This type of analysis has recently demonstrated specific environmental factors such as general health in men and relationship satisfaction in women to influence sleep quality (Barclay *et al.*, 2012). A bivariate twin model may also be used to examine the genetic overlap between sleep and health outcomes or between the seven components of the PSQI. Bivariate analysis on the seven components of PSQI in young adults has shown substantial genetic overlap yet environmental heterogeneity between the PSQI components (Barclay *et al.*, 2010b). Using the bivariate model on a longitudinal study design, we can also investigate whether different sets of genes contribute to sleep quality at different periods of life or if there is an overlap of genes. It is also possible that the impact of the environment on sleep may vary based on the presence of specific genes, resulting in a genotype \times environment interaction effect. If this were the case, genes may play a larger role than is suggested in the present study, and future gene \times environment interaction effects should be examined. Gene–environment correlations, in which genes that influence one trait influence exposure to specific environments, can also be assessed using a twin design. Gene \times environment and gene–environment correlation analysis has demonstrated the influence of negative life events with sleep quality (Barclay *et al.*, 2011). Understanding the etiology of sleep disorders has significant public health implications. Examining the extent to which genes and the environment impact the development of sleep disorders may help to inform treatment approaches.

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CONFLICT OF INTEREST

No conflicts of interest declared.

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