Genetic and Environmental Influences on Infant Sleep

WHAT’S KNOWN ON THIS SUBJECT: Twin studies provide a natural experiment that can determine the extent of genetic and environmental influences on sleep behavior. Previous studies have indicated that genes contribute moderately to sleep.

WHAT THIS STUDY ADDS: In the largest pediatric study to date, we demonstrate that the shared environment strongly influences sleep behavior in infants, with no gender differences in the results. This research provides strong impetus to future work identifying the key modifiable environmental drivers.

abstract

BACKGROUND: Sleep duration is attracting increasing attention in relation to chronic disease risk, but few large-scale studies have investigated the determinants of sleep characteristics in early life. In this study we used data from a large, population-based twin study to examine genetic and environmental influences on sleep duration and sleep difficulties in infancy.

METHODS: Participants were 1931 pairs of young twins (3862 children) from the Gemini twin birth cohort. Sleep patterns were assessed at 15 months by using a modification of the Brief Infant Sleep Questionnaire completed by parents. Outcomes included nighttime and daytime sleep duration and frequency of night waking.

RESULTS: Twin analyses showed that nighttime sleep duration was predominantly influenced by the shared environment (66%, confidence interval [CI] 63%–70%) with a modest genetic effect (26%, CI 22%–30%). A similar pattern was observed for daytime nap duration (shared environment: 57%, CI 53%–61%; genetic effect: 37%, CI 33%–41%) and sleep disturbance (shared environment: 55%, 44%–64%) with a genetic effect of 40% (30%–51%). These estimates were similar for boys and girls.

CONCLUSIONS: These results indicate an important contribution of the shared family environment as well as genes to children’s sleep behavior. There is a need for research to identify specific environmental determinants that could provide targets for interventions to improve sleep quality. Pediatrics 2012;129:1091–1096

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KEY WORDS: twin, sleep, infant, environment, gene

ABBREVIATIONS
A — additive genetic component of variance
AIC — Akaike Information Criterion
C — shared environmental component of variance
CI — confidence interval
DZ — dizygotic
E — unique environmental component of variance
MZ — monozygotic

Drs Wardle and van Jaarsveld designed the Gemini study; Drs Fisher and Wardle planned these analyses; Dr Fisher analyzed the data; Drs Llewellyn and van Jaarsveld provided statistical guidance; Drs Fisher and Wardle wrote the paper; Drs van Jaarsveld and Llewellyn critically reviewed the manuscript; and all authors approved the final draft for submission.

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There is growing evidence that short sleep is associated with adverse health outcomes, including cardiovascular disease, cancer, impaired immune function, and psychiatric disorder. Recently, there has also been interest in the possibility that short sleep is a modifiable determinant of weight gain. Average sleep duration has declined substantially over the past few decades, which has led the Centers for Disease Control and Prevention to term this an “unrecognized public health problem,” although a recent review indicated that the evidence for a secular decline in pediatric sleep is less clear. Nevertheless, the importance of adequate sleep for child development is unequivocal. The observation that siblings can vary substantially in their sleep characteristics despite sharing a home environment points to the influence of “nature” as well as “nurture.” Twins provide a fortuitous natural experiment that makes it possible to quantify genetic and environmental influences on any phenotype by taking advantage of the fact that identical (monozygotic [MZ]) twins share all their segregating genes and dizygotic (DZ) twins share on average 50%, while both MZ and DZ twins share a common family environment in childhood. In a sample of adult twins from the Washington Twin Registry, approximately a third of the variation in sleep duration was attributed to additive genetic effects. Sleep disturbance has also been shown to be moderately heritable in adults (~40%), and in a study of young adult twins, both sleep quality and diurnal preference (“early risers” versus “night owls”) showed significant genetic effects. There have been comparatively few pediatric twin studies of sleep. One study involving 300 twin pairs found that sleep difficulties in middle childhood showed some genetic influence, although the moderate sample size meant that confidence intervals (CIs) spanned zero. A recent Italian study (n = 314 pairs) of 18-month-old infants found that variation in sleep patterns was predominantly due to shared environmental factors. However, neither study was powered to detect small effects. The aim of the current study was therefore to investigate environmental and genetic influences on sleep duration and sleep problems in infancy in a large twin birth cohort.

METHODS

The Gemini study has been described in detail previously. Briefly, it is a population-based cohort study of young twins in the United Kingdom focusing on the determinants of early childhood weight trajectories. A total of 2402 families with twins born in England and Wales between March and December 2007 (36% of all live twin births) agreed to participate and returned completed baseline questionnaires when twins were ~8.2 months old (SD 2.2, range 4.0–20.3 months). The questionnaire containing the sleep questions reported in this study was completed by 1931 families (80%) when twins were ~16 months old (mean 1.8, SD 1.1, range 14.0–27.4 months). Less than 1% of the cohort had a diagnosed developmental disorder at 15 months. As expected in twins, 15% of the sample were born preterm (<37 weeks), and 6.5% were very low birth weight (categorized as <2 SD from the mean). Because the numbers of children with diagnosed disorders were small, these children were included. All analyses were repeated excluding very low birth weight infants; however, results did not change. Gemini families are comparable to UK national twin statistics on gender, zygosity, gestational age, and birth weight, although in common with other population-based samples, ethnic minorities and lower-socioeconomic status groups were underrepresented, and parents were slightly healthier than average with respect to diet, smoking rates, and BMI. To determine zygosity in same-gender twin pairs, parents completed a 20-item questionnaire, which has shown >95% accuracy against polymorphic DNA markers in 18-month-old twins. In the present sample, zygosity was uncertain in 68 pairs, and they were excluded from these analyses. Informed written consent was provided by all parents. Ethical approval was granted by the University College London Committee of non–National Health Service Human Research.

Sleep Behavior

Sleep was assessed by using modified items from the Brief Infant Sleep Questionnaire for children, which has been shown to be reliable and valid against actigraphy. Parents reported a number of aspects of their children’s sleep behavior including usual bedtime and wake time (from which nighttime sleep duration was calculated) and daytime nap duration. Parents also reported whether each child regularly woke up during the night (yes/no). Children were classified as having sleep disturbance if they woke up even 1 night a week on a regular basis.

Statistical Analyses

All analyses were adjusted for age at questionnaire completion and child gender. Standardized residuals were used for all analyses. Twin-twin intraclass correlations were computed for preliminary evidence of genetic influence. Higher MZ than DZ correlations indicate some genetic influence, DZ correlations that are more than half the MZ correlations suggest some shared environmental influence, and MZ correlations that are <1 provide evidence of unique environmental effects or measurement error. Structural equation modeling was used to estimate the additive genetic (A), the shared
environment (C), and the unique environment (E) parameters (the latter also including error of measurement) and generate CIs. For the sleep disturbance variable (yes/no), a threshold model for dichotomous data was used. Parsimony of submodels (CE, AE, and E) was tested with 2 goodness of fit statistics: change in $\chi^2$ and Akaike information criterion (AIC). To test for gender differences in genetic or environmental parameters, full gender-limitation models were run. A null model (not allowing any gender differences) was preferred for every sleep parameter, so boys and girls were combined for the analyses. Quantitative twin analyses were carried out by using MX Maximum likelihood Structural Equation Modeling Software (version 32; Virginia Commonwealth University, Richmond, VA).

RESULTS

Sleep Behavior

Participant characteristics are presented in Table 1. Children's bedtimes ranged from 5:00 PM to 11:30 PM, but the majority went to bed between 6:00 PM and 8:00 PM. Morning wake times ranged from 5:00 PM to 11:30 PM, but the majority of the infants woke between 6:00 AM and 8:00 AM. Almost half (44%) of the children experienced regular sleep disturbance. There were small gender differences in sleep patterns; boys slept for slightly longer than girls during the day (1.87 vs 1.81 hours; $P < .001$), and girls slept slightly longer than boys at night (11.74 vs 11.55 hours; $P < .001$), but there were no gender differences in sleep disturbance ($P > .05$).

Sleep behaviors stratified by zygosity are presented in Table 1. Importantly for the twin analyses, there were no significant differences in mean values between MZ and DZ twins in any aspect of sleep behavior (all $P > .05$).

Genetic and Environmental Influences on Sleep Behavior

Intraclass correlations for sleep behavior for the whole sample are presented in Table 2. For bedtimes, both MZ and DZ twins correlated exactly, suggesting that this was purely shared environmental; therefore, heritability analyses were unnecessary. MZ correlations were higher than DZ correlations for morning wake time, nighttime sleep duration, daytime nap duration, and sleep disturbance, suggesting some genetic effects. However, in all cases, DZ correlations were more than half the MZ correlations, indicative of shared environmental influence.

<table>
<thead>
<tr>
<th>TABLE 1 Participant Characteristics</th>
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<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>Age, mo</td>
</tr>
<tr>
<td>Female, %</td>
</tr>
<tr>
<td>Nighttime sleep duration, h per night</td>
</tr>
<tr>
<td>Daytime nap duration, h per d</td>
</tr>
<tr>
<td>Sleep disturbance, % experiencing</td>
</tr>
</tbody>
</table>

Values are means (SD) unless otherwise stated. n: number of infants in the sample with valid data.

<table>
<thead>
<tr>
<th>TABLE 2 Intraclass Correlations for Sleep Behavior</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Bedtime</td>
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<tr>
<td>Wake time</td>
</tr>
<tr>
<td>Nighttime sleep duration</td>
</tr>
<tr>
<td>Daytime nap duration</td>
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<tr>
<td>Sleep disturbance (yes/no)</td>
</tr>
</tbody>
</table>

All correlations significant at $P < .001$. Parentheses indicate 95% CIs.

DISCUSSION

The results of this study indicate that both nature and nurture influence sleep, although over all the measured sleep parameters, the shared environment influence was strongest. This is the first infant study large enough to examine gender differences in infant sleep behavior and demonstrated that the extent of genetic and environmental influence was similar for girls and boys. These findings provide a strong impetus for research into the specific environmental influences on sleep that might offer promising targets for intervention. Unsurprisingly, bedtime at this age was entirely shared environmental. However, in this study, as in many others, we did not have information on how long it took children to fall asleep after they were in bed (sleep latency), which could show more within-pair variation. We found that wake time was partially influenced by genes, consistent with evidence from adult samples showing genetic influence on sleep-wake patterns. For example, data from adults have indicated genetic influence on being a “morning” versus an “evening” person, and evening diurnal preference shows shared genetic influence with poorer sleep quality.

There is considerable interest in nighttime sleep duration as a potential risk factor for weight gain. All twin studies
in children and adults have demonstrated significant environmental influence on sleep,13,18,20,21 but few pediatric studies have been powered to distinguish shared and nonshared environmental effects. The results of the current study demonstrate that sleep duration is likely to be modifiable through the shared environment, which in infants and young children is predominantly the home setting and the parents. However, research is needed to identify the specific environmental influences. The best evidence is for television viewing, which is negatively associated with children’s sleep duration.22,23 However, the majority of studies are cross-sectional, and therefore, it is not clear whether shorter sleep or higher television viewing comes first. Nonetheless, given that television viewing is not only associated with worse sleep but also with inactivity and overweight,24,25 advising parents to reduce television time in problem sleepers seems likely to be a safe option. Early introduction of solid foods (<4 months) and maternal antenatal depression have been associated with shorter sleep at 1 and 2 years, and in the same study, attendance at a child care center outside the home was also associated with shorter sleep at 2 years.26

In terms of the associations between sleep and weight, 1 study in 1870 adult twin pairs demonstrated that insomnia and obesity had ~10% of genes in common.27 Similar analyses in pediatric twin studies could examine whether the sleep-weight association shows common genetic or environmental influence, and the Mendelian randomization principle could be used to test whether the association is likely to be causal.

Another consistent shared environment influence on sleep is socioeconomic status,28 although to date no specific processes underlying this association have yet been identified. So-called “sleep hygiene” has also been associated with childhood sleep patterns. Good sleep hygiene constitutes a number of shared environmental factors such as having no television in the bedroom, consistent bedtime routines, bedtimes earlier than 9:00 PM for children up to 10 years, children of all ages being allowed to fall asleep independently (no parent present), and limiting caffeinated soft drinks.29 Future research should identify other modifiable aspects of the shared environment that influence sleep as well as find ways of promoting positive sleep hygiene, especially in lower–socioeconomic status groups, where sleep problems are more prevalent.30

Almost half the children in our study experienced some level of sleep disturbance in the form of regular night waking, similar to the rate of occasional or usual night waking in studies of 8-year-old twins (40%)13 and singletons (43%).31 It is reassuring that similar rates of sleep disturbance are seen in singletons and twins, indicating that twins are not keeping one another awake. In our sample of infants, genetic factors explained 40% of the variance in reports of sleep disturbance. This is consistent with results from a study of twins followed from age 8 to age 10 which showed stability in sleep disturbance and common genetic influence.

### TABLE 3 Estimates of Genetic and Environmental Influence on Infant Sleep Behavior in the Gemini Birth Cohort

<table>
<thead>
<tr>
<th>Model</th>
<th>Estimates of Variance Components</th>
<th>Model Fit</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>A</td>
<td>C</td>
</tr>
<tr>
<td>Wake time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE*</td>
<td>0.38 (0.34–0.43)</td>
<td>0.56 (0.51–0.60)</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.81 (0.79–0.82)</td>
</tr>
<tr>
<td>AE</td>
<td>0.93 (0.93–0.94)</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Nighttime sleep duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE*</td>
<td>0.26 (0.22–0.30)</td>
<td>0.66 (0.63–0.70)</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.83 (0.82–0.85)</td>
</tr>
<tr>
<td>AE</td>
<td>0.92 (0.91–0.93)</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Daytime nap duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE*</td>
<td>0.37 (0.33–0.41)</td>
<td>0.57 (0.53–0.62)</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.82 (0.80–0.85)</td>
</tr>
<tr>
<td>AE</td>
<td>0.94 (0.93–0.95)</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sleep disturbance (yes/no)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE*</td>
<td>0.40 (0.30–0.51)</td>
<td>0.55 (0.44–0.64)</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.85 (0.80–0.86)</td>
</tr>
<tr>
<td>AE</td>
<td>0.96 (0.94–0.98)</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
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</tbody>
</table>

ΔAIC, change in AIC; Δχ², change in χ²; LL, log likelihood; df, degrees of freedom. Parentheses indicate 95% CIs.

* Best fitting model.
at the 2 time points\textsuperscript{32} and with previous pediatric studies which have found a significant genetic influence.\textsuperscript{13} However, little progress has been made in identifying specific genes,\textsuperscript{31} although the \textit{CLOCK} and \textit{PER} genes have been linked with circadian rhythms.\textsuperscript{33,34}

To our knowledge, only 1 other infant study has demonstrated shared environmental influences on sleep behavior. Brescianini et al\textsuperscript{14} studied 18-month-old Italian twins (314 pairs) and found results were similar to ours, with the shared environment explaining 64\% of results were similar to ours, with the shared environment explaining 64\% of nighttime sleep duration (compared with 66\% in our study), with moderate genetic influence. This consistency is important because the Mediterranean sleep culture is different from that of the United Kingdom or the United States, being characterized by comparably late bedtimes for children. For example, mean nighttime sleep duration in the Italian study was 9.7 hours compared with 11.7 hours in ours. It therefore appears genetic and environmental influences on sleep behavior. Use of parent report is a limitation, but this is common to larger studies. The simple yes/no categorization of sleep disturbance may miss valuable information on extremely sleep disturbed children versus those who wake only 1 or 2 times per week. However, the percentage experiencing regular night waking was similar to other studies that used more detailed measures.\textsuperscript{13,31} The unique environment component (which also contains measurement error) in our results was small, supporting the reliability of the measures. Our sample was predominantly white, so we could not explore ethnic differences in sleep behavior, but it is fairly representative of the UK population.

CONCLUSIONS
Sleep patterns in early childhood reveal influences of nature and nurture, indicating that a better understanding of both the biological and environmental pathways is needed to design interventions to improve sleep.

ACKNOWLEDGMENTS
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We would like to thank the Gemini families who are participating in the study and the Office of National Statistics for their help in recruitment.

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10. Heath AC, Kendler KS, Eaves LJ, Martin NG. The biological and environmental influences of nature and nurture, in-
THE BENEFIT OF DESSERT FOR BREAKFAST: I will never forget the arguments I had with my parents over what I should eat for breakfast. Under the influence of numerous television advertisements for cereals jam-packed with cookies, marshmallows, and other sugary treats, I longed for the day when my parents would accept these sweet cereals as nourishing food rather than dessert. Unfortunately for me, it was not until recently that scientists have been able to provide any evidence in support of dessert for breakfast. According to a recent publication in Steroids (Volume 77, Issue 4: March 10, 2012), including sweets such as chocolate and cake in your first meal of the day may be the key to maintaining weight loss. Researchers randomized 144 obese, non-diabetic adults into two groups; one group consumed a high carbohydrate, high protein breakfast (including a dessert item), while the second group consumed a low carbohydrate breakfast. Both groups had the same total daily calorie intake: 1,400 calories for women and 1,600 calories for men. After 16 weeks, both groups lost the same amount of weight: approximately 32 pounds. However, over subsequent 16 weeks, those on the “dessert with breakfast” plan lost an additional 13 pounds, while those on the low carbohydrate plan gained back all but three pounds of the weight lost. In addition, the group eating dessert with breakfast reported higher satiety ratings, significantly fewer cravings for a variety of foods, and had lower measured postprandial levels of the hunger-inducing hormone ghrelin when compared to the group eating a low carbohydrate breakfast. These findings support the importance of meal satisfaction in addition to calorie counting when considering a diet plan. While this research might have come too late for me to win arguments with my parents, I am excited at the prospect of incorporating these findings into my adult morning routine.

Noted by Leah H. Carr, BS, MSIII
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