ARTICLE

A Genetic Decomposition of the Association Between Parasomnias and Dyssomnias in 8-Year-Old Twins

Alice M. Gregory, PhD

Objective: To estimate genetic and environmental influences on parasomnias and dyssomnias and their association in 8-year-olds.

Design: Parents of twins completed the Children's Sleep Habits Questionnaire.

Setting: Families were primarily tested at the Institute of Psychiatry, London, England.

Participants: A total of 300 pairs of 8-year-old twins and their parents participated in the study.

Main Outcome Measures: Sleep difficulties in children.

Results: Individual differences in parasomnias and dyssomnias were largely explained by genes (accounting for 50% and 71% of the variances, respectively). The rest of the variances were mainly due to nonshared environmental influences. A moderate association was found between parasomnias and dyssomnias ($r=0.42$), which was mainly accounted for by genetic influences (87%). The genetic correlation between parasomnias and dyssomnias was moderate ($r=0.61$). In contrast, the nonshared environmental correlation was small ($r=0.10$).

Conclusions: The decomposition of the association between parasomnias and dyssomnias suggests that there may be different manifestations of shared underlying genetic risks for sleep problems partly dependent on nonshared environmental influence.

Arch Pediatr Adolesc Med. 2008;162(4):299-304

THE *DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS* (Fourth Edition)[1] distinguishes 2 main categories of primary sleep disorders, parasomnias and dyssomnias, both of which may be experienced by children.[2] Previous genetic research focusing on children has highlighted both genetic and environmental influences on specific sleep problems assessed individually (eg, sleepwalking and nightmares[3]) and sleep problems defined as a single category without distinguishing parasomnias and dyssomnias.[4,5] Certain parasomnias and dyssomnias are known to co-occur in childhood,[6,7] although little is known about the reasons for these associations. To address this issue, this article examines phenotypic and genetic associations between parasomnias and dyssomnias in a sample of twins aged 8 years.

Parasomnias are characterized by atypical behavior or physiologic events that occur in specific periods of sleep and include a range of difficulties, such as sleepwalking and bedwetting. Information is accumulating about both genetic and environmental risk factors for these disorders, with research showing that both types of influence are important in explaining individual differences in these sleep problems.[6,8] Previous research has also examined the association among different types of parasomnias, showing that they co-occur in both children and adults and that this co-occurrence in adults can be partly explained by genes.[3]

Dyssomnias are characterized by an unusual amount, quality, or timing of sleep and among other things include both insomnia and breathing-related sleep disorder. As with parasomnias, twin studies have revealed that both genetic and environmental factors have a role in the etiology of these difficulties in both children[6] and adults.[9-11]

Genetic analyses can provide information concerning reasons for the associations between disorders.[12] Such analyses are potentially useful in the hunt for specific genetic or environmental influences on difficulties. For example, a high genetic correlation between different disorders (such as that found between anxiety and depression[13,14]) suggests that once we have identified specific genes associated with one disorder these may be worth examining in relation to the other disorder. Information about genetic influences on sleep difficulties is potentially useful in identifying individuals at risk for difficul-

Author Affiliations:
Department of Psychology, Goldsmiths College, University of London, and Institute of Psychiatry, King's College, London, England.

©2008 American Medical Association. All rights reserved.
Downloaded From: http://archpedi.jamanetwork.com/ on 01/21/2017

ties. It is then possible to intervene to reduce the likelihood of difficulties developing. For these reasons, this study examined the extent to which parasomnias and dyssomnias co-occur during middle childhood and estimated genetic and environmental influences on this association.

METHODS

PARTICIPANTS

All participants are members of the Emotions, Cognitions, Heredity and Outcome (ECHO) study, which consists of 300 twin pairs aged 8 years (range, 8 years 2 months to 8 years 11 months) at wave 1 of data collection. ECHO is a spin-off study from the longitudinal Twins Early Development Study (TEDS[15]), focusing on twins born in England and Wales during 1994-1996. Data collection took place at the Institute of Psychiatry, London, England, with the exception of a few families who were visited in their homes. The ECHO study received ethical approval from the Maudsley Hospital Ethics Committee, London. Informed consent from parents was obtained through the mail before data collection.

Twins were selected for inclusion in the ECHO study sample based on their anxiety at 7 years. Anxiety was focused on when selecting participants because the current data were collected as part of a study investigating anxiety and links with other difficulties (eg, sleep problems). This extremes design was used to maximize power. Selecting participants by focusing on anxiety scores at the 7-year-old assessment is not a concern because the selected nature of the sample is corrected in all analyses.

Of the 5745 families in TEDS, parental data were available for 5343 twin-pairs, and 1378 of these families contained at least 1 child (or proband) scoring in the top 15% for parent-reported anxiety at 7 years. Of these families, 967 were excluded for various reasons (eg, 1 twin had a major medical condition). This left 411 potential proband pairs. An additional 30 families had moved, leaving 381 proband families to be invited to participate, of whom 247 pairs took part (65%). For the control subjects (n=3965 pairs), the same criteria were applied, excluding 2794 pairs. From the remaining 1171 potential control families, a random 92 pairs were invited to participate, of whom 53 participated (58%). The total number of families participating when the twins were 8 years of age was therefore 300, comprising 43 monozygotic male pairs, 57 monozygotic female pairs, 29 dizygotic male pairs, 53 dizygotic female pairs, 117 dizygotic opposite sex pairs, and 1 pair of unknown zygosity (who refused to provide DNA). After testing, data from 11 twin pairs (4%) were considered unusable because at least 1 of the twins had neurologic impairments, autistic spectrum disorders, severe receptive language impairments, or persistent difficulties with attention. An additional 10 families (3%) did not have scores for the sleep measure reported herein because of missing data. Fifty-seven percent of the initial sample was female and 43% male. Most families who participated in the ECHO study were white (n=256 [87%]). Further information about the demographics of the sample can be found elsewhere.[6,16]

PROCEDURES AND INSTRUMENTS

Zygosity

A parent-rated instrument was used to assign twin zygosity in the TEDS sample when the twins were 18 months old. This measure assigned zygosity accurately in 95% of cases when validated against DNA (for further discussion of zygosity ascertainment in the TEDS sample, see the article by Price et al[17]).

Anxiety Selection Variable

Anxiety was examined in the TEDS sample when the participants were aged 7 years using the parent-report Anxiety Related Behaviors Questionnaire.[18] Twins with at least 1 member scoring in the top 15% of this measure were selected as the high-anxiety pairs in the ECHO study, whereas control pairs scored below this cutoff. The entire sample was analyzed as 1 group, taking this selection process into account.

Children's Sleep Habits Questionnaire

Parents reported on their children's sleep problems using a 33-item version of the Children's Sleep Habits Questionnaire (CSHQ[7]). Each item was rated on a 3-point scale (1 indicating rarely to 3 indicating usually). The CSHQ consists of 8 subscales, focusing on bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night waking, parasomnias, sleep-disordered breathing, and daytime sleepiness. When completing the CSHQ, parents were asked to report on the most recent typical week. The reliability and validity of this measure are demonstrated elsewhere.[7,19]

The focus of this article is on the parasomnias scale of the CSHQ (comprising 7 items including "child talks during sleep" and "child grinds teeth during sleep") and a measure of dyssomnias (comprising 10 items taken from 4 subscales of the CSHQ: sleep-onset delay, sleep duration, night waking, and sleep-disordered breathing). The internal consistencies for parasomnias ($\alpha=.58$) and dyssomnias ($\alpha=.62$) were moderate, reflecting the various sleep problems within each general category.

STATISTICAL ANALYSES

Skew

Both sleep problem variables were skewed (skew >1) and therefore were log transformed (reducing the skew to <1) for analyses. Log-transformed data are reported unless otherwise specified. Of note, all analyses were rerun on raw (untransformed) data, and substantively identical results were obtained.

Selected Data

All analyses were conducted in Mx,[20] which is one of the most popular statistical programs designed to deal with genetically sensitive data. The selected sample (details reported previously) was used because we could only see a small proportion of the total TEDS participants and selecting from the extremes increases not only the power but also the likelihood of including children with clinically significant difficulties. To correct for ascertainment, analyses on all variables, including descriptive statistics, and genetic analyses were conducted jointly with the 7-year screening variable from the TEDS sample. This technique is somewhat similar to using a weight (for further information, see other articles reporting data from the ECHO study[6,16]).

Genetic Analyses

Twin studies compare within-pair similarity for groups of monozygotic twins, who are genetically identical, and dizygotic twins, who share half their segregating genes.[12] This information can

©2008 American Medical Association. All rights reserved.
Downloaded From: http://archpedi.jamanetwork.com/ on 01/21/2017

be used to estimate additive genetic influences, environmental influences that make family members similar (shared environmental influences), and environmental influences that make family members different (nonshared environmental influences) on single traits and correlations between traits. The bivariate correlated factors model reported herein allows influences on parasomnias to correlate with the same factors on dyssomnias. Consequently, the correlations between parasomnias and dyssomnias are mediated via genetic, shared, and nonshared environmental routes (**Figure**). As with other analyses, the selection variable was included in these analyses to control for the selected nature of the sample.

The fit statistic provided by Mx for raw data modeling is minus twice the log likelihood (–2LL) of the observations. This provides a relative measure of fit because the differences between –2LLs between models are distributed as χ^2. To examine the overall fit of the genetic model, it is necessary to compare its –2LL to that of a saturated model. In a saturated model, the maximum number of parameters is estimated to describe the variance-covariance and means of the tested variables and to provide a perfect fit to the data. The Akaike Information Criterion, which was calculated as $\chi^2 - 2 \times df$, considers the number of parameters being estimated and provides a further fit index (lower, negative values indicate a better fit).

RESULTS

The raw (untransformed) mean scores for parasomnias and dyssomnias at 8 years of age are given in **Table 1**. No significant differences were found in levels of the sleep problems between boys and girls. The phenotypic correlation between parasomnias and dyssomnias was moderate ($r = 0.42$). Table 1 also gives the cross-twin correlations for parasomnias and dyssomnias. For both sets of cross-twin correlations, the monozygotic correlation is greater than the dizygotic correlation, suggesting genetic influence. Although the monozygotic correlations are greater than twice the magnitude of the dizygotic twin correlations, suggesting possible genetic dominance (where there is interaction of different alleles at a locus), the sample size was too small to differentiate additive genetic influence and dominance. Furthermore, preliminary (unreported) analyses showed that for each phenotype, models that included additive genetic, shared, and nonshared environmental influences provided a better fit to the data compared with models that included additive genetic, dominance, and nonshared environmental influences. The cross-twin cross-trait correlations (eg, the associations between parasomnias in twin 1 and dyssomnias in twin 2) were $r = 0.39$ for monozygotic twins and $r = 0.10$ for dizygotic twins.

Consistent with estimates derived from twin correlations, the results of model-fitting univariate data (reported in **Table 2**) revealed significant genetic influences on both parasomnias and dyssomnias (eg, genetic influences explained 50% of the variance of parasomnias). Nonshared environmental influences were also significant and accounted for 48% and 26% of the variance of parasomnias and dyssomnias, respectively. The confidence intervals (which included zero) suggest that shared environmental influences did not have a significant role.

Table 2 also presents the results from the bivariate model. The genetic, shared, and nonshared environmental estimates on parasomnias and dyssomnias were similar to those obtained from the univariate models. The bivariate genetic correlation (the overlap between genes that influence parasomnias and dyssomnias) suggests that there is overlap between genes that influence both difficulties ($r = 0.61$). Overall, genes are most important in explaining the association between parasomnias and dyssomnias (accounting for 87% of the covariance between the two). Shared environmental influences on the sleep problems are negligible, but these influences appear to be identical for both parasomnias and dyssomnias ($r = 1$), although overall they still account for a small proportion of the association between parasomnias and dyssomnias (5% of the covariance). A small overlap was found between the nonshared environmental influences for parasomnias and dyssomnias ($r = 0.10$), and nonshared environment accounted for little of the association between the 2 difficulties (explaining 8% of the covariance). Each model appeared to fit the data adequately as suggested by the negative Akaike Information Criterion values and nonsignificant *P* values, suggesting that the models do not fit the data significantly less well than the perfect models.

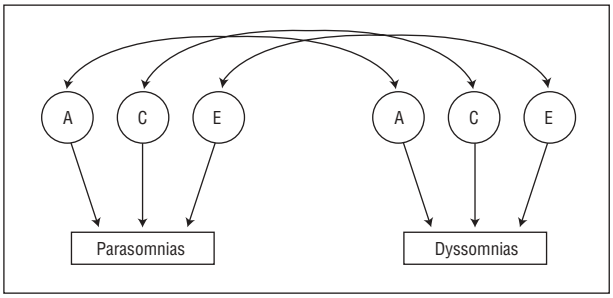

Figure. Correlated factor solution path diagram. Model shown for 1 twin. A indicates additive genetic influence; C, shared environmental influence; and E, nonshared environmental influence.

Table 1. Means (SDs) and Cross-Twin Correlations of Parasomnias and Dyssomnias at 8 Years[a]

Variable	Parasomnias	Dyssomnias
Total, mean (SD)	8.40 (1.73)	12.09 (2.41)
Male, mean (SD)	8.44 (1.82)	12.09 (2.47)
Female, mean (SD)	8.37 (1.66)	12.08 (2.36)
Cross-twin correlations		
Monozygotic	0.58	0.77
Dizygotic	0.14	0.23

[a] Raw (untransformed) means (SDs) are reported. The parasomnias scale includes 7 items, and the dyssomnias scale includes 10 items. Correlations are conducted on log-transformed data. All numbers account for the selected nature of the sample.

COMMENT

This study found a moderate overlap between parasomnias and dyssomnias, and individual differences in each category of difficulty were explained largely by genetic and nonshared environmental influences. The novel finding here is that there was substantial genetic overlap between these 2 types of sleep problems, suggesting that

©2008 American Medical Association. All rights reserved.
Downloaded From: http://archpedi.jamanetwork.com/ on 01/21/2017

Table 2. Parameter Estimates (95% Confidence Intervals) From the Genetic Models[a]

Phenotypes	Influences			Genetic Model Fit			
	A	C	E	$\Delta\chi 2$	Δdf	*P* Value	AIC
Estimates from univariate models							
Parasomnias	0.50 (0.31 to 0.63)	0.02 (0.00 to 0.14)	0.48 (0.36 to 0.63)	65.96	57	.20	–48.04
Dyssomnias	0.71 (0.57 to 0.80)	0.02 (0.00 to 0.12)	0.26 (0.19 to 0.38)	62.89	57	.28	–51.11
Estimates from bivariate model							
Univariate estimates							
Parasomnias	0.51 (0.33 to 0.63)	0.02 (0.00 to 0.14)	0.47 (0.36 to 0.61)	126.33	111	.15	–95.67
Dyssomnias	0.71 (0.57 to 0.80)	0.02 (0.00 to 0.12)	0.27 (0.19 to 0.38)		As previously		
Bivariate correlations							
Parasomnias and dyssomnias	0.61 (0.45 to 0.79)	1 (–1 to 1)	0.10 (–0.10 to 0.29)		As previously		
Proportion of correlation between parasomnias and dyssomnias due to A, C, and E influences	0.87	0.05	0.08		As previously		

Abbreviations: A, additive genetic influence; AIC, Akaike Information Criterion; C, shared environmental influence; E, nonshared environmental influence.
[a] All analyses are conducted on log-transformed data. All analyses considered the selected nature of the sample. $\Delta\chi^2$ indicates change in minus twice the log likelihood between the saturated model and the genetic model; Δdf, change in degrees of freedom between the saturated model and the genetic model.

genes that influence parasomnias influence dyssomnias and vice versa. Overall, the moderate association between parasomnias and dyssomnias was largely explained by genes with smaller environmental influence.

The finding that parasomnias and dyssomnias cooccur agrees with previous literature demonstrating associations between these difficulties.[7] Clinical knowledge concerning specific sleep difficulties supports links between these 2 categories of sleep problems. For example, it is known that excessive sleepiness (a possible feature of dyssomnias) may increase the chances of sleepwalking (a parasomnia).

In line with previous research, a genetic influence was seen on both parasomnias and dyssomnias.[3,9,10] The strong genetic correlation between the 2 types of difficulties agrees with previous studies that highlight genetic overlap between diverse sleep problems, including different pairs of parasomnias[3] and insomnia and sleepiness.[21] This genetic overlap leads to speculation as to which genes are associated with both sets of difficulties. As with other complex phenotypes, there is a lack of replicated associations between specific genes and sleep difficulties. Nevertheless, *clock* genes have been linked to sleep difficulties, including insomnia,[22] and more specifically, *Period* genes are important in sleep timing.[23] Furthermore, a range of sleep problems, including insomnia and parasomnias, have been linked to symptoms of depression,[16,24] and genetic overlap occurs between symptoms of sleep problems and depression. This suggests that polymorphisms identified with regard to depression, including genes related to monoaminergic neurotransmission, neurotoxic and neurotrophic processes, and activation of the hypothalamic-pituitary axis, may be candidates for further exploration with regard to sleep problems.[25,26]

Besides genetic influence, nonshared environmental influence also played a central role in explaining individual differences in parasomnias and dyssomnias. Many environmental factors have now been considered in association with sleep problems in children, and links have been made between sleep difficulties and family disorganization, maternal depression, school demands, suffering bullying, and a host of life events.[4,27-30] Although influences such as these are often considered environmental, it is widely accepted that genetic propensities can moderate both exposure and sensitivity to such environmental influences. The correlation between nonshared environmental influences on parasomnias and dyssomnias was small, suggesting that nonshared environmental influences on these difficulties were largely distinct. It is easy to see how environmental influences could lead to one type of difficulty and not another. For example, high levels of exposure to television could be associated with certain sleep difficulties (eg, sleep-wake transition) but not others (eg, sleep-disordered breathing[31]). Overall, the results of this study suggest that there may be a differential manifestation of shared underlying genetic risks for sleep problems partly based on nonshared environmental influences.

The finding of negligible shared environmental influence on parasomnias and dyssomnias is unsurprising given the rarity of shared environmental influences on traits in adults and to a lesser extent children.[12] This supports the idea that environmental influences tend to work in a way that makes children within a family different and not similar.[32]

The results of this study should be considered alongside the limitations. The first limitation concerns the sample size. The thorough assessment of variables meant that it was infeasible to include a larger number of twin pairs. The modest sample size meant that there was no power to look at the associations between individual sleep problems (as opposed to combining difficulties into parasomnias and dyssomnias). This point is noteworthy because previous research examining the overlap between different pairs of parasomnias has revealed differing levels of genetic overlap (eg, the genetic covariation between sleepwalking and sleep talking was greater than that between sleep talking and nightmares[3]). Nevertheless, despite the modest sample size, there was power to highlight genetic influences that explain the association between parasomnias and dyssomnias. The second limitation concerns the examination of sleep problems in the

©2008 American Medical Association. All rights reserved.
Downloaded From: http://archpedi.jamanetwork.com/ on 01/21/2017

full range. There was no power to investigate whether the magnitude and type of genetic and environmental influences on sleep problems are the same at the extremes as in the full range, and this is an issue that may be worthwhile addressing in larger twin samples. Although appropriate given the research question, the third limitation concerns the use of the twin method, for which concerns have been raised.[33] The final limitation to be discussed concerns the employment of a parent-rated questionnaire to assess childhood sleep problems. Different phenotypic and genetic estimates have been obtained using different methods to assess sleep problems (eg, parent vs child self-report).[6] Nevertheless, this method of assessing sleep problems is appropriate given the size and nature of the study.

Despite limitations, this work has at least 3 sets of implications. The first concerns clinical assessment of sleep problems. As highlighted elsewhere,[7] we demonstrated that different types of sleep problems co-vary. This emphasizes the likely benefit of obtaining detailed information about both parasomnias and dyssomnias in children who present with a sleep problem. The familiality of the sleep problems reported herein also suggests that it may be worth inquiring about the sleep of family members when assessing patients.

The second set of implications concerns future research. Previous research has highlighted genetic overlap among different types of parasomnia,[3] suggesting that it is worth examining whether genes found to influence one type of parasomnia also influence another. The results reported herein go further to suggest that genes that influence certain parasomnias may also influence certain dyssomnias and vice versa.

The final set of implications concern nosology. The finding that parasomnias and dyssomnias are phenotypically and genetically overlapping could have implications for the conceptualization of these problems.

This article focuses on 8-year-olds, and the findings reported herein are not necessarily applicable to other age groups. Indeed, there is clear evidence that traits can become more or less heritable throughout life (eg, a recent report[34] highlighted age as a moderator of the association between a polymorphism in the *PER3* clock gene and diurnal preference). In addition to paying close attention to developmental issues, researchers also need to examine ways in which genetic and environmental factors interact. Groundbreaking research in this area has demonstrated that sensitivity to environmental insults may be moderated by specific genes in relation to a host of difficulties, and a recent report revealed that a *PER3* polymorphism is associated with individual differences in decrement in cognitive performance after sleep loss.[35] Finally, to have a clear understanding of the mechanisms by which genes and the environmental factors have their effects, it is now essential to identify further specific genetic and environmental influences on sleep patterns and problems and to elucidate the ways in which these influence the brain and behavior.

Accepted for Publication: October 8, 2007.
Correspondence: Alice M. Gregory, PhD, Department of Psychology, Goldsmiths College, University of London, Lewisham Way, New Cross, London SE14 6NW, England (a.gregory@gold.ac.uk).
Author Contributions: Dr Gregory had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Financial Disclosure: None reported.
Funding/Support: The ECHO study was supported by a Career Development Award from the UK Medical Research Council to Thalia C. Eley, PhD (Institute of Psychiatry).
Additional Contributions: Thalia Eley, PhD, collected data, obtained funding, oversaw the conduction of the ECHO Study, and commented on an earlier draft of the manuscript; Simon Archer, PhD, Kay Jones, MSc, and Tom Willis, PhD, provided comments on an earlier draft of the manuscript; David Clark, PhD, and Peter McGuffin, PhD, provided scientific input about the ECHO study; Megan Crawford proofread an earlier draft of the manuscript; Georgina Hosang, Jenn Lau, PhD, Fiona Mcleod, Jasmine Singh, and Lucy Stirling, DClinPsy, collected data for the ECHO study; and Maria Napolitano, MPhil, was project coordinator for the ECHO study.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
2. Mindell JA. Sleep disorders in children. *Health Psychol*. 1993;12(2):151-162.
3. Hublin C, Kaprio J, Partinen M, Koskenvu M. Parasomnias: co-occurrence and genetics. *Psychiatr Genet*. 2001;11(2):65-70.
4. Gregory AM, Eley TC, O'Connor TG, Rijsdijk FV, Plomin R. Family influences on the association between sleep problems and anxiety in a large sample of preschool aged twins. *Pers Individ Dif*. 2005;39:1337-1348.
5. van den Oord EJ, Verhulst FC, Boomsma DI. A genetic study of maternal and paternal ratings of problem behaviors in 3-year-old twins. *J Abnorm Psychol*. 1996;105(3):349-357.
6. Gregory AM, Rijsdijk FV, Eley TC. A twin-study of sleep difficulties in school-aged children. *Child Dev*. 2006;77(6):1668-1679.
7. Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep*. 2000;23(8):1043-1051.
8. Hublin C, Kaprio J. Genetic aspects and genetic epidemiology of parasomnias. *Sleep Med Rev*. 2003;7(5):413-421.
9. Heath AC, Kendler KS, Eaves LJ, Martin NG. Evidence for genetic influences on sleep disturbances and sleep patterns in twins. *Sleep*. 1990;13(4):318-335.
10. McCarren M, Goldberg J, Ramakrishnan V, Fabsitz R. Insomnia in Vietnam era veteran twins: influence of genes and combat experience. *Sleep*. 1994;17(5):456-461.
11. Dauvilliers Y, Maret S, Tafti M. Genetics of normal and pathological sleep in humans. *Sleep Med Rev*. 2005;9(2):91-100.
12. Plomin R, DeFries JC, McClearn GE, McGuffin P. *Behavioral Genetics*. 4th ed. New York, NY: Worth Publishers; 2001.
13. Eley TC, Stevenson J. Exploring the covariation between anxiety and depression symptoms: a genetic analysis of the effects of age and sex. *J Child Psychol Psychiatry*. 1999;40(8):1273-1284.
14. Thapar A, McGuffin P. Anxiety and depressive symptoms in childhood: a genetic study of comorbidity. *J Child Psychol Psychiatry*. 1997;38(6):651-656.
15. Trouton A, Spinath FM, Plomin R. Twins Early Development Study (TEDS): a multivariate, longitudinal genetic investigation of language, cognition and behavior problems in childhood. *Twin Res*. 2002;5(5):444-448.
16. Gregory AM, Rijsdijk FV, Dahl RE, McGuffin P, Eley TC. Associations between sleep problems, anxiety and depression in twins at 8 years of age. *Pediatrics*. 2006;118(3):1124-1132.
17. Price TS, Freeman B, Craig I, Petrill SA, Ebersole L, Plomin R. Infant zygosity can be assigned by parental report questionnaire data. *Twin Res*. 2000;3(3):129-133.
18. Eley TC, Bolton D, O'Connor TG, Perrin S, Smith P, Plomin R. A twin study of anxiety-related behaviours in pre-school children. *J Child Psychol Psychiatry*. 2003;44(7):945-960.

©2008 American Medical Association. All rights reserved.
Downloaded From: http://archpedi.jamanetwork.com/ on 01/21/2017

19. Owens JA, Maxim R, Nobile C, McGuinn M, Msall M. Parental and self-report of sleep in children with attention- deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med*. 2000;154(6):549-555.
20. Neale MC. *Mx: Statistical Modeling*. 4th ed. Richmond: Department of Psychiatry, Medical College of Virginia; 1997.
21. Watson NF, Goldberg J, Arguelles L, Buchwald D. Genetic and environmental influences on insomnia, daytime sleepiness, and obesity in twins. *Sleep*. 2006; 29(5):645-649.
22. Serretti A, Benedetti F, Mandelli L, et al. Genetic dissection of psychopathological symptoms: insomnia in mood disorders and *CLOCK* gene polymorphism. *Am J Med Genet B Neuropsychiatr Genet*. 2003;121(1):35-38.
23. Toh KL, Jones CR, He Y, et al. An hPer2 phosphorylation site mutation in familiar advanced sleep phase syndrome. *Science*. 2001;291(5506):1040-1043.
24. Vandeputte M, de Weerd A. Sleep disorders and depressive feelings: a global survey with the Beck depression scale. *Sleep Med*. 2003;4(4):343-345.
25. Huezo-Diaz P, Tandon K, Aitchison KJ. The genetics of depression and related traits. *Curr Psychiatry Rep*. 2005;7(2):117-124.
26. Levinson DF. The genetics of depression: a review. *Biol Psychiatry*. 2006;60(2): 84-92.
27. Kahn A, Van de Merckt C, Rebuffat E, et al. Sleep problems in healthy preadolescents. *Pediatrics*. 1989;84(3):542-546.
28. Lam P, Hiscock H, Wake M. Outcomes of infant sleep problems: a longitudinal study of sleep, behavior, and maternal well-being. *Pediatrics*. 2003;111(3): e203-e207. http://www.pediatrics.org/cgi/content/full/111/3/e203. Accessed January 14, 2008.
29. Sadeh A. Stress, trauma, and sleep in children. *Child Adolesc Psychiatr Clin N Am*. 1996;5:685-700.
30. Williams K, Chambers M, Logan S, Robinson D. Association of common health symptoms with bullying in primary school children. *BMJ*. 1996;313(7048): 17-19.
31. Paavonen EJ, Pennonen M, Roine M, Valkonen S, Lahikainen AR. TV exposure associated with sleep disturbances in 5-to 6-year-old children. *J Sleep Res*. 2006; 15(2):154-161.
32. Harris JR. *The Nurture Assumption: Why Children Turn Out the Way They Do*. New York, NY: Free Press; 1998.
33. Martin N, Boomsma DI, Machin G. A twin-pronged attack on complex trait. *Nat Genet*. 1997;17(4):387-392.
34. Jones KH, Ellis J, von Schantz M, Skene DJ, Dijk DJ, Archer SN. Age-related change in the association between a polymorphism in the *PER3* gene and preferred timing of sleep and waking activities. *J Sleep Res*. 2007;16(1):12-16.
35. Viola AU, Archer SN, James LM, et al. *PER3* polymorphism predicts sleep structure and waking performance. *Curr Biol*. 2007;17(7):613-618.

Announcement

Trial Registration Required. In concert with the International Committee of Medical Journal Editors (ICMJE), *Archives of Pediatrics and Adolescent Medicine* will require, as a condition of consideration for publication, registration of all trials in a public trials registry (such as http://ClinicalTrials.gov). Trials must be registered at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005. For trials that began enrollment before this date, registration will be required by September 13, 2005, before considering the trial for publication. The trial registration number should be supplied at the time of submission.

For details about this new policy, and for information on how the ICMJE defines a clinical trial, see the editorials by DeAngelis et al in the September 15, 2004 (2004; 292(11):1363-1364) and June 15, 2005 (2005;293(23): 2927-2929) issues of *JAMA*. Also see the Instructions to Authors on our Web site: www.archpediatrics.com.

©2008 American Medical Association. All rights reserved.
Downloaded From: http://archpedi.jamanetwork.com/ on 01/21/2017