Sleep Problem Risk for Adolescents with Sickle Cell Disease: Socio-demographic, Physical, and Disease-Related Correlates

Cecelia R. Valrie, Ph.D.[1,2], **Krystal L. Trout, M.A.**[2], **Kayzandra E. Bond, Ph.D.**[2,3], **Rebecca J. Ladd, Ph.D.**[4], **Nichelle L. Huber, B.A.**[2], **Kristen J. Alston, Ph.D.**[5], **Alicia M. Sufrinko, Ph.D.**[6], **D. Erik Everhart, Ph.D.**[2], and **Beng R. Fuh, MD**[7]

[1]Department of Psychology, Virginia Commonwealth University, Richmond, Virginia

[2]Department of Psychology, East Carolina University, Greenville, North Carolina

[3]Monroe-Meyer Institute for Genetics and Rehabilitation, University of Nebraska Medical Center, Omaha, Nebraska

[4]Division of Bio-Behavioral Medicine, Department of Psychiatry, Medical University of South Carolina, Charleston, South Carolina

[5]Department of Family Medicine, University of Mississippi Medical Center, Jackson, Mississippi

[6]Sports Medicine Concussion Program, Department of Orthopaedic Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

[7]Department of Pediatrics, East Carolina University, Greenville, North Carolina

Abstract

The aims of the current study were to investigate whether SCD incurs an additional risk for poor sleep over and above the influence of socio-demographic factors (i.e., race and sex) during adolescence, and to explore the relationships between socio-demographic, physical (i.e., age and pubertal status), and disease-related factors (i.e., SCD genotype and hydroxyurea use) on sleep problem risk during adolescence. Black adolescents, aged 12–17, with SCD (n= 53) were recruited from regional pediatric SCD clinics in the southeast and a sample of healthy Black adolescents (n= 160) were recruited from middle and high schools. Regression analyses indicated that SCD was uniquely related to sleeping more, and worse sleep quality over and above the influence of socio-demographic factors. Having a more severe SCD genotype was related to worse sleep quality and higher pubertal status was related to sleeping longer during the week. Results indicate the need for systematic assessments of sleep problems, with more a focus on youth with more severe genotypes and higher pubertal status. Future research should focus on characterizing trajectories of sleep problems in this population, identifying key risk factors, and elucidating mechanisms linking risk factors to sleep problem risk to aid in tailoring interventions for this population.

Corresponding Author: Cecelia Valrie, Ph.D., Virginia Commonwealth University, Department of Psychology, 806 W. Franklin St, Box 842018, Richmond, VA 23284, Office Phone: 804-827-1562, Fax: 804-828-2237, cvalrie@vcu.edu.

Keywords

sickle cell disease; sleep; adolescence; puberty

Introduction

Youth with sickle cell disease (SCD), a family of genetic blood disorders seen primarily in people of African or Mediterranean descent [1], are at high risk of sleep disturbance[2–3]. Results from polysomnography studies indicate that approximately 36% of children and adolescents with SCD experience sleep disordered breathing (SDB) [4], and 23% experience periodic limb movement disorder [5]. Also, 21–41% of youth with SCD report some form of insomnia [6], a behavioral sleep disorder characterized by trouble falling asleep, staying asleep, or both [7]. Poor sleep patterns in individuals with SCD have been related to increased pain, risk of stroke, high health care utilization, and high negative mood [8–11] which is consistent with findings in adults with SCD [12–13]. Notably, when examining sleep in youth with SCD, researchers have tended to either utilize combined samples of children and adolescents or focus exclusively on children. This is a significant gap in the literature given that adolescence is a time period of increased risk for insufficient sleep and disrupted sleep patterns in healthy adolescents due to a range of physical and socio-demographic factors [14–16]. There are no studies to date that have investigated whether SCD infers an additional risk of poor sleep in adolescents with SCD in the context of other socio-demographic risk factors known to impact sleep in healthy adolescents (e.g., race and sex). Also, research is needed to investigate the unique relationships between socio-demographic, physical, and disease-related factors and sleep problem risk in adolescents with SCD, which may aid in the development of more targeted treatments for this population.

Race and sex are socio-demographic factors associated with sleep in healthy adolescents that may predispose adolescents with SCD to poor sleep. The majority of individuals with SCD are Black [1], and findings from a nationally representative sample of healthy youth using time-diaries found that Black adolescents report sleeping less on weekdays and weekends compared to White, Hispanic, and Asian adolescents [14]. These findings are consistent with recent studies using actigraphy that found that Black adolescents sleep less, and evidence more fragmented sleep than white adolescents [17–18]. Notably, Black and White adolescents tend to report equivocal rates of subjective sleep quality and symptoms of insomnia [17–19]. Also, studies have indicated that female adolescents tend to evidence worse sleep quality and more daytime sleepiness [17], as well as more symptoms of insomnia [19], while male adolescents tend to sleep less than female adolescents [18]. Notably, being female was related to more sleep anxiety, but not other sleep problems, in a sample of children with SCD [20]. The one study that investigated the role of socio-demographic factors on sleep problem risk in youth with SCD compared children, aged 4–10 years, with SCD to a healthy control group of children who were demographically similar based on race, sex, and age [20]. Findings indicated that above the influence of these socio-demographic factors, SCD placed children at higher risk of night awakenings and sleep disordered breathing problems.

As for additional factors that may increase sleep problem risk within the adolescent SCD population, a physical factor associated with sleep problem risk during adolescence is the onset of puberty. Puberty generally coincides with the onset of adolescence in healthy youth and is associated with a shift in circadian rhythm, the body's natural cycle that regulates the timing of sleepiness and wakefulness, resulting in a sleep phase delay [21]. This translates to adolescents feeling more alert and less sleepy later in the night than during childhood, and approximately a two hour delay in the onset of sleep during this developmental period. Combined with early high school start times, this often leads to adolescents consistently receiving less than the recommended 8–10 hours of sleep per night. Also, research has related higher pubertal status to more symptoms of insomnia in adolescents [22]. However, the onset of puberty in individuals with SCD is frequently delayed [23], and, subsequently, the shift in circadian rhythm that accompanies the onset of puberty may also be delayed for this population. This may make it so that pubertal status is a more salient marker of sleep problem risk than age. Notably, findings from a study of children with SCD found that older age was related to more bedtime resistance and sleeping longer [20]. These findings are inconsistent with research indicating sleep need in healthy youth decreases over time [24], and may indicate that the accumulating physical burden of SCD may be increasing sleep need in this population. It is important to examine the unique effects of pubertal status and age on sleep problem risk during adolescence in this population.

Disease-related factors that may be related to sleep problem risk in adolescents with SCD include SCD genotype and hydroxyurea use. SCD genotype is often used as an indicator of disease severity as the HbSS and HBSβ^{0}thal genotypes are related to more sickle cell complications, including more frequent and severe pain [25]. And previous studies have indicated a strong relationship between pain and poor sleep in youth with SCD [3, 10]. A study of children with SCD found that SCD genotype was related to parasomnia symptoms but not to other indicators of poor sleep, including sleep duration, night wakings, sleep disordered breathing, and daytime sleepiness [20]. This is in contrast to the body of research indicating that SCD genotype is related to sleep disordered breathing risk [26]. Hydroxyurea use has been associated with decreased SCD symptoms, including less frequent and severe vaso-occlusive pain crises, in youth [27–28]; however, the relationship between hydroxyurea use and sleep is not well-researched. One study found that hydroxyurea use was related to higher nocturnal and awake oxygen saturations, but not to rates of obstructive sleep apnea [29]. Overall, the relations between SCD genotype, hydroxyurea use, and sleep problem risk in adolescents with SCD needs further investigation.

Identifying whether SCD provides additional risk for poor sleep patterns in adolescence in the context of socio-demographic factors is essential for determining appropriate intervention targets for improving sleep in this population. The current study compared Black adolescents with SCD to a healthy control group of Black adolescents. The primary aim was to investigate whether SCD incurs an additional risk for poor sleep patterns over and above the influence of socio-demographic factors (e.g., race and sex) during adolescence. It was hypothesized that Black adolescents with SCD would evidence worse sleep than healthy Black adolescents, and that over and above the influence of age and sex, SCD would place adolescents at increased risk of poor sleep patterns. The secondary aim was to explore the relationships between socio-demographic, physical (e.g., puberty and

age), and disease-related factors (SCD genotype and hydroxyurea use) on sleep problem risk during adolescence. This was accomplished by investigating the relationships between the physical, socio-demographic, and disease-related factors and sleep problem risk within a sample of adolescents with SCD.

Materials and Methods

Participants and Procedure

Youth with SCD were recruited from three regional pediatric SCD clinics in the southeast, and were interviewed as part of an IRB-approved project examining sleep and pain in youth with SCD. Inclusion criteria for the larger study included that the youth had experienced at least one pain episode (i.e., at least 20 minutes of SCD pain) in the past year, as indicated by their medical record or the adolescent or guardian's response to a screening question. This definition of a SCD episode was taken from the Structured Pain Interview [30] and these screening criteria have been used in previous studies of youth with SCD [10, 31]. Additional inclusion criteria for the current study included that the youth had to be between 12 and 17 years of age, and self-identify as Black, African, or African American.

Due to the larger study, exclusion criteria included having a comorbid pain condition (n = 1), currently participating in a sleep intervention (e.g., taking a medication prescribed for sleep or on continuous positive airway pressure therapy; n = 3), currently receiving chronic blood transfusions (n = 5), having a neurocognitive impairment that would impede the youth's ability to complete surveys (n = 2), a history of extreme noncompliance as indicated by their pediatric SCD provider or continuous no-shows to scheduled interview (n = 11), or other mental health/family issue that would impede their ability to participate in the study as indicated by their pediatric SCD provider (n = 12). An additional 11 possible adolescent participants were excluded due to other issues that would have impacted their ability to complete the larger study (e.g., moving, not being allowed to use technology), 9 declined, and 13 could never be scheduled for interview.

The final sample included 53 of the 120 adolescents with SCD who meet inclusion criteria, and the final sample did not significantly differ from the total participant pool based on age ($t = -.79$, p = .43). No other demographics were gathered on possible participants. The majority of the participants with SCD were female (58%, N = 31) and had HBSS genotype (51%, N = 27), while 37.74% (N = 20) had HBSC, 5.66% (N = 3) had HBSβ^{0}thal, and 5.66% (N = 3) had HBSβ$^+$thal. Also, 66% (N = 35) were currently on hydroxyurea. The healthy control group participants included 160 adolescents recruited as part of an IRB-approved study of sleep in a multi-ethnic sample of middle and high school students from a rural, low income school in the region of one of the SCD clinics [32]. Adolescents were included in the study if they met all of the following criteria: 1) between 12 and 17 years of age, and 2) self-identified as Black, African, or African American. The healthy control group adolescents completed demographic and sleep measures at their respective schools. The majority of the control group were female (57%, N = 89).

Measures

Demographic and Disease-Related Information—For adolescents with SCD, participants' age in years, sex, race, SCD genotype, and whether they currently taking hydroxyurea were collected by guardian report, and confirmed using the participants' electronic medical records. Adolescents in the healthy control group self-reported age in years, sex, and race.

Pubertal Development—Adolescents with SCD completed the 5-item Self-Rating Scale for Pubertal Development [33]. Changes of specific physical indicators of pubertal development are rated on a scale ranging from not yet started = 1 to seems complete = 4. There are separate forms for boys and girls, with girls completing an item concerning whether they have started menstruation that is scored as no = 1 and 4 = yes. The scores across items are averaged to produce an overall Pubertal Development Score. The measure has been reported to be reliable and has been validated against pediatrician and parent reports of pubertal development [33]. Internal consistency for the total scores for the current sample of adolescents with SCD was .77.

Sleep Duration—Sleep duration for participants with and without SCD was gathered using self-report sleep information forms. All participants were asked to report what time they went to sleep and woke up on weekdays and weekends. The difference between sleep onset and wake times was used to calculate duration of sleep in minutes on weekdays and weekends. There is evidence of the validity of adolescents' reports of their weekday and weekend sleep durations when compared to daily diaries and actigraphy [34].

Behavioral Sleep Quality—Adolescents completed the 28-item Adolescent Sleep Wake Scale (ASWS) [35]. Using a one month reference interval, the frequency of sleep behaviors were reported using a 6-point response set (always, frequently, often, sometimes, not often, never). The measure includes five subscales assessing problems going to bed (i.e., "I have trouble making myself go to bed at bedtime"), falling asleep (i.e., "I have trouble going to sleep"), maintaining sleep (i.e., "During the night, I am very restless"), reinitiating sleep (i.e., "After waking up during the night, I have trouble going back to sleep"), and returning to wakefulness (i.e., "I have trouble getting out of the bed in the morning"). The scale also produces a composite total behavioral sleep quality score. The ASWS has been reported to be valid and reliable when used with various pediatric populations [36]. Internal consistency for the total scores for current sample of adolescents with SCD was .78, and for the current healthy adolescent sample was .85.

Data Analyses

Data was analyzed using SAS 9.3 for Windows. Descriptive statistics, including the means, standard deviations, and ranges, were calculated. To examine the influence of race, t-tests were calculated to compare the Black adolescents with SCD to the control group of healthy Black adolescents on the sleep variables. Then to assess for possible covariates for the subsequent regression analyses, chi-squares and t-tests were calculated comparing adolescents with SCD to the healthy control group of adolescents on sex and age. To test the hypothesis that, over and above the impact of age, sex, and race, SCD would place

adolescents at increased risk of poor sleep patterns, a series of regression models predicting sleep variables using SCD status, age, and sex were calculated with the combined sample of adolescents with and without SCD. To explore the relationship between socio-demographic, physical, and disease-related factors and sleep problem risk, correlations and t-tests were calculated between the variables of interest within the sample of adolescents with SCD.

Results

The Influence of SCD on Sleep of Adolescents in the Context of Socio-Demographic Factors

Means and standard deviations for the sleep variables for adolescents with SCD and the healthy control group adolescents are reported in Table 1. T-tests were calculated comparing the samples. Adolescents with SCD reported sleeping more on weekdays and weekends, and reported worse total sleep quality than the healthy Black adolescents. Also, as indicated by the subscale scores on the ASWS, adolescents with SCD reported more problems going to bed, falling asleep, maintaining sleep, and reinitiating sleep after waking in the night than the healthy Black adolescents. Notably, the adolescent SCD group and the healthy adolescent control group did not significantly differ based on sex ($\chi^2 = 0.05$, $p = .82$). However, the healthy control group adolescents ($M = 15.36$ years, $SD = 1.49$ years) were significantly older than the adolescents with SCD ($M = 14.72$, $SD = 1.50$; $t = 2.71$, $p < .01$).

To examine the unique contribution of SCD status on sleep patterns of Black adolescents while controlling for the effects of age and sex, simultaneous regression models were calculated predicting sleep variables using the combined sample of adolescents with SCD and healthy Black adolescents (See Table 2). The model predicting weekday sleep durations was significant and accounted for 10% of the variance ($F(3,202) = 8.71$, $p < .01$). SCD status uniquely accounted for 8% of the variance, such that having SCD was related to longer weekday sleep durations. The model predicting weekend sleep durations was significant ($F(3, 198) = 12.10$, $p < .01$) and accounted for 14% of the variance. SCD status uniquely accounted for 14% of the variance, such that having SCD was related to longer weekend sleep durations. The model predicting total sleep quality was significant ($F(3, 206) = 4.52$, $p < .01$) and accounted for 5% of the variance. SCD status uniquely accounted for 4% of the variance, such that having SCD was related to poorer total sleep quality.

Relations between Socio-demographic, Physical, and Disease-Related Factors and Sleep Problem Risk in Adolescents with SCD

For the adolescents with SCD, females ($M = 10.13$, $SD = 1.67$) reported more weekend sleep than males ($M = 8.41$, $SD = 2.48$; $t = -2.78$, $p < .01$). However, there were no differences in weekday sleep duration ($t = 0.82$, $p = .42$) or total sleep quality ($t = -.56$, $p = .58$) based on sex. The mean Puberty score for the adolescents with SCD was 2.91 ($SD = 0.68$, Range = 1–4). Higher pubertal status was significantly correlated with less weekday sleep ($r = .37$, $p < .01$), but was not correlated with weekend sleep duration or total sleep quality ($r = .10$, $p = .47$ and $r = .03$, $p = .81$, respectively). Also, age was not significantly correlated with weekday sleep duration ($r = -.16$, $p = .24$), weekend sleep duration ($r = .25$, $p = .07$), or total sleep quality ($r = -.02$, $p = .91$). T-tests were calculated comparing SCD

group members with severe genotypes (HBSS and HBSβ^{0}thal) to those with other genotypes (HBSC and HBSβ$^+$thal) on the sleep variables. Adolescents with SCD with more severe genotypes ($M = 3.86$, $SD = 0.50$) reported worse total sleep quality than adolescents with SCD with other genotypes ($M = 3.50$, $SD = 0.56$; $t = -2.43$, $p = .02$). However, the subgroups of adolescents with SCD did not differ on weekday or weekend sleep durations ($t = 0.74$, $p = .46$ and $t = 0.34$, $p = .74$, respectively).

T-tests also indicated that adolescents on hydroxyurea did not differ from adolescents not on hydroxyurea on weekday sleep duration ($t = -0.76$, $p = .45$), weekend sleep duration ($t = -0.82$, $p = .41$), or total sleep quality ($t = 0.16$, $p = .87$).

Discussion

The primary aim of the current study was to investigate whether SCD places adolescents at an additional risk of poor sleep. Consistent with our hypothesis, adolescents with SCD reported sleeping more on weekdays and weekends, and reported worse total sleep quality than the healthy Black adolescent control group. They particularly reported more problems going to bed, falling asleep, maintaining sleep, and reinitiating sleep after waking in the night, all indicators of insomnia [7]. In addition, regression analyses indicated that having SCD was related to sleeping longer on weekdays and weekends and poorer sleep quality over and above the influence of socio-demographic factors associated with poor sleep risk. Notably, the average reported sleep duration for the adolescents with SCD was in the recommended range of 8–10 hours [24], while the average reported sleep duration for the healthy adolescents was lower than recommended. However, current recommendations are based on the sleep needs of healthy adolescents and may not be appropriate for youth with SCD, who commonly experience anemia. Research to establish sleep recommendations associated with optimal functioning for youth with SCD is needed. Overall, these findings provide further support for the need to provide routine sleep evaluations as part of comprehensive SCD care.

Particularly notable is that the sample was limited to youth who experience pain during adolescence. As pain has been associated with poorer sleep [3] and the experience of pain is an indicator of more severe disease severity via its connection to other SCD symptoms [25, 45–46], this may have exacerbated the differences noted between adolescents with SCD and healthy Black adolescents. For example, the largest difference noted between adolescents with SCD and the healthy adolescents was on the maintaining sleep subscale. This might have been due to pain during the night leading to night awakenings. However, the current findings also inform intervention efforts with the most severe patients with SCD, as individuals who experience SCD pain early in life are more likely to experience medical complications throughout their lifetime, including chronic pain during adulthood [25, 37]. The current findings support the inclusion of sleep-focused interventions as a part of comprehensive care for youth with SCD who experience pain. This is consistent with treatment recommendations for other pediatric pain populations that note the need to assess and manage sleep to improve pain management and functional outcomes [3]. Also, future studies should include a sample of youth with SCD who do not experience pain to provide information on the sleep problem risk faced by that subpopulation.

The current study also examined the relations between socio-demographic, physical, and disease-related factors and sleep problem risk in adolescents with SCD. Adolescents with more severe SCD genotypes reported worse total sleep quality, and higher pubertal status was related to sleeping less during the week. These findings provide information concerning specific subpopulations within the adolescent SCD population that may be at greater risk for poor sleep. However, additional research is needed to determine exact mechanisms linking SCD genotypes and puberty to poor sleep patterns to provide more precise targets for intervention. Possible factors linking SCD genotypes to poor sleep patterns include SDB, stroke, and pain. Individuals with more severe genotypes are at higher risk of SDB [26], stroke [38], and pain [25], and these factors have also been linked to poor sleep patterns [2–3, 8, 39]. As for pubertal status, the findings are consistent with research in healthy youth indicating that puberty is accompanied by a circadian rhythm shift which conflicts with early high school start times and often results in adolescents sleeping less than recommended during the week [21].

Findings also indicated that the relation between sex and sleep problem risk in adolescents with SCD was minimal, with females sleeping longer on weekends than males. These findings are consistent with previous research in children with SCD that indicated that sex was not strongly related to sleep problem risk [20]. In addition being on hydroxyurea was not related to sleep problem risk in this population, which is consistent with findings from a study of youth with SCD that found hydroxyurea use was not related to rates of obstructive sleep apnea [29]. Although hydroxyurea use generally leads to reductions in SCD symptoms that may have initially lead to disrupted sleep, such as pain [28–29], once poor sleep patterns are established they may be reinforced by other factors. This would be consistent with Spielman's 3P Model of Insomnia that proposes that after insomnia has been triggered by precipitating factors, different perpetuating factors maintain or exacerbate sleep difficulties, such as altered bedtime behaviors or beliefs concerning sleep [40]. Therefore, research is needed to examine possible precipitating factors, such as sleep hygiene and cognitions, as well as additional sociodemographic factors that may increase sleep problem risk in the adolescent SCD population, including asthma symptoms and socioeconomic status (SES). Findings from the study of children with SCD indicated that those with asthma and those living in a lower SES environment evidenced more total sleep problems [20].

Beyond what is detailed above, additional limitations may have impacted the overall findings, and point to areas for future research. Sleep was only assessed via self-report. Notably, insomnia symptoms are generally assessed via self-report measures, and subjective self-assessments of sleep are generally correlated with objective evaluations of sleep [33, 41]. Pubertal status was also only assessed via self-report, while the gold standard is via examination by a physician or hormonal evaluation. However, the measure used has been validated against both physician and parental reports of maturation [33]. Also, the study did not assess aspects of sleep beyond sleep duration and insomnia symptoms, such as SDB and PLM disorder, which are primarily assessed via polysomnography (e.g., an overnight sleep study) [42–44]. Future research should include both subjective and objective sleep evaluations, such as sleep actigraphy or polysomnography, and should assess multiple aspects of sleep. Given the goals of the larger study, the current investigation excluded individuals actively on treatments for sleep disorders, which may have led to an

underestimation of sleep problems in the adolescent SCD population. Lastly, the current study adds to the picture of sleep problems experienced by youth with SCD; however, it does not address the gap in the knowledge as to when sleep problems initially appear in this population, and the trajectory of sleep problems in this population over time. Future research utilizing longitudinal methodologies to identify onset and trajectories of sleep problems as individuals with SCD would better inform prevention and intervention efforts.

Overall, findings from the current study highlight the unique influence of SCD on sleep problems, particularly insomnia symptoms, during adolescence. Poor sleep patterns in this population have been related to a range of poor health outcomes, including increased pain, stroke risk, and higher health care utilization [8–11]. Our findings also indicate that youth with more severe SCD genotypes, and those in later stages of pubertal development are at higher risk of disrupted or insufficient sleep. This suggests a need for systematic assessments of sleep problems, with possibly more in-depth evaluations of sleep problems in youth who experience pain, those with more severe genotypes and those further along in their pubertal development. There is also the need for the development and implementation of sleep interventions tailored for this population. Interventions may include education on sleep hygiene, cognitive behavioral therapy for insomnia (CBT-I), and sleep medications [3]. Future research focused on characterizing trajectories of sleep problems in this population, identifying additional key risk factors specific to SCD, and elucidating mechanisms linking risk factors to sleep problem risk can aid in tailoring existing behavioral and medical interventions for this population.

Acknowledgments

References

1. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. The Lancet. 2010; 376:2018–2031.

2. Gileles-Hillel A, Kheirandish-Gozal L, Gozal D. Hemoglobinopathies and sleep – The road less traveled. Sleep Medicine Reviews. 2015; 24:57–70. [PubMed: 25679069]

3. Valrie CR, Bromberg MH, Palermo T, et al. A systematic review of sleep in pediatric pain populations. J Dev Behav Pediatr. 2013; 34:120–128. [PubMed: 23369958]

4. Samuels MP, Stebbens VA, Davies SC, et al. Sleep related upper airway obstruction and hypoxaemia in sickle cell disease. Arch Dis Child. 1992; 67:925–929. [PubMed: 1308102]

5. Rogers VE, Marcus CL, Jawad AF, et al. Periodic limb movements and disrupted sleep in children with sickle cell disease. Sleep: Journal of Sleep and Sleep Disorders Research. 2011; 34:899–908.

6. Hankins JS, Verevkina NI, Smeltzer MP, et al. Assessment of Sleep-Related Disorders in Children With Sickle Cell Disease. Hemoglobin. 2014; 38:244–251. [PubMed: 24941261]

7. [Accessed June 8, 2016] What is Insomnia?. National Heart, Lung, and Blood Institute website. Dec 13. 2011 http://www.nhlbi.nih.gov/health/health-topics/topics/inso

8. Caboot JB, Allen JL. Pulmonary complications of sickle cell disease in children. Current opinion in pediatrics. 2008; 20:279–287. [PubMed: 18475096]

9. Dampier C, Lieff S, LeBeau P, et al. Health-related quality of life in children with sickle cell disease: a report from the Comprehensive Sickle Cell Centers Clinical Trial Consortium. Pediatric blood & cancer. 2010; 55:485–494. [PubMed: 20658620]

10. Valrie CR, Gil KM, Redding-Lallinger R, et al. Brief report: Sleep in children with sickle cell disease: An analysis of daily diaries utilizing multilevel models. J Pediatr Psychol. 2007; 32:857–861. [PubMed: 17400602]

11. Valrie C, Gil K, Lallinger-Redding R, et al. Brief Report: Daily mood as a mediator or moderator of the pain-sleep relationship in children with sickle cell disease. J Pediatr Psychol. 2008; 33:6. [PubMed: 17890285]

12. Moscou-Jackson G, Allen J, Kozachik S, et al. Acute Pain and Depressive Symptoms: Independent Predictors of Insomnia Symptoms among Adults with Sickle Cell Disease. Pain Manag Nurs. 2015:1–9. [PubMed: 25591502]

13. Wallen GR, Minniti CP, Krumlauf M, et al. Sleep disturbance, depression and pain in adults with sickle cell disease. BMC Psychiatry. 2014; 14:207. [PubMed: 25047658]

14. Adam EK, Adam EK, Snell EK, et al. Sleep Timing and Quantity in Ecological and Family Context: A Nationally Representative Time-Diary Study. Journal of Family Psychology. 2007; 21:4–19. [PubMed: 17371105]

15. Bartel KA, Gradisar M, Williamson P. Protective and risk factors for adolescent sleep: A meta-analytic review. Sleep medicine reviews. 2015

16. Gradisar M, Gardner G, Dohnt H. Recent worldwide sleep patterns and problems during adolescence: A review and meta-analysis of age, region, and sleep. Sleep Med. 2011; 12:110–118. [PubMed: 21257344]

17. Matthews KA, Hall M, Dahl RE. Sleep in healthy black and white adolescents. Pediatrics. 2014; 133:e1196.

18. Moore M, Kirchner HL, Drotar D, et al. Correlates of adolescent sleep time and variability in sleep time: The role of individual and health related characteristics. Sleep Med. 2011; 12:239–245. [PubMed: 21316300]

19. Roberts RE, Roberts CR, Chan W. Ethnic differences in symptoms of insomnia among adolescents. Sleep. 2006; 29:359. [PubMed: 16553022]

20. Daniel LC, Grant M, Kothare SV, et al. Sleep patterns in pediatric sickle cell disease. Pediatric blood & cancer. 2010; 55:501–507. [PubMed: 20658622]

21. Micic G, Lovato N, Gradisar M, et al. The etiology of delayed sleep phase disorder. Sleep medicine reviews. 2016; 27:29–38. [PubMed: 26434674]

22. Zhang J, Chan NY, Lam SP, et al. Emergence of sex differences in insomnia in adolescents: A large-scale school-based study. Sleep. 2016; 39(8):1563–1570. [PubMed: 27091537]

23. Barden E, Kawchek DA, Ohene-Frempong K, et al. Body composition in children with sickle cell disease. The American Journal of Clinical Nutrition. 2002; 76:218–225. [PubMed: 12081838]

24. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: Methodology and results summary. 2015

25. Platt OS, Thorington BD, Brambilla DJ, et al. Pain in sickle cell disease. Rates and risk factors. N Engl J Med. 1991; 325:11–16. [PubMed: 1710777]

26. Rogers VE, Lewin DS, Winnie GB, et al. Polysomnographic characteristics of a referred sample of children with sickle cell disease. J Clin Sleep Med. 2010; 6(4):374–381. [PubMed: 20726287]

27. Charache S, Terrin ML, Moore RD, et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. Inversigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. N Engl J Med. 1995; 332(20):1317–1322. [PubMed: 7715639]

28. Green NS, Barral S. Emerging science of hydroxyurea therapy for pediatric sickle cell disease. Pediatr Res. 2014; 75(1–2):196–204. [PubMed: 24252885]

29. Narang I, Kadmon G, Lai D, et al. Higher nocturnal and awake oxygen saturations in children with sickle cell disease receiving hydroxyurea therapy. Ann Am Thorac Soc. 2015; 12(7):1044–1049. [PubMed: 25970812]

30. Gil KM, Williams DA, Thompson RJ Jr, et al. Sickle cell disease in children and adolescents: The relation of child and parent pain coping strategies to adjustment. J Pediatr Psychol. 1991; 16(5): 643–663. [PubMed: 1744811]

31. Gil KM, Carson JW, Porter LS, et al. Daily stress and mood and their association with pain, health-care use, and school activity in adolescents with sickle cell disease. J Pediatr Psychol. 2003; 28(5): 363–373. [PubMed: 12808013]

32. Sufrinko AM, Valrie CR, Lanzo L, et al. Empirical validation of a short version of the Adolescent Sleep-Wake Scale using a sample of ethnically diverse adolescents from an economically disadvantage community. Sleep Med. 2015; 16:1204–1206. [PubMed: 26429746]

33. Carskadon MA, Acebo C. A self-administered rating scale for pubertal development. J Adolesc Health. 1993; 14(3):190–195. [PubMed: 8323929]

34. Wolfson AR, Carskadon MA, Acebo C, et al. Evidence for the validity of a sleep habits survey for adolescents. Sleep. 2003; 26:213–216. [PubMed: 12683482]

35. LeBourgeois MK, Giannotti F, Cortesi F, et al. The relationship between reported sleep quality and sleep hygiene in Italian and American adolescents. Pediatrics. 2005; 115:257–265. [PubMed: 15866860]

36. Lewandowski AS, Toliver-Sokol M, Palermo TM. Evidence-Based Review of Subjective Pediatric Sleep Measures. Journal of Pediatric Psychology. 2011; 36:780–793. [PubMed: 21227912]

37. Baum KF, Dunn DT, Maude GH, et al. The painful crisis of homozygous sickle cell disease. A study of the risk factors. Archives of internal medicine. 1987; 147:1231–1234. [PubMed: 3606281]

38. Ohene-Frempong K, Weiner SJ, Sleeper LA, et al. Cerebrovascular accidents in sickle cell disease: rates and risk factors. Blood. 1998; 91(1):288–294. [PubMed: 9414296]

39. Mims KN, Kirsch D. Sleep and Stroke. Sleep Medicine Clinics. 2016; 11:39–51. [PubMed: 26972032]

40. Spielman AJ, Glovinsky PB. The varied nature of insomnia. Case studies in insomnia. 1991:1–15.

41. Mouthon A, Huber R. Methods in Pediatric Sleep Research and Sleep Medicine. Neuropediatrics. 2015; 46:159–170. [PubMed: 25961599]

42. Pockett C, Kirk V. Periodic limb movements in sleep and attention deficit hyperactivity disorder: Are they related? Paediatrics & child health. 2006; 11:355–358. [PubMed: 19030304]

43. Roland P, Rosenfeld R, Brooks L, et al. Clinical Practice Guideline: Polysomnography for Sleep-Disordered Breathing Prior to Tonsillectomy in Children. Otolaryngology–Head and Neck Surgery. 2011; 145:S15.

44. Rogers VE, Gallagher PR, Marcus CL, et al. Capturing PLMS and their variability in children with sickle cell disease: Does ankle activity monitoring measure up to polysomnography? Sleep Med. 2012; 13:1013–1020. [PubMed: 22841030]

45. Ballas SK. Current issues in sickle cell pain and its management. Hematology/the Education Program of the American Society of Hematology. American Society of Hematology. Education Program. 2007; 2007:97–105.

46. Chaturvedi S, DeBaun MR. Evolution of sickle cell disease from a life-threatening disease of children to a chronic disease of adults: The last 40 years. American Journal of Hematology. 2016; 91:5–14. [PubMed: 26547630]

TABLE 1

Sleep Differences between Black Adolescents with and without SCD

	Black Adolescents with SCD (N = 53)		Healthy Black Adolescents (N = 160)		
	M	*SD*	*M*	*SD*	*t*
Weekday Sleep Duration (hrs)	8.21	1.64	7.06	1.51	−4.66 **
Weekend Sleep Duration (hrs)	9.44	2.18	6.97	2.95	−6.41 **
Total Sleep Quality	3.70	0.55	4.05	0.68	3.39 **
Bed	3.51	0.80	3.80	0.98	1.99 *
Falling Asleep	3.77	0.71	4.13	0.89	2.63 **
Maintaining Sleep	3.88	0.93	4.34	1.02	2.91 **
Reinitiating Sleep	4.50	0.96	4.81	0.79	2.32 *
Waking	2.86	0.96	3.17	1.16	1.79

**
p < .01,

*
p < .05

Author Manuscript   Author Manuscript   Author Manuscript   Author Manuscript

TABLE 2

Regression Models Predicting Sleep using the Combined Sample of Black Adolescents with and without SCD

	Weekday Sleep Durations ($n = 206$)			Weekend Sleep Durations ($n = 202$)			Total Sleep Quality ($n = 210$)		
	F		Adjusted R^2	F		Adjusted R^2	F		Adjusted R^2
	8.71[**]		.10	12.10[**]		.14	4.52[**]		.05
	β	t	Partial R^2	β	t	Partial R^2	β	t	Partial R^2
Age	−0.16	−1.99[*]	.02	0.09	1.40	.01	0.03	0.48	.00
Sex	−0.04	−0.65	.00	0.14	2.08[*]	.02	−0.12	−1.77	.01
SCD Status	0.20	4.30[**]	.08	0.38	5.68[**]	.14	−.20	−2.96[**]	.04

[**] p < .01,

[*] p < .05