Objective To investigate the pain-sleep relationship in children with sickle cell disease (SCD) and the influence of stress and pain medication use on this relationship. Method Children with SCD (n = 20; aged 8–12 years) completed daily diaries assessing sleep, pain, stress, and pain medication use for up to 2 months. Data analyzed using multilevel modeling. Results High daily pain was related to poor sleep quality that night and poor sleep quality was related to high pain the following day. High stress was related to less sleep. High same-day pain and pain medication attenuated the impact of pain on sleep quality. Conclusion Results highlight the importance of sleep in addressing functioning in children with chronic pain, knowledge which may help patients and their families better manage the child’s pain. Behavioral pain interventions may be improved by the inclusion of strategies to encourage proper sleep hygiene and address sleep issues.

Key words children; diary; pain; sickle cell disease; sleep.

Sickle cell disease (SCD) is a family of genetic blood disorders characterized by frequent pain episodes (Shapiro et al., 1995). Several studies have reported a high prevalence of sleep disordered breathing in children with SCD (Samuels, Stebbens, Davies, Picton-Jones, & Southall, 1992) and have linked sleep disordered breathing to increased pain, central nervous system events, such as stroke, and decreased cognitive functioning through nocturnal hypoxia (Kirkham & Datta, 2006; Setty, Stuart, Dampier, Brodecki, & Allen, 2003). Notably, there have been few studies of other sleep problems in children with SCD and their possible link to disease symptoms (Jacob et al., 2006; Shapiro et al., 1995; Valrie, Gil, Redding-Lallinger, & Daeschner, in press). Findings from these studies suggest that SCD pain is negatively related to sleep quality and sleep duration in children and adolescents. However, the research is primarily descriptive in nature.

In our prior study (Valrie et al., in press), 24 children and their parents completed baseline assessments of the children’s sleep, pain, and stress and then, the children completed daily diaries of their sleep, pain, stress, and pain medication use for up to 8 weeks. Baseline reports of higher pain severity were related to baseline reports of poorer sleep quality. The strength of this negative relationship was exacerbated by high stress. Children’s baseline reports were also fairly consistent with their own daily diary reports and their parents’ baseline reports, providing support for the reliability and validity of the diaries.

In the current study, we used the diary data to examine temporal patterns of sleep and pain and to investigate the influence of daily stress and pain medication use on the pain-sleep relationship. We hypothesized that high daily pain during the day would be related to poorer sleep quality and shorter sleep duration during the night. We also tested the alternate relationship that poor sleep quality and less sleep during the night would be related to higher pain the next day. Finally, we hypothesized that the magnitude of the negative pain-sleep relationships would be amplified at increasing levels of stress and attenuated by the children’s pain medication use.

Method Participants

Participants and their guardians were recruited during regularly scheduled appointments from two outpatient university clinics located in the Southeast. A health care provider screened all potential participants for medical
contraindications (e.g., neurological impairment that would lead to difficulties completing the diaries, co-morbid medical conditions unrelated to SCD). Only children who had at least one pain episode (pain attributed to SCD by the children that lasted at least 20 min) in the past year were eligible. Pain episode information was obtained from the children’s medical file or the children or their guardians’ response to a screening question. The sample consisted of 20 children with SCD (13 girls and 7 boys) aged 8–12 years (M = 10.1 years, SD = 1.07 years) who completed a minimum of seven daily diaries following a baseline assessment (Valrie et al., in press). The mean level of maternal education was 12.7 years (SD = 2.10 years, range = 7.5–16 years). Of the 20 children, 14 (70%) had sickle cell anemia, 5 (25%) had sickle thalassemia, and 1 (5%) had sickle thalassemia.

**Procedures**

The Institutional Review Boards at the respective universities approved the procedures. Notably, the guardians were shown the diaries, informed of the procedure, and asked to assist their children with the process if needed. The current study adopted Butz and Alexander’s (1991) recommendations for conducting diary studies with 7–12-year old children with a chronic illness. The diary was made to be appropriate for the children’s reading level, the study period was limited to 8 weeks to minimize fatigue, and we used reward to enhance completion rates.

**Daily Diary of Sleep, Pain, Stress, and Pain Medication Use**

Sleep

The following sleep items were based on a diary used with children with juvenile rheumatoid arthritis (JRD) (Schanberg et al., 2000). To assess sleep quality, children were asked to rate on a 100 mm horizontal visual analogue scale (VAS), ranging from “did not sleep well” (0 mm) to “slept very well” (100 mm), how well they slept the night before. “Slept very well” indicated that the children felt well rested and refreshed after the night of sleep and “Did not sleep well” indicated that the children did not. To assess sleep duration, children were asked to report what time they went to sleep the night before and what time they woke up. Children were asked to complete the sleep section after awakening in the morning and the remainder of the sections before going to bed.

Pain

Children were asked to report whether they experienced any SCD pain during the day, and then to rate the average level of their pain by placing a vertical mark on a 100 mm horizontal VAS with ratings ranging from “hurting a whole lot” (0 mm) to “not hurting at all” (100 mm). Research (Gil et al., 2000; 2003) has provided support for the reliability and validity of the VAS in assessing SCD pain in children and adolescents.

**Stress**

Stress was assessed by the Daily Events Inventory (Schanberg et al., 2000). The measure consisted of 17 negative daily events, such as “argued with parents” and “was made fun of”. The daily event total was calculated by summing the number of negative daily events endorsed by the children. The scale was found to have satisfactory internal reliability (r = .70) and was predictive of daily fatigue, stiffess, and cutting back on activities in children with juvenile rheumatoid arthritis (Schanberg et al., 2000).

**Pain Medication Use**

Children were asked an open-ended question: “What medications did you take today?” Responses were coded as either nonopioid analgesics, herein referred to as analgesics, or opioid analgesics using Medline Plus <http://medlineplus.gov>, a service of the US National Library of Medicine and the National Institutes of Health. Previous studies have reported valid results when utilizing similar strategies to assess daily medication use in children and adolescents with SCD (Dampier, Ely, Brodecki, & O’Neal, 2002; Gil et al., 2000).

**Results**

**Diary Completion and Descriptive Diary Information**

The children completed a total of 712 days out of a possible 1120 days (20 children × 7 days per week for 8 weeks), representing a completion rate of 64%. On average, children completed 36 diary days (SD = 19) with a range 7–56 days. Also, t-tests and chi-squares were calculated to compare the baseline characteristics of diary completers (n = 20) and noncompleters (n = 4). Both groups were similar except that completers were significantly more likely to be female (x^2 = 5.67, p = .02). This is qualified by the fact that all of the diary noncompleters were boys. The 7 boys in the study completed 277 diaries (M = 40 diaries, SD = 21) and the 13 girls completed 435 diaries (M = 33 diaries, SD = 19). Gender was not significantly related to number of diaries completed (r = -.15, p > .05). Also, gender was entered as a covariate in all of the multilevel models and did not
significantly predict sleep quality, sleep duration, or pain severity. Pearson product correlations were calculated to examine what baseline characteristics were related to completing more diaries. Number of diaries was positively related to the likelihood that children had used opioids to manage their pain prior to the study ($r = .53, p = .02$).

Across all diaries, the average sleep quality rating was 84.41 (SD = 25.91, range = 0–100) and mean sleep duration was 8.8 h per night (SD = 1.66 h, range = 2–17 h). Sixteen of the 20 children experienced pain during the course of the study with pain reported on 22.24% of total diary days; however, pain medication was taken on 25.91% of pain days when using the sub-sample of children who took medication. For this sub-sample, pain medication use was only reported on 9.20% of total diary days; however, pain medication was taken on 71.05% of pain days when using the sub-sample of children who took medication. Six children reported taking no medication, seven children reported taking an analgesic, and four children reported taking an opioid. Pain medication use was only reported on 9.20% of total diary days; however, pain medication was taken on 71.05% of pain days when using the sub-sample of children who took medication. For this sub-sample, analgesics were used on 26.31% of pain days, opioids were used on 55.26% of pain days, and a combination of analgesics and opioids were used on 10.53% of pain days.

### Multilevel Random Effects Models Predicting Sleep Duration, Sleep Quality, and Pain Severity

High pain severity ($\beta = -3.72, p < .01$), high analgesic use ($\beta = -6.96, p < .01$) and high opioid use ($\beta = -6.02, p = .03$) were inversely related to sleep quality at night (Table I). In addition, the interaction between pain severity and analgesic use ($\beta = 2.81, p = .02$) was related to sleep quality, indicating that the relationship between pain severity and sleep quality was influenced by analgesic use. The online interactive calculator for probing interactions developed by Preacher, Curran, and Bauer (in press) was used to statistically examine the relationship between pain severity and sleep quality when children took analgesic medication and when children did not. The calculator estimated simple slopes displaying the pain-sleep quality relationship given children’s analgesic medication use. When an analgesic was not taken, the simple slope was $-5.98$ ($z = -5.09, p < .04$), indicating that high pain was related to lower sleep quality. In contrast, when an analgesic was taken, the simple slope was $.20$ ($z = .05, p = .96$), indicating that the relationship between pain severity and sleep quality was attenuated by taking an analgesic. Regarding sleep duration, high stress during the day was related to less sleep that night ($\beta = -3.72, p < .01$) was inversely related to high SCD pain the next day. Perhaps poor sleep

### Table I. Multilevel Random Effects Analyses Predicting Sleep Quality, Sleep Duration, and Pain Severity

<table>
<thead>
<tr>
<th></th>
<th>Sleep quality (N = 561)</th>
<th>Sleep duration (N = 540)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>$t$</td>
</tr>
<tr>
<td>Pain</td>
<td>$-3.72$</td>
<td>$-2.91^{**}$</td>
</tr>
<tr>
<td>Stress</td>
<td>$0.53$</td>
<td>$0.53$</td>
</tr>
<tr>
<td>Pain*stress</td>
<td>$-0.32$</td>
<td>$0.26$</td>
</tr>
<tr>
<td>Analgesic use</td>
<td>$-6.96$</td>
<td>$-2.59^{**}$</td>
</tr>
<tr>
<td>Pain*analgesic use</td>
<td>$2.81$</td>
<td>$2.29^*$</td>
</tr>
<tr>
<td>Opioid use</td>
<td>$-6.02$</td>
<td>$-2.24^*$</td>
</tr>
<tr>
<td>Pain*opioid use</td>
<td>$0.14$</td>
<td>$0.16$</td>
</tr>
</tbody>
</table>

Note: Level 2 covariates in each model consisted of age, gender, level of maternal education, SCD type, and aggregated person-means for the independent diary variables used in the models. The level 1 covariate of week day vs. weekend day was predictive of sleep duration and was included in the final multilevel model predicting sleep duration. Results indicate that children sleep longer on the weekend than during the week ($\beta = 0.35, t = 2.49, p = .01$).

*p < .05, **p < .01.

### Discussion

High daily pain was related to poor sleep quality during the night, a finding consistent with previous studies (Jacob et al., 2006; Shapiro et al., 1995; Valrie et al., in press). Pain may interfere with sleep at night, because the pain persists and causes discomfort, or because pain might disrupt underlying sleep mechanisms (Onen, Onen, Courpon, & Dubray, 2005). Findings also indicated that poor sleep quality during the night was related to high SCD pain the next day. Perhaps poor sleep,
quality during the night lowers children’s pain threshold (Onen et al., 2005). Another possibility is that poor sleep may be an indicator of biological factors related to the onset of a pain episode, such as level of oxygen in the blood. Taken together, these results support the hypothesis that there is a cyclic relationship between pain and sleep.

Stress did not evidence a moderating influence on the pain-sleep relationship, but instead evidenced a more direct influence on SCD pain and sleep. These findings are consistent with the majority of research that shows that stress is related to shorter sleep duration (Sadeh, 1996). In addition, the finding that high stress is related to high same-day pain in younger children with SCD is consistent with research examining this relationship in adolescents with SCD (Gil et al., 2003). As for pain medication use, results do support the hypothesis that pain medication had an attenuating effect on the impact of pain on sleep. Specifically, when children took an analgesic, pain was no longer predictive of sleep quality. However, taking an analgesic or an opioid was related to poor sleep quality that night regardless of pain severity. Also, inconsistent with past research (Onen et al., 2005) pain medication use was not related to sleep duration. This finding may be due to the fact that the current study was only assessing sleep during the night. Possibly children were taking naps during the day in response to the sedative effects of taking a pain medication.

Limitations of the present study include that all of the measures were self-report and actual completion time of the diaries could not be verified. Also, the range of sleep information was limited by the children’s awareness of their sleep and may have been biased by other factors, such children’s previous sleep experiences or their overall views of their sleep (Sadeh, 1996). Future research should incorporate more objective, time-sensitive measurement approaches, such as the use of sleep actigraphy. More objective measures would allow researchers to attain more accurate measures of total sleep time by taking into account the number and length of wakening periods during the night. Another limitation is the small sample size and the restricted age range, which may make it difficult to generalize these results to the general population of children with SCD. However, research by Curran and Muthén (1999) does indicate that a large number of repeated measures per participant compensates for having a smaller sample size. In our study, the focus was to examine the relation between factors at the daily observation level within individuals versus the group level, thus the small sample size is offset by the large number of observations. Moreover, the sample size is comparable to other published diary studies (Gil et al., 2000; 2003).

In conclusion, the current study highlights that sleep plays an important role in the functioning of children who experience illness-related pain. Future research needs to examine the connection between poor sleep quality and other important factors, such as nocturnal hypoxia, and sleep disordered breathing (Setty et al., 2003). Also, future research should take a careful look at how health care use is related to sleep in children with SCD. Specifically, it should distinguish between “weak” and “strong” opioids and between pain medications administered at home versus those administered in a health care setting. The current study may have underestimated the impact of pain medication use on sleep in this population due to the use of more potent medications during acute situations faced in hospital settings. Also, pain management strategies beyond pain medication use should be examined. Results from the current study indicated that not all children who experience pain use pain medication. It is important to make sure that those children are able to manage their pain effectively and also to supplement pain medication use with alternative strategies to reduce the negative impact of pain medication use on sleep. Lastly, research on sleep could help by promoting good sleep hygiene among children who experience illness-related pain, and possibly improve behavioral pain interventions (Gil et al., 2001) by encouraging the inclusion of strategies to promote proper sleep hygiene.

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