Daily Pain and Sleep in Children with Sickle Cell Disease:
An Analysis of Daily Diaries Utilizing Multilevel Models

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ABSTRACT

Cecelia R. Valrie: Daily Pain and Sleep in Children with Sickle Cell Disease:
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(Under the direction of Karen M. Gil, Ph.D.)

This study investigated the temporal relationship between pain and sleep in children with sickle cell disease (SCD) and examined the influence of additional stressors and pain medication practices on this relationship. To accomplish the goals of the study, 20 children with SCD aged 8 to 12 years of age completed daily diaries for approximately 5 weeks. These diaries were analyzed using multilevel models. Results were consistent with the hypothesis that there is a cyclic relationship between high SCD pain and poor sleep. Specifically, high levels of daily SCD pain were significantly related to poor sleep quality that night. Also, poor sleep quality during the night was significantly related to high SCD pain that day. Poor sleep quality appeared to be the stronger predictor in the pain-sleep cycle. Additional stressors and pain medication use did not evidence a substantial impact on the relationship between SCD pain and sleep, but instead evidenced more direct influences on SCD pain and sleep aspects. Clinical and policy implications include the possible benefits of raising awareness among clinicians, policymakers, patients, and their parents about the interaction between the child's symptoms and sleep patterns. Additional research should study how other disease symptoms may influence sleep and how sleep may influence other disease symptoms. In addition, this research should examine the role of disease management strategies implemented by the child and his/her family on these relationships.

ACKNOWLEDGEMENTS

TABLE OF CONTENTS

LIST OF TABLES

TABLE OF FIGURES

CHAPTER 1

INTRODUCTION

Sleep is seen as a core component of preventive health that is commonly ignored both clinically and in relation to research on health issues (Dement, 2002; National Center on Sleep Disorders Research [NCSDR], 2003). Theories concerning the functions of sleep fall into three basic categories: restorative, behavioral, and mental functions. The restorative theories are based on the notion that sleep's primary purpose is to rejuvenate the mind and body, though there is some controversy concerning what portions of the body are being renewed or how this process is accomplished (Adam & Oswald, 1977; Hobson, 1988; Horne, 1983a, 1988). The behavioral theories of sleep, which are largely based on evolutionary theory, view sleep as a way of saving energy and avoiding threat to life through "adaptive non-responding" during parts of the day when food is not readily available (Meddis, 1975; Moorcroft, 1993; Webb, 1983). In contrast, mental theories of sleep promote sleep as a time when new learning is solidified into memory (McGaugh, Jenson, & Martinez, 1979) and a time when one's mood can be regulated after dealing with the stress of the day (Horne, 1983b; Kramer, 1993).

In children and adolescents, poor sleep patterns have been found to be associated with deficits in neurobehavioral functioning, poor academic performance, daytime sleepiness, depressed mood, and behavior problems (Levy, Gray-Donald, Leech, Zvagulis, & Pless, 1986; National Sleep Foundation, 2000; Sadeh, Gruber, & Raviv, 2003; Kirmil-Gray, Eagleston, Gibson, & Thoresen, 1984; Smedje, Broman, & Hetta, 2001; Vignau et al., 1997;

Wolfson & Carskadon, 1998). Research also indicates that children and adolescents with a chronic illness are at increased risk for poor sleep (NCSDR, 2003). However, research still needs to be done to investigate the mechanisms that might explain this association. In addition, exploring the relationship between chronic illness and poor sleep patterns might be useful in explaining the process by which chronic illness leads to increased risk of behavioral, emotional, school, and social adjustment problems in children and adolescents (Barbarin, 1990; Boekaerts & Roder, 1999; Thompson & Gustafson, 1996). Research needs to be done to explore whether poor sleep habits are contributing to or exacerbating the existing medical symptoms of individuals with a chronic illness (NCSDR, 2003).

The current study is designed to examine the relationship between daily pain, a disease symptom strongly associated with sickle cell disease (SCD), and daily sleep patterns of children with SCD. Specifically, the study is investigating the impact of daily pain on daily sleep and the impact of daily sleep on daily pain in this population. In addition, the current study is focused on exploring the influence of factors associated with the experience and management of SCD pain, stress and pain medication use, on the relationship between pain and sleep in children with SCD.

Overview of SCD

SCD is a family of genetic blood disorders affecting approximately 1 in 600 African Americans (Steinberg, 1999). It is characterized by the overabundance of sickle hemoglobin in red blood cells (Bunn, 1997; Steinberg, 1999). When red blood cells deoxygenate, the sickle hemoglobin in the cells polymerize or aggregate into large polymers, which causes the cells to convert from their normal round, "donut" shape to a crescent or "sickle" shape. Cells temporarily return to their former shapes when they are re-oxygenated in the lungs, but as the

2

cells continuously go through the cycle of oxygenation, they begin to maintain their sickle shapes and are irrecoverably damaged (Sickle Cell Disease Guideline Panel, 1993). These new sickle-shaped cells are sticky, brittle, and have shorter life spans than normal red blood cells. This leads to anemia, the body's inability to supply a sufficient amount of oxygen to various organs, and vaso-occlusion, blockages in small and large blood vessels, which occur because of the tendency for sickle cells to attach to arterial walls (Steinberg, 1999). It also leads to a number of other acute and chronic health problems such as strokes, leg ulcers, and kidney dysfunction.

The severity of SCD symptoms varies greatly from patient to patient (Steinberg, 1999). This variability is best typified by the most prevalent complication associated with SCD, pain due to tissue damage. Severe pain episodes, characterized as unanticipated and intense pain periods ranging from hours to weeks, usually occur a few times a year during childhood and adolescence (Shapiro et al, 1995). Onset of these episodes can occur as early as 6 months, though some individuals never experience SCD pain throughout their lifetime (Dampier & Shapiro, 2003). The likelihood of experiencing a SCD pain episode increases with age, with approximately 54% of children with SCD between the ages of 0 and 9 years and 67% between the ages of 10 and 19 years experiencing SCD pain. Also, the severities of pain episodes, which can range from mild to severe, vary greatly even within individuals across their lifetime. However, usually when pain occurs often during early or middle childhood, the same or greater frequencies and severities are seen throughout the adolescent and adult years (Baum, Dunn, Maude, & Serjeant, 1987; Platt et al., 1991).

Since pain is the most salient complication of SCD, most researchers have chosen to focus on factors related to pain such as intensity, duration, and the number of pain episodes

during a given year as a meaningful index of disease severity. SCD pain in children and adolescents has been examined as it relates to health care use, school related outcomes, social outcomes, and, to a lesser extent, sleep (Fuggle, Shand, Gill, & Davies, 1996; Gil et al., 2000; Shapiro et al., 1995).

<u>Aspects of Sleep</u>

To appreciate the potential impact that pain can have on sleep and that sleep can have on pain in children with SCD, it is first useful to understand the context of typical sleep patterns and disruptions. Sleep is primary regulated by two unique physiological systems: the sleep-wake homeostatic system and the circadian timing system (Mindell, Owens, & Carskadon, 1999). The sleep-wake homeostatic system determines the depth and duration of sleep as a function of prior sleep patterns. It tries to ensure that an individual experiences a baseline level of sleep duration and rapid-eye movement (REM) sleep by creating a "rebound" effect (Carskadon, 2002). If a person does not experience their baseline level of sleep, the individual's body will try to make up for it during future sleep episodes. In contrast, the circadian timing system provides the structure of sleep, including the timing of sleep and waking (Carskadon, 2002). An individual's baseline level of sleep duration and REM sleep is believed to be set by the circadian timing system. Notably, there are developmental changes in an individual's circadian timing system over time as evidenced by the systemic changes in optimal sleep duration over the life span and the percentage of sleep that is REM sleep versus non-REM sleep over the life span (Carskadon, 2002; Mindell et al., 1999). Disruptions in either of these regulatory systems appears to hinder the functions of sleep, possibly leading to the multitude of negative outcomes associated with poor sleep patterns. The three aspects of sleep examined in the present study are sleep duration, sleep

irregularity, and sleep quality. Possibly these aspects of sleep are linked to negative outcomes because changes in these aspects disrupt the core regulatory systems.

An individual's optimal sleep duration is defined as the sleep duration that would produce "optimal daytime performance with minimal sleepiness" (NCSDR, 2003). Failure to meet that optimal sleep duration leads to difficulties in functioning. Decreases in sleep duration have been connected to daytime sleepiness, mood problems, and detriments in school performance and the ability to learn in children and adolescents (Carskadon, 1990; Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001; Fredriksen, Rhodes, Reddy, & Way, 2004; Taras & Potts-Datema, 2005). In addition, sleep restriction has been associated with behavior problems, vulnerability to accidents and drugs, and disorders related to the sleep/wake behaviors in adolescents (Carskadon, 1990). Notably, research indicates that even a difference of an hour in sleep duration can lead to significant effects on daytime sleepiness and neurobehavioral functioning in school-age children (Sadeh et al., 2003). Also, results from Fredriksen et al.'s (2004) study, which followed 2259 children from grade 6 to grade 8, indicated that children who experienced less sleep over time reported heightened depressive symptoms and low self-esteem.

As for sleep regularity, research has shown that keeping the sleep/wake times consistent, even if they are not the circadian set sleep/wake times, can still lead to optimal functioning. Theorists have speculated that regulating the sleep/wake cycle into an organized and stable process is connected to the development of the central nervous system and the brain's inhibitory and control systems, thus making stability of sleep/wake times the important issue (see Gruber, Sadeh, & Raviv, 2000). In addition, though sleep irregularity is linked to sleep duration (e.g., sleep restriction and the subsequent "rebound effect" due to

less than optimal sleep duration can lead to sleep irregularity), the influence of sleep irregularity has been consistently found to impact functioning over and above the effects of sleep duration (Acebo & Carskadon, 2002; Bates, Viken, Alexander, Beyers, & Stockton, 2002; Billard, Alperovitch, Perot, & Jammes, 1987).

Sleep irregularity has been related to deficits in school performance, daytime sleepiness, depressed mood in girls, sleep/wake behavior problems and utilization of sleeping pills in adolescents (Billard et al., 1987; Giannotti & Cortesi, 2002; Manber, Bootzin, Acebo, & Carskadon, 1996; Strauch & Meier, 1988; Wolfson & Carskadon, 1998). In addition, research in infants has indicated that greater variability in sleep/wake patterns is a risk factor for later behavioral and developmental difficulties (Thoman, 1990; Thoman, Deneberg, Sievel, Zeidner, & Becker, 1981; Tynan, 1986). As for research on pre-pubescent children, results from Acebo and Carskadon's (1993) study utilizing 5th graders indicated that sleep irregularity is negatively related to teacher reported school functioning. Also, sleep irregularity has been related to preschool adjustment and behavior problems and appears to be a characteristic of children with ADHD (Bates et al., 2002; Gruber et al., 2000).

Notably, sleep irregularity in the adolescent studies and Acebo and Carskadon's (1993) study was quantified as the difference between week day sleep/wake patterns versus weekend sleep/wake patterns. This quantification is consistent with the research indicating that a discrepancy between week day and weekend sleep/wake patterns develops around the onset of puberty. Also, LaBerge et al.'s (2001) examined the sleep patterns of 1,146 children aged 10 to 13 years in relation to their pubertal status, ranging from prepubertal to late pubertal. They found that on average their sample delayed their weekend sleep onset by

about one hour and that the difference between the week day and weekend sleep onset times increased as pubertal status increased. Only two studies examining children, Gruber et al.'s (2000) study and Bates and associates' (2002) study examining sleep in pre-pubescent children, have investigated the link between daily sleep irregularity and daytime functioning. Overall, findings indicate a connection between sleep irregularity and negative functioning. However, more research needs to be done, specifically examining the influence of daily sleep irregularity and sleep irregularity in pre-pubescent children.

There are numerous ways of quantifying sleep quality (Knab & Engel-Sittenfeld, 1983). For the current study, sleep quality is viewed as the subjective component of sleep and is characterized by how the individual felt about his/her night of sleep (Hartmann, 1971). Thus, quality is defined by how the individual would characterize the night of sleep (good or poor) and how rested and relaxed the individual felt upon awaking. Quantification of this subjective evaluation of sleep quality is commonly done by asking individual's to rate the quality of their sleep or how well rested they felt, sometimes with them responding on a visual analogue scale (Knab & Engel-Sittenfeld 1983). Sleep quality characterized in this way has been related to sleep continuity, depth of sleep, and sleep efficiency, which is the percent of time the child actually sleeps between the first time they go to sleep and the last time they awaken before getting up from bed (Akerstedt, Hume, Minors, & Waterhouse, 1994; Tikotzky & Sadeh, 2001; Zammit, 1988). Notably, reports are mixed regarding whether sleep quality is related to sleep duration, with some results indicating that ratings of poor sleep quality are related to shorter sleep durations (Alapin et al., 2000; Hartmann, 1971; Levy, et al., 1986) and some results indicating that ratings of sleep quality are not related to sleep duration (Meijer, Habekothe, & van den Wittenboer, 2000; Meijer & van den

7

Wittenboer, 2004; Totterdell, Reynolds, Parkinson, & Briner, 1994). However, research does consistently indicate that high sleep efficiency, a factor strongly related to sleep quality ratings, is related to shorter sleep durations (Meijer & van den Wittenboer, 2004; Sadeh et al., 2003; Tikotzky & Sadeh, 2001).

In relation to functioning, poor sleep quality has been related to mood dis-regulation factors, such as symptoms of anxiety, depression, and irritability, in children and adolescents (Kirmil-Gray et al., 1984; Manni et al., 1997; Meijer & van den Wittenboer, 2004). In addition, sleep quality appears to be indirectly related to school performance through symptoms of anxiety (Meijer & van den Wittenboer, 2004), and research indicates that poor sleep efficiency is related to lower achievement motivation and working memory (Meijer et al., 2000; Steenari et al., 2003). Lastly, poor sleep, as characterized by high sleep fragmentation and low sleep efficiency, is related to behavior and thought disorder problems, lower executive control, and difficulties with sustained attention and behavioral inhibition (Sadeh et al., 2003).

Developmental considerations associated with sleep. As mentioned earlier, sleep patterns undergo systematic changes over the lifespan. The most notable changes in sleep patterns occur during the birth to young adult years. There is a high incidence of sleep problems during infancy, ranging from sudden infant death syndrome to sleep continuity problems (Lin-Dyken & Dyken, 1996). In contrast, the sleep patterns experienced during childhood, the time between infancy and the onset of puberty, are considered to be the "gold standard of sleep quality" (Dement, 2002; Lin-Dyken & Dyken, 1996). This is due to a number of factors, such as the low incidence of sleep disorders during this time, and the low level of daytime sleepiness experienced by this population. Thus, sleep duration and sleep

patterns are fairly regular, and ratings of sleep quality are generally "good". However, adolescence is found to be a time of high sleep deprivation, irregular sleep patterns, and daytime sleepiness associated with social, school-related, and biological changes (Carskadon, 2002; National Sleep Foundation, 2000). For example, recent research and theory into the role of physical maturation on sleep processes suggests that puberty may influence both the sleep-wake homeostatic system and the circadian timing system in such a way as to promote less sleep and more irregular sleep onset times (Carskadon, 2002). Thus, taking into account pubertal stage is advocated as an essential part of research on sleep processes in children. Given the relative high quality of sleep during the childhood years and the absence of the numerous psychosocial factors associated with adolescence, it may be easier to distinguish the disruptive influence of specific factors on sleep patterns during this time period. The current study examines children during the childhood period in the age range of 8 to 12 years.

Lastly, though optimal sleep duration has been investigated in adolescent and adult populations, systematic research is still needed to determine the range of optimal sleep duration during the early childhood years (NCSDR, 2003). Research has shown that though there is individual variation in the amount individuals generally sleep during the night, individuals appear to share similar optimal sleep durations. Research has also shown that children between the ages of 5 to 12 years generally sleep between 8 and 11 hours per night with individual variability displayed, primarily due to age, circadian rhythm, and environment (Lin-Dyken & Dyken, 1996; NCSDR, 2003; Sheldon, 2002). In one of the few studies examining sleep patterns in young children (Fisher, Pauley, and McGuire, 1989), questionnaires were administered to parents of 870 children, ranging from grades 1 to 6,

assessing sleep-related behaviors in their children. For children between 8.5 and 11.5 years of age, 62.1% of the boys and 60% of the girls were reported to have slept an average of 8-9 hours per night. Also, 35% of the boys and 38.2% of the girls were reported to have slept an average of 10-11 hours per night. As age increased the total amount of sleep decreased.

The Influence of SCD Pain on Sleep

An examination of the literature on sleep in populations experiencing pain indicates that pain and poor sleep patterns are closely related. Onen, Onen, Courpron, and Dubray (2005) reviewed literature investigating the link between pain and sleep in a number of different pain populations, including individuals experiencing postoperative pain, burns, coronary heart disease, rheumatic diseases, cancer, headache, and chronic pain without any identified physical cause. Findings from these studies indicated that pain is associated with sleep loss, sleep disturbance (e.g., changes in the distribution of REM sleep), decreased sleep efficiency, and fragmented sleep. Some of the mechanisms proposed to account for the relationship between pain and poor sleep patterns in these populations included the experience of pain episodes during the night, the disturbance of underlying sleep mechanisms by the condition causing the pain, and the impact of pain medication taken to combat the pain experience. Another issue emphasized in the review was the cyclical nature of the relationship. That is, not only does pain impact sleep patterns, but sleep patterns impact the pain experience. Poor sleep patterns appear to make one vulnerable to the pain experience by lowering one's pain threshold (Onen et al., 2005). Thus, poor sleep patterns could possibly exacerbate the individual's existing pain condition. However, more research is needed to fully investigate the impact of sleep on pain as well as the proposed cyclic relationship between pain and sleep in children and adults. In addition, most of the research in this area is

10

with adults. So, more research needs to be done examining these relationships in children and adolescents.

As for children and adolescents with SCD, the majority of studies examining sleep in this population focus on obstructive sleep apnea (a condition were "breathing stops or gets very shallow while sleeping"), which has a prevalence rate of 36% versus the 2% prevalence rate observed in the overall child population (National Heart, Lung, and Blood Institute, 2006; Samuels, Stebbens, Davies, Picton-Jones, & Southall, 1992). There have been relatively few studies that have examined other sleep issues in this population. Barbarin's (1999) study involved interviewing children with SCD and their families. Children, but not adolescents, reported a significantly larger number of sleep problems than a control group matched on race, age, sex, mother's marital status, and socioeconomic status. This result is consistent with the earlier hypothesis that the influences of SCD on sleep patterns may be masked during adolescence due to developmental differences in sleep patterns. Barbarin (1999) also found that both SCD groups reported higher levels of fatigue than did their controls.

Of the remaining studies, three also examined samples consisting of both adolescents and children with SCD. In Walco and Dampier's (1990) study, parents of children and adolescents with SCD were interviewed. About 12% of the parents reported that their child's pain "never or rarely" disturbed their child's sleep, 29% reported that pain "sometimes" disturbed their child's sleep, 29% reported that pain "often" disturbed their child's sleep, and 20% reported that pain "always" disturbed their child's sleep. Shapiro and associates (1995) conducted a diary study of 18 children with SCD aged 8 to 17 years who experienced frequent SCD pain. The children and adolescents completed an average of 264

home-based diaries per child and as part of that diary they were asked whether they had a good or poor night of sleep, as well as whether they experienced SCD-related pain that day. During days participants reported experiencing SCD-related pain, 43% reported poor sleep patterns; whereas, on days participants reported experiencing no pain, only 3% reported poor sleep patterns. Participants also reported sleeping less on nights following a day in which pain occurred. Lastly, Jacob et al. (2006) had 27 children and adolescents with SCD who were hospitalized due to pain complete daily diaries. Findings indicated that the children and adolescents evidenced disruptions in their sleep/wake patterns throughout their stay in the hospital and that pain was positively related to disruptions in these patterns.

The only study to exclusively focus on children examined the relationships between SCD pain, stress, and sleep patterns in 24 children with SCD aged 8 to 12 years (Valrie, Gil, Redding-Lallinger, & Daeschner, 2005). Results indicated that high SCD pain severity is related to poor sleep quality and that as daily stress increased, the negative relationship between high pain severity and poor sleep quality was amplified. In addition, high pain frequency was associated with less sleep, but only when daily stress was low. High daily stress was associated with longer sleep durations. As part of Valrie et al.'s (2005) study, a subset of 20 of the 24 children completed daily diaries assessing SCD pain, stress, and sleep. The data were aggregated for each child. In comparison to the results of the interview data, the models using the aggregated diary data did not support a relationship between pain, stress, and sleep in children with SCD. However, properties of aggregated data may have made it difficult to detect associations among the variables of interest. For example, information concerning the variability in pain, the variability in sleep, and the relationship between the variability in pain to the variability sleep was suppressed by aggregating the

data. Also, the full benefits of utilizing diary data were not realized with this strategy. For example, the investigation of temporal relationships between the variables of interest could not be done when aggregating the data. Lastly, the analysis method used to investigate the diary data was less than optimal.

Overall, these findings suggest that SCD pain is negatively related to sleep quality and sleep duration. However, the research in this area is limited and the influence of sleep patterns on SCD pain has not been explored. Also, results from Valrie et al.'s (2005) study emphasize the need to examine the influence of other factors on the relationship between SCD pain and sleep. The following section discussed two factors, stress and pain medication use, strongly related to the SCD pain experience and that were considered as moderators on the relationship between SCD pain and sleep in the current study.

Possible Moderating Factors

Stress. Stress has been uniquely linked to both sleep and SCD pain. As highlighted in the earlier section, stress is the only factor that has been examined as a possible moderator on the relationship between SCD pain and sleep. Stress refers to the strain caused by "unusual events, change, or threat of change demanding special biobehavioral or psychological adaptive responses by the individual to maintain psychophysiological equilibrium and well-being" (Sadeh, 1996; Sadeh & Gruber, 2002). In addition, a stressor is identified as "the event that triggers the change or the threat" (Sadeh & Gruber, 2002). Within the broader spectrum of assessing stress as it relates to disease, the current study focuses on events and experiences as they are uniformly related to considerable adaptive strain. This perspective is known as the environmental perspective and was seen as the most

appropriate approach for the current study due to the focus in the health literature on stress aspects related to the environmental approach (Cohen, Kessler, & Gordon, 1995).

There are three types of stressors: (1) major changes affecting large numbers of people, such as natural disasters, (2) major changes affecting one or a few people, such as divorce, and (3) daily hassles, which are everyday occurrences that arise from daily living (Lazarus & Cohen, 1977). Since most research studies have found that daily hassles, in contrast to major life events, are more strongly linked to adaptation and health, daily hassles as an indicator of stress has been emphasized in most research (Delongis, Coyne, Dakof, Folkman, & Lazarus, 1982). Research suggests that because major life events may trigger a host of daily hassles, daily hassles may mediate the effects of major life events, particularly in children and adolescents (Sorensen, 1993). For children, the primary daily hassles appear to come from peer interaction, academics, and family interaction, and many of these stressors have far-reaching and negative correlates.

With respect to the relationship between stress and sleep, the general finding is that stressful or traumatic events prompt poor sleep quality and disturbance in normal sleep patterns (Partinen, 1994; Sadeh, 1996). However, there is a controversy in the literature concerning the nature of the exact disturbance in sleep patterns. The majority of research examining the influence of stress on sleep indicates that stress leads to delayed onset of sleep, shorter sleep durations, and more night awakenings. However, results from a limited number of studies, including Valrie et al.'s (2005) study of the influence of stress on sleep in children with SCD, have indicated that high stress is related to deeper, more continuous sleep with longer duration. To explain these conflicting findings, Sadeh (1996), guided by Selye's (1956) general adaptive syndrome theory, postulated two conflicting adaptive responses to

stress that an individual's sleep-wake system can employ: the "turn-on" response and the "shut-off" response. The "turn-on" response is when stress triggers increased vigilance and tension due to the physiological activation of the sympathetic adrenergic system. Thus, this response leads to the response consistently seen in the majority of the literature, which includes difficulties with sleep onset and lightly disrupted sleep. In contrast, the "shut-off" response is when the organism systematically copes with the stressor by withdrawing from it, which then leads to deeper sleep and longer sleep duration. However, this coping mechanism is also still linked to poor subjective sleep quality.

Extending Sadeh's (1996) theory of two adaptive responses, Sadeh and Gruber (2002) proposed an integrative model of stress and sleep. Their theory postulates that the sleep-wake system is merely a component of the body's stress management system and thus, the matching of the sleep response to stress is a function of numerous stress and coping factors, including characteristics of the stressor. If the stressor is appraised as acute, the individual's adaptation system will choose a more direct coping approach to the stressor. Therefore, when the organism is primed to directly cope with the stressor, the "turn-on" response, which is related to vigilance, will be activated. In contrast, if the stressor is appraised as chronic, the individual's adaptation system will choose a response directed toward conserving one's energy to deal with the strain associated with the stressor. Thus, the "shut-off" response, which allows the organism to withdraw temporarily from the stressor as well as conserve one's resources, will be activated.

There are acute and chronic aspects of daily hassles. Unlike major life events, daily hassles are ongoing stressors in a person's life linked to everyday living. All individuals experience a certain baseline level of stress associated with daily hassles and this baseline

level can be viewed as chronic stress. However, daily fluctuations around this baseline level of stress, especially sudden increases and decreases, can be viewed as the acute aspect of daily hassles. Thus, the way in which researchers choose to measure daily hassles should have an impact on the nature of the relationship seen between stress and sleep patterns. Consistent with this hypothesis, when stress was assessed as the baseline level of daily hassles experienced over a month period in Valrie et al.'s (2005) study, stress was found to be related to longer sleep duration. In contrast, the current study assessed stress as the daily fluctuations in daily hassles around an individual's mean level of hassles, which lead to the hypothesis that in the current study, stress would be related to less sleep and more sleep irregularity. Also, it was hypothesized that stress would be related to poor sleep quality as both the "turn-on" and "shut-off" responses to stress are associated with poor subjective reports of sleep quality (Sadeh & Gruber, 2002).

In children with chronic illness, the symptoms associated with the illness, such as SCD pain, have also been characterized as significant stressors (Thompson & Gustafson, 1996). Given the variability in occurrence, duration, and intensity of SCD pain, it can be viewed as an acute stressor, which according to Sadeh and Gruber's (2002) theory would lead to the activation of "turn-on" response. This conceptualization is consistent with the results of Valrie et al.'s (2005) study that indicated that high SCD pain is related to shorter sleep duration and poorer sleep quality.

In relation to the influence of stress on SCD pain, stress appears to be related to higher same-day SCD pain, possibly due to an increased sensitivity to the pain experience or an exacerbation of existing disease symptoms. Two studies utilizing adult samples measured summary levels of stress and found retrospective reports of stress to be predictive of SCD

symptomatology, pain intensity, and activity reduction (Leavell & Ford, 1983; Porter et al., 1998). Two additional studies using adult samples measured stress concurrently with other variables of interest by having the participants complete daily diaries (Porter, Gil, Carson, Anthony, & Ready, 2000; Gil et al., 2004). This procedure enabled investigators to look at the temporal ordering of stress in relation to the other variables. Overall findings indicated that daily stress was related to same-day pain and pain two days later in adults with SCD. In one study with adolescents (Gil et al., 2003), 37 adolescents with SCD between the ages of 13 and 17 completed daily diaries assessing pain, stress, mood, activity, and health care use for approximately three months. Daily stress was related to same day pain, health care use, and activity reduction in school and social areas. Valrie et al.'s (2005) study is one of the few studies that has examined daily stress in children with SCD below the age of 13. However, it did not investigate the relationship between stress and SCD pain.

Medication Use. The use of pain medication is recommended as part of the standard treatment for reducing SCD pain (Jacob, 2001). SCD pain severity is usually experienced in low to moderate levels, and although more severe pain episodes are sometimes treated in clinics, hospitals, and emergency rooms, SCD pain is usually managed with nonopioid and opioid analgesics at home (Dampier, Ely, Brodecki, & O'Neal, 2002; Gil et al., 2000; Porter et al., 1998; Shapiro et al., 1995). Nonopioid analgesics, herein referred to by their popular name "analgesics", are generally inexpensive, can be obtained without prescription, and work by affecting nociceptors where pain impulses begin to reduce an individual's perception of their pain (Jacob, 2001). In addition, they reduce the inflammatory response associated with the cause of the pain and are generally recommended for mild to moderate SCD pain.

In contrast, opioid analgesics, herein referred to by their popular name "narcotics", are only available through prescription and work by "binding to opioid receptors within and outside the central nervous system" (Jacob, 2001). In regard to pharmacologically treating SCD, narcotics have been encouraged for treatment of moderate to severe SCD pain by the American Pain Society (APS), but only for individuals who do not respond to analgesics or whose pain is too great to be treated by nonopioid analgesics alone. However, there is some controversy associated with the use of narcotics to treat SCD pain. Concerns about narcotic use appear to center around the addictive quality of opioids and side effects associated with the medications. While analgesics have only minimal side effects and are not addictive, narcotics are addictive and have numerous serious side effects, including constipation, nausea, and sedation. Recommendations from the APS include utilizing narcotics for only a short duration of at most 24 hours (Jacob, 2001).

Pain medication may have an impact on the relationship between SCD pain and sleep both by reducing SCD pain and by altering current sleep patterns. Research indicates that high SCD pain is related to high same day pain medication use in adults and adolescents with SCD (Gil et al., 2000; Gil et al., 2003; Gil et al., 2004; Porter et al., 1998). In addition, results from Dampier and associates' (2002) diary study of 37 children and young adults with SCD aged 6 to 21 years examined the amount of pain reduction associated with different pain medications. Analgesics were associated with a 13% to 18% reduction in SCD pain, narcotics were associated with a 23% to 26% reduction in pain, and a combination of analgesics and narcotics were associated with a 40% to 57% reduction in pain. As for the influence of pain medications on sleep patterns, longer sleep durations have been clearly noted as an established side effect of narcotics (Onen et al., 2005). In addition, though

18

analgesics have less severe side effects, their use has been linked to delayed sleep onset, increased awakenings, and lower sleep efficiencies in healthy individuals. However, the effects of analgesics are not as well-established.

<u>The Current Study</u>

For the current study, children with SCD were asked to complete daily diaries assessing the variables of interest (e.g., sleep, SCD pain, stress, and pain medication use) for up to 8 weeks. This methodology is particularly appropriate for the current study given the daily fluctuations in the variables of interest and the focus on examining the temporal associations among these variables to assist in establishing causal inferences (Stone, Kessler, & Haythornwaite, 1991). In addition to these advantages, it has been noted that daily diary reports may reduce recall bias and increase accuracy of reporting acute minor changes in symptoms and other variables of interest (Butz & Alexander, 1991; Stone et al., 1991; Verbrugge, 1980). Lastly, children's reports of their own daily activities may provide more comprehensive information concerning their daily lives than parental reports (Spilsbury et al., 2004).

Daily diaries are one of the most common ways of assessing sleep patterns, are found to be highly correlated with cross-sectional sleep data, and are often used to validate other sleep measures (Knab & Engel-Sittenfeld, 1983; Wolfson et al., 2003). They have also been used frequently to assess daily pain, medication use, and health care utilization in children and adolescents with SCD, some as young as 4 years of age (Connor-Warren, 1996; Dampier et al., 2002; Gil et al., 2000; Gill, Shand, Fuggle, Dugan, & Davies, 1997; Fuggle et al., 1996; Maikler, Broome, Bailey, & Lea, 2001; Shapiro et al., 1995). Butz and Alexander (1991) generated recommendations for diary methods with children by examining a study of

7 to 12 year old children with asthma who were asked to complete daily diaries assessing their symptoms for eight weeks. Some recommendations include biweekly rewards to help maintain high compliance rates, making sure that the diary is at the appropriate reading level for the children, and limiting the study period to eight weeks to reduce fatigue related to completing the diary. All of these strategies were implemented in the current study.

The current investigation was conducted in the research laboratory of Karen M. Gil, Ph.D. and builds upon the current daily diary projects examining stress and pain in adolescents and adults with SCD, specifically by (1) extending the project to younger children and (2) expanding the concepts studied to include sleep patterns. The sample used for the current investigation was the subset of 20 of the 24 children with SCD aged 8 to 12 used in a previous investigation (Valrie et al., 2005) that completed daily diaries. As part of that investigation, daily reports of sleep duration, sleep quality, SCD pain, and stress were compared to the child's baseline reports. Children's reports across the two methods were consistent with two notable exceptions. The average sleep quality score for the diary data was higher than what was reported during the baseline interview, and the children reported significantly more pain days in the diaries than during their baseline interview. Both of these findings are consistent with previous results indicating that higher rates of minor events are generally reported in daily diaries than during interviews. Specifically for the pain reports, these findings are consistent when comparing studies by Gil and associates that use interview (Gil, Abrams, Phillips, & Keefe, 1989; Gil, Williams, Thompson, & Kinney, 1991) versus the diary method (Gil et al., 2000; Gil et al., 2003; Porter et al., 1998) to assess SCD pain in adolescents and adults. They are also consistent with other research showing that the

frequency of pain episodes reported by children during an initial interview was about half what they subsequently recorded in daily diaries (Fuggle et al., 1996; Gill et al., 1997).

In the current study, information was gathered in the baseline assessment on individual level factors that may influence sleep patterns above and beyond the impact of pain (e.g., pubertal level, depressive symptoms, week day versus weekend day). These factors were investigated as possible covariates to be controlled when predicting sleep variables.

Hypotheses

The primary goal of the current study was to investigate the relationship between daily pain and sleep patterns in young children with SCD. It was hypothesized that high daily SCD pain would be related to shorter sleep duration, high sleep irregularity, and poorer sleep quality the same night. The alternate relationship was also examined, which was the influence of daily sleep patterns on SCD pain. It was hypothesized that shorter sleep duration, high sleep irregularity, and poor sleep quality would be related to high SCD pain the next day. Previous research has suggested that in the bi-directional relationship between pain and stress, pain is the more powerful factor in the cycle (Gil et al., 2003; Gil et al., 2004). Consistent with these findings, it was hypothesized that pain was the more powerful predictor in the pain-sleep cycle and that this would be evidenced by the magnitude of the impact of pain on sleep.

The secondary goal of the current study was to investigate the influence of stress and pain medication use on the relation between SCD pain and sleep (see Figure 1). It was hypothesized that the relationship between SCD pain and sleep would be moderated by stress, such that high daily pain would be related to shorter sleep duration, high sleep

irregularity, and poorer sleep on the same night, and the magnitude of this relationship would be amplified at increasing levels of stress. Also, it was hypothesized that the relationship between daily sleep and SCD pain would be moderated by stress, such that shorter sleep duration, high sleep irregularity, and poor sleep quality would be related to high pain on the next day, and the magnitude of this relationship would be amplified at increasing levels of stress.

In regards to pain medication use, it was hypothesized that the relationship between SCD pain and sleep would be moderated by pain medication use, such that high pain would be related to shorter sleep duration, high sleep irregularity, and poorer sleep quality the same night, and the magnitude of this relationship would be attenuated by the child's medication use on the same day. In addition, it was hypothesized that the attenuating effect of pain medication use on the relationship between pain and sleep would be moderated by the type of pain medication taken. Narcotics have a stronger impact on reducing pain and a stronger connection to the alteration of sleep patterns by producing longer sleep durations than analgesics (Dampier et al., 2002; Onen et al., 2005). Thus, it was hypothesized that narcotic use would have more of a buffering impact than analgesic use.

CHAPTER 2

METHOD

Participants

Participants and their guardians were recruited from the University of North Carolina at Chapel Hill (UNC-Chapel Hill) and East Carolina University (ECU) outpatient SCD clinics during their regularly scheduled clinic appointments. Hospital personnel screened all possible participants for medical contraindications for participation (e.g., neurological impairment, confounding medical condition). In addition, by the entry criterion of the study, all participants had experienced at least one episode of SCD pain in the past year. The sample used for the present investigation consisted of 20 children with SCD aged 8 to 12 years who completed daily diaries a baseline assessment. These children were part of a larger study (Valrie et al., 2005); only children who completed diaries were included in the present study. This sample consisted of 13 girls and 7 boys who had a mean age of 10.1 years of age (SD = 1.07 years). The mean level of maternal education was 12.7 years (SD = 2.10 years) with a range of 7.5 to 16 years. Of the 20 children, 14 (70%) had sickle cell anemia, 5 (25%) had hemoglobin SC, and 1 (5%) had sickle thalassemia. The children completed a total of 712 days out of a possible 1120 days if all participants had completed 8 weeks of diary days, representing a completion rate of 64%. On average, children completed 36 diary days (SD = 19) with a range 7 to 56 days. All participants were African American.

Informed consent was obtained from participants and their guardians according to procedures approved by the Institutional Review Boards at UNC-Chapel Hill and ECU. Then participants and their guardians completed a baseline interview. As part of the baseline interview, the children were administered the Children's Depression Inventory and a Puberty Scale, and the guardians were administered a Demographic form. The parents were compensated $15 and the children were compensated $5 for the baseline interview. At the conclusion of the baseline interview, the children were instructed on how to complete the daily diaries and were asked to complete the daily diaries for up to 8 weeks. They were then given a packet containing 4 weeks worth of diaries and 4 stamped, addressed envelopes and were asked to mail the diaries back to the investigator on a weekly basis. Once the participant completed 3 weeks worth of diaries, he/she was sent a packet containing the remaining 4 weeks worth of diaries and 4 stamped, addressed envelopes. To aid them in identifying accurate sleep onset and waking times, participants were given a digital clock. Also, to encourage their continued participation, the children were called weekly and/or sent written feedback and were given $5 compensation for each complete week of diaries.

Measures: Child Daily Diary

The daily diary used in the present study was a modified version of diaries used in two prior studies: a diary assessing daily pain occurrence and intensity, health care use, and activity reduction in adolescents with SCD between the ages of 13 and 18 year (Gil, 1994) and a diary assessing daily pain occurrence, activity reduction, mood, stress, and perceived control in children with juvenile rheumatoid disease (JRD) between the ages of 7 and 15 years (Schanberg et al., 2000). The diary assessed sleep, pain, stress, medication use, and

mood. The section on mood was not used in the present study. Children were instructed on how to complete the diaries during the initial interview. In the morning, children recorded information on their previous night's sleep and in the evening, children completed the sections assessing daytime sleepiness, pain, stress, medication use, and mood. Results from Valrie et al.'s (2005) study, which compared information from the diary to information gathered during the children's retrospective interview, are presented in Table 1. As mentioned earlier, the results between the two methods were consistent with two notable exceptions. The children reported a higher average sleep quality score and more pain days on the diaries than indicated during interview. However, both of these findings are consistent with previous results indicating that higher rates of minor events are generally reported on daily diaries than during interviews and thus, indicates that the data provided by the diaries is valid.

Sleep. The sleep section was based on the Children's Sleep Behavior Scale (Fisher et al., 1989), a diary used with children with JRD (Schanberg et al., 2000), and the BEARS sleep assessment instrument (Owens, 2002). To assess sleep quality, children were asked to rate on a 100mm horizontal visual analogue scale (VAS), ranging from "did not sleep well" (0mm) to "slept very well" (100mm), how well they slept the night before. The distance of the child's mark from the left end of the scale was measured in millimeters, and this score was the primary rating of sleep quality for the present study. Children were also asked to report what time they went to sleep the night before and what time they woke up that morning. To assess sleep irregularity, the difference was calculated between the sleep onset time of the current night and the child's average sleep onset time. To assess sleep duration, the difference was calculated between the sleep onset time and the sleep cessation time. The

children were also asked a number of other questions about their sleep patterns to assess general sleep demographics for this population, such as number of wakings during the night and daytime sleepiness. The question assessing daytime sleepiness, which was a yes/no question asking "Did you feel tired today?", was the only portion of the sleep section to be completed in the evening.

Research views diary assessments of sleep patterns as a reliable and valid measure of sleep patterns (Knab & Engel-Sittenfeld, 1983; Wolfson et al., 2003). In relation to examining sleep in children, the majority of sleep diary studies use parental report. However, recent research has provided support for the reliability and validity of child completed daily sleep logs when compared to objective measures, such as actigraphy (Gaina, Sekine, Chen, Hamanishi, & Kagamimori, 2004; Sadeh, Raviv, & Gruber, 2000)

Pain. In this section of the diary, children were asked to report whether they experienced any SCD pain during the day. If so, they were asked to rate the average level of their pain by placing a vertical mark on a 100mm horizontal VAS with ratings ranging from "not hurting at all" (0mm) to "hurting a whole a lot" (100mm). This mark was the primary rating of pain intensity. When the child reported no SCD pain it was rated as a 0mm response. Research has provided support for the reliability and validity of the VAS in assessing daily SCD pain in children and adolescents when compared to child, parent, and physician interviews and concurrent parent diary reports (Gil et al., 2000; Valrie et al., 2005; Walco & Dampier, 1990). As for the descriptor of "average" level of pain, research has established the validity of this measure in assessing SCD pain and other acute pain problems, such as postoperative pain, in adolescents when compared to parent interview data (Gil, Ginsberg, Muir, Sullivan, & Williams, 1992; Graumlich et al., 2001; Walco & Dampier,

1990). In addition, "average" daily adolescent SCD pain ratings using the VAS were positively related to daily stress, lower rating of daily positive mood, and daily health care utilization, including medication use (Gil et al., 2003). Also, high "average" daily pain ratings of children and adolescents with JRD were negatively related to daily mood (Schanberg et al., 2000).

Stress. Stress was measured with the Daily Events Inventory. The Daily Events Inventory consists of 17 negative daily events, such as "argued with parents" and "was made fun of" (see Table 4). These 17 items are modified versions of items from instruments developed by Gil and associates (1987) and Grant and Compas (1995), and were used in a recent diary study by Schanberg et al. (2000). Children were told to indicate whether the event occurred that day. The daily event total was calculated by summing the number of negative daily events endorsed. There were also 11 additional items on the scale that consist of positive daily events and illness-related events, such "stay home from school" and "had trouble getting out of bed". These items were not scored as part of the measure. The scale has satisfactory internal reliability (r = .70) and was predictive of daily disease symptoms in children with JRD (Schanberg et al., 2000).

Medication Use. The medication section consisted of an open-ended question asking "What medications did you take today?" The responses were then coded to assess whether or not the child took a narcotic and/or analgesic medication that day.[1] Previous studies have reported valid results when utilizing similar diary methods to assess medication use in children and adolescents with SCD (Connor-Warren, 1996; Dampier et al., 2002; Gil et al., 2000; Maikler et al., 2001). In these reports, higher SCD pain was positively related to

higher medication use, and Gil et al. (2000) reported consistency between adolescent and parent reports of medication use in adolescents with SCD.

<u>Measures: Baseline Reports</u>

<u>Depression.</u> The Children's Depression Inventory (CDI) is a 27 item questionnaire (Kovacs, 1977) used to assess the severity of depression in children aged 7 to 17 years. It examines a variety of depressive symptoms, including negative mood, ineffectiveness, negative self-esteem, interpersonal problems, and anhedonia. The children's overall raw scores were converted to T-scores with a mean of 50 and a standard deviation of 10. Higher scores are associated with higher severity of depressive symptoms. The measure has adequate reliability and validity (Doerfler, Felner, Rowlison, Raley, & Evans, 1988; Finch, Saylor, Edwards, & McIntosh, 1987; Helsel & Matson, 1984; Hodges & Craighead, 1990).

<u>Pubertal Development.</u>   The Rating Scale for Pubertal Development (Puberty Scale) is a 5-item questionnaire (Carskadon & Acebo, 1993) designed to be a noninvasive measure of physical development and overall maturation in school age children. There are separate versions of the questionnaire for boys and girls. Both versions assess changes in height, body hair, and skin complexion. The girl version also assesses breast growth and menstruation and the boy version assesses voice and facial hair transformation. Children were classified on a 1 to 5 scale ranging from pre-pubertal to post-pubertal development. The measure has adequate reliability and validity (Carskadon & Acebo, 1993).

<u>Demographic Information Form.</u> Guardians completed a basic demographic information sheet. The information gathered included the guardian's employment type, marital status, and educational background. In addition, the guardians reported the child's age, sex, type of SCD, and pain medications used in the past two weeks.

CHAPTER 3

DATA ANALYSIS

Multilevel models, also known as hierarchical linear models, were used to examine the relations among daily reports of sleep, SCD pain, stress, and pain medication use controlling for individual level factors (e.g., age, gender, type of SCD). Multilevel models utilize systems of regression equations to model data with a hierarchical or clustered structure (Hox, 1998). The structure of the data for the current project was considered clustered, because it consists of repeated reports nested within each individual participant. Multilevel models allow for a separate examination of the influence of individual level factors (e.g., demographic and other baseline measures) and observation level factors (e.g., the daily fluctuations in sleep, SCD pain, stress, and pain medication use). This procedure is done by conceptualizing the clustered data as "consisting of units grouped at different levels" (Goldstein, 1995). For the current study, level 1 units of observation consist of the repeated daily reports and the level 2 units are individual characteristics (Raudenbush & Bryk, 2002). Level 1 factors include daily sleep, pain, stress, and pain medication reports. When utilized as predictor variables, the fixed effects of these factors were modeled to examine how they relate to the dependent variable. Level 2 factors for the current investigation, which consist of time-invariant covariates, include age, gender, type of SCD, level of pubertal growth, depressive symptoms, and person-centered means of the level 1 independent variables (Snijders & Bosker, 1999). The fixed effects of the level 2 variables were modeled to control

for their relationship to the dependent variables. The random effects (e.g., freely varying) components of these models consist of individuals' intercepts, which allows for the modelingof the relationships between the dependent and independent variables when individuals randomly vary in relation to their mean level of the dependent variable (e.g., sleep quality, sleep duration, sleep irregularity, and pain severity).

<u>Advantages of Multilevel Modeling</u>

There are numerous advantages of utilizing multilevel modeling to examine daily dairy data. For example, the procedure allows for the modeling of both within-person and between-person variance, which is necessary to attain the goals of the current study. The purpose of the current study is to examine the influence of daily fluctuations in the level 1 independent variables on the dependent variables, while controlling for the influence of between-person variance, as modeled by level 2 variables. Given this focus, Kreft, de Leeuw, and Aiken (1995) advise using a specific centering strategy that allows the researcher to separate the within-person and between-person variance during the analysis, while not impacting the slopes between the level 1 independent and dependent variables. This strategy, as outlined by Schwartz and Stone (1998), is done by creating a distinct within-person variable and between-person variable for each diary variable. The within person variable, which is created by subtracting the mean of each individual from his observations and creating a person centered variable, is said to be pure. Because it contains no between-person variance, it should not be correlated with any between-person variables. This person-centered variable models the influence of the daily fluctuations of a variable relative to the child's average experience. In addition, person-centering the level 1 predictor variables reduces unnecessary collinearity between the predictor variables and their interaction terms.

To further help with interpretation, the standard deviations for these centered variables were set to 1.

In contrast, the between-person variable used is the mean for each individual and is entered into the analysis to model the between-person variance associated with the variable. Overall, this strategy allows the researcher to control for the impact of individual level differences, including individual differences in the level 1 variable, while separately investigating the influence of the day-to-day fluctuations in the level 1 variable on the dependent variable.

Another advantage of multilevel models is that this approach does not entail aggregating the within-person variables, which, due to differing numbers of observations per person, can lead to heteroskedasticity (Schwartz & Stone, 1998). Heteroskedasticity, which violates an assumption of the ordinary least squared regression, is when the variance of the error is not constant. This condition can be caused by un-modeled systematic error associated with the aggregated individual differences. Also, autocorrelation, which is when two observations of an individual are more similar because of their closeness in time, can be corrected in multilevel models (Schwartz & Stone, 1998). This correction is done by applying a continuous first-order autoregressive error structure to all diary variables. Two additional advantages are that multilevel models utilize observations instead of individuals as the primary unit of analysis, which leads to an expanded number of degrees of freedom, and they allow for missing data, which is a common occurrence with daily diary data (Porter et al., 2000; Porter et al., 1998).

<u>Multilevel Models for Study Hypotheses</u>

Data were entered into Excel Spreadsheets for transport into SAS for Windows. All data were double entered and compared to eliminate any errors. Multilevel models were generated using PROC MIXED in SAS (Singer, 1998) and the use of the restricted maximum likelihood method. Tests for autocorrelation were significant, indicating that autocorrelation was significantly present for models predicting the sleep variables and pain. Thus, a continuous-time, autoregressive, within-person error structure was applied to all models in the current study.

Each multilevel model controlled for the following level 2 covariates: demographic variables (e.g., age, gender, maternal education, and SCD type) and aggregated person-means for the independent diary variables used in the models. Pubertal level, depressive symptoms, and week day versus weekend day were considered as possible covariates in the models predicting sleep variables.

<u>Daily SCD pain predicting daily sleep.</u> Three multilevel models were calculated to test hypotheses examining the role of daily pain in predicting daily sleep. The models used daily SCD pain to predict (1) sleep quality, (2) sleep duration, and (3) sleep irregularity that night.

<u>Daily sleep predicting daily pain.</u> One multilevel model was calculated to test the alternative relationship examining the role of daily sleep in predicting daily pain. The model used daily sleep duration, daily sleep irregularity, and daily sleep quality to predict SCD pain the next day.

<u>Daily stress and daily pain medication use moderating the relationship between pain and sleep.</u> To test the hypothesis examining stress as a moderator of the relationship between

pain and sleep, stress and the interaction between SCD pain and stress were entered into the three multilevel models predicting daily sleep duration, sleep irregularity, and sleep quality. In addition, to test the hypothesis examining stress as a moderator of the relationship between sleep and pain, stress, the interaction between sleep duration and stress, the interaction between sleep irregularity and stress, and the interaction between sleep quality and stress were entered into the multilevel model predicting daily SCD pain.

To test the hypothesis examining pain medication use as a moderator of the relationship between pain and sleep, analgesic use, the interaction between SCD pain and analgesic use, narcotic use, and the interaction between SCD pain and narcotic use were entered into the three multilevel models predicting daily sleep duration, sleep irregularity, and sleep quality.

Significant interactions found were statistically probed utilizing the online interactive calculator for probing interactions developed by Preacher, Curran, and Bauer (2004) and based on techniques discussed in Bauer and Curran (2005). Specifically, the calculator was utilized to calculate the region of significance of the simple slope relating the relationship between one of the predictor variables and the dependent variable as a function of the other predictor variable, the moderator. This procedure informs the researcher at which values of the moderator the relationship is significantly different from 0. Calculation of the region of significance can only be done when the moderator is continuous.

In addition, the calculator was used to calculate simple intercepts and slopes describing the above described relationship at particular values of the moderator. In the case of a continuous moderator, the high value was designated as one standard deviation above the mean, the medium value was designated as the mean, and the low value was designated

as one standard deviation below the mean. However, in the case of a categorical moderator, the first and second moderator values was equal to 0 and 1, with 0 representing one category and 1 representing another category. These values allowed the researcher to discuss the direction of the relationship between the predictor variable and the dependent variable at varying levels of the moderator. In addition, z-scores were calculated to examine whether the intercept and slope of the lines produced were significantly different from 0. See Bauer and Curran (2005) for more detailed information on calculating the region of significance, simple intercepts, and simple slopes for probing interactions in multilevel modeling.

CHAPTER 4

RESULTS

Information Concerning Diary Completion

This section presents information concerning what baseline factors appeared to be

related to diary completion. First, the baseline information for the 20 children who

completed both the baseline interview and diary portion of the study is compared to data of 4

children who completed the baseline interview, but did not complete the diary portion of the

study. Of the 4 individuals designated as non-completers, 3 did not complete any diaries and

one sent in diaries for calendar dates that had not yet occurred. T-tests and chi-squares were

calculated to compare baseline interview characteristics of the diary completers and non-

completers (see Tables 2a and 2b). According to analysis, diary completers were similar to

diary non-completers, except that completers were significantly more likely to be female (x^2

= 5.67, p = .02). However, this is qualified by the fact that all of the diary non-completers

were boys.   The small sample size used for the analyses may have compromised the ability

to detect significant differences between the groups.

Pearson product correlations were calculated to examine what baseline characteristics

were related to completing more diaries (see Table 3). Number of diaries completed was

negatively related to puberty status (r = -.60, p = .03) and positively related to the likelihood

that the child has used narcotics to manage pain (r = .53, p = .02). Notably, children with

high puberty scores tended to report high pain severity (r = .67, p = .01), high stress (r = .49,

$p = .09$), and be girls ($r = .58$, $p = .04$). Narcotic use was not significantly related to any other baseline characteristics.

<u>Descriptive Information</u>

On average, children reported experiencing poor sleep on 12.61% of diary days (SD = 11.49%; range = 0 to 45.45%) with about 15% reporting no "poor" sleep nights. Across all diaries, the average sleep quality rating was 84.41 (SD = 25.91), the mean sleep duration was 8.8 hours (SD = 1.66 hours), and, in relation to sleep irregularity, the average sleep onset time was 10:09 pm (SD = 91 minutes). Children also reported having difficulty with sleep onset on a total of 32.26% of days, waking during the night on a total of 30.04% of days, and daytime sleepiness on a total of 40.60% of days.

Sixteen of the 20 children experienced pain during the course of the study. Across the diaries, pain was reported on 22.24% of the diaries and the average pain severity on pain days was 48.73 on a 100 point scale (SD = 27.20, range = 2 to 100). For the current study, a pain episode was defined as occurring between the period of the time when the child reports first experiencing pain and the time when the child reports no longer experiencing pain. Given the nature of the diaries, a pain episode can encompass one or multiple days. Children reported experiencing a mean of 3.2 pain episodes during the course of the study (range = 1 to 11 episodes). In addition, children reported experiencing a mean of 1.2 multiple-day pain episodes (range = 0 to 3). The majority of multiple-day pain episodes lasted between 2 to 4 days. However, 2 children reported pain episodes lasting between 6 to 7 days and 1 child reported experiencing pain on all but one of the 34 days he/she completed diaries.

The mean number of stress events endorsed was 1.77 (SD = 2.02) on the 17-event scale. The mean number of stress events endorsed was 2.56 on pain days (SD = 2.57) and

1.58 on non-pain days (SD = 1.80). This difference was significant (t = -4.44, p < .01).

Further information concerning the endorsement of specific stress items on the scale is

presented in Table 4. All stress items were endorsed at least once during the course of the

study. In addition, children significantly endorsed stressors on a higher percentage of pain

days than non-pain days.

Eighteen of the 20 children in the study reported on their medication use. Six

children reported taking no medication, 7 children reported taking an analgesic, 4 children

reported taking a narcotic, 6 children reported taking a non-pain, sedating medication, and 10

children reported taking another type of medication. All of the children who reported using

an analgesic or a narcotic experienced multiple-day pain episodes. In contrast, children who

reported using no pain medication during the course of the study ranged from children who

experienced no pain to a child who experienced up to 7 consecutive pain days. Of note, the

parents of the child who experienced 7 consecutive pain days, but did not take a pain

medication during the study, had communicated to the SCD physician a reluctance to

medicate their child.

Though pain medication use was only reported on 9.20% of total diary days, pain

medication was taken on 41.54% of pain days, and on 71.05% of pain days when using the

sub-sample of children who took a pain medication. Analgesics were never used on non-pain

days and narcotics were only used twice on non-pain days. The majority of children who

used a pain medication reported using it over a period of consecutive days, usually ranging

from 2 to 4 days. Notably, the child who experienced pain on all but one diary day used a

drug coded as a narcotic in the current study, Amitriptyline, 25 consecutive days. This

finding is consistent with the fact that Amitriptyline is commonly prescribed for chronic

(long-term) use. Additional information concerning the types of medications taken and diary days on which specific types were taken is presented in Tables 5a and 5b.

Non-pain medication use was reported on 44.59% of diary days.[2] Six of the 10 children who used a non-pain medication reported taking a non-pain medication throughout the entire study period. These results are consistent with chronic (long-term) usage guidelines commonly recommended for the majority of non-pain medications reported in the study, such as hydroxyurea and folic acid. In addition, 13 of the children completed the Puberty Scale and 17 of the children completed the CDI during the baseline interview. The puberty scores ranged from 1 to 4 (i.e., prepubertal to late pubertal development), and the mean puberty scale score was 2.54 (SD = 1.05), which is in the early puberty range. As for the CDI, the mean score was 46.12 (SD = 5.38, range = 37 to 53) and all of the children's scores were within one standard deviation of the mean or below, suggesting little to no clinical levels of depressive symptoms in this sample.

Correlations

Pearson product correlations were calculated for the diary variables used in the subsequent analysis (see Table 6). Pain, stress, and medication use during the day and sleep variables collected that night were used in the analysis. Due to the bias of the standard errors, p- values were not reported. Instead, trends in the data, as evidenced by correlations above .10, are discussed. High pain severity appeared to be related to poor sleep quality (r = -.32,) and high sleep irregularity (r = .13). In addition to pain, high analgesic use (r = -.13) and high narcotic use (r = -.29) appeared to be related to poor sleep quality. High stress (r = .19), high narcotic use (r = .23), and less sleep (r = -.46) appeared to be related to high sleep irregularity.

Intercept Only Models Predicting Sleep and Pain

Four intercept only models, which are equivalent to an ANOVA, were calculated to provide baseline calculations of between- and within-individual variance for the planned models predicting sleep quality, sleep duration, sleep irregularity, and pain (Raudenbush & Bryk, 2002; Snijders & Bosker, 1999). The sum of the error variance components represents the total variance of the diary level variables and can be found in Tables 7 and 8. These models allow for the calculation of the intra-class correlation (ICC). The ICC represents the proportion of the total variability for a specific dependent variable that is accounted for by individual differences associated with each child and is calculated by dividing the between individual variability by the total variability of the dependent variable. For sleep quality, the ICC is .25, indicating that 25% of the variance in sleep quality is due to individual variability. For the remaining dependent variables, 32% of the variance in sleep duration, 32% of the variance in sleep irregularity, and 18% of the variance in pain severity appears to be due to individual variability. Conversely, this indicates that 75% of the variance in sleep quality, 68% of the variance in sleep duration and sleep irregularity, and 82% of the variance in pain severity appears to be due to within subject variability.

Multilevel Random Effects Models Predicting Sleep Quality, Sleep Duration, and Sleep Irregularity

A series of multilevel random effects models were calculated to examine the associations between SCD pain, stress, and medication use and (1) sleep quality, (2) sleep duration, and (3) sleep irregularity the following night (see Tables 9 to 11). 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.

Pubertal level and depressive symptoms were not predictive of any of the daily sleep variables; thus they were excluded from the final multilevel models predicting sleep. This was not surprising given the limited ranges of the two variables. Overall, no level 2 variables significantly predicted any of the sleep variables. Level 1 predictors in each model consisted of pain severity, stress, analgesic use, narcotic use, and the various interaction terms representing the association between pain severity and stress, and pain severity and the medication use variables.[3] The level 1 covariate of week day versus weekend day was uniquely predictive of sleep duration and was included in the final multilevel model predicting sleep duration.

Sleep Quality. For the model predicting sleep quality (see Table 9), the estimate of within-individual variance was significant and the difference between this estimate and the within-individual estimate of the intercept only model indicated that the level 1 variables in the model accounted for 8.24% of the variance in sleep quality's within-individual variability. An examination of the fixed effects indicated that on a day-to-day basis, high pain severity (Beta = -3.72, p < .01), high analgesic use (Beta = -6.96, p < .01) and high narcotic use (Beta = -6.02, p = .03) were uniquely related to poorer sleep quality that night. In addition, the interaction between pain severity and analgesic use (Beta = 2.81, p = .02) was uniquely related to sleep quality, indicating that the relationship between pain severity and sleep quality was influenced by analgesic use. Notably, the estimate of the between-individual variance was also significant and indicated that even after controlling for the level 2 covariates, there was still a significant amount of variability in the intercept associated with individual-level factors. Also, the estimate of the autocorrelated effect was significant and

indicated that the autocorrelated structure of the data was not accounted for by the level 1 factors in the model.

The online interactive calculator (Preacher et al., 2004) was used to statistically examine the relationship between pain severity and sleep quality when the child took analgesic medication and when the child did not (see Figure 2). When an analgesic was not taken, the simple intercept associated with the relationship between sleep quality and pain severity was 95.63 ($z = 11.00$, $p < .01$) and the simple slope was -5.98 ($z = -5.09$, $p < .04$). When an analgesic was taken, the simple intercept associated with the relationship was 81.09 ($z = 6.58$, $p < .01$) and the simple slope was .20 ($z = .05$, $p = .96$). These relationships are graphically displayed in Figure 2. High pain severity was defined as 2 standard deviations above the mean and low pain severity was defined as 2 standard deviations below the mean. Taken together, results suggest that when the child used an analgesic, the negative relationship between pain severity and sleep quality was decreased. However, examination of the figure also suggests that given the strength of the negative influence of analgesic use on sleep quality, the benefits of taking an analgesic to buffer against the effects of pain may only be fully realized when the child is experiencing an extremely high level of pain relative to their usual pain experience.

Sleep Duration. For the model predicting sleep duration (see Table 10), the estimate of within-individual variance was significant and the model indicated that the level 1 variables accounted for 6.73% of the variance in sleep duration's within-individual variability. An examination of the fixed effects indicated that on average, children sleep longer on the weekend than during the week (Beta = 0.35, $p = .01$). Moreover, high stress was uniquely related to less sleep that night (Beta = -0.13, $p = .04$). Notably, the estimate of

the between-individual variance was significant, but the estimate was higher than the between-individual variance in the intercept only model. This result appears to be a consequence of the restricted maximum likelihood method of estimation, possibly associated with the number of level 2 covariates controlled in the model relative to the level 2 sample size of 18. The estimate of the autocorrelated effect was significant and indicated that the autocorrelated structure of the data was not accounted for by the level 1 factors in the model.

Sleep Irregularity. For the model predicting sleep irregularity (see Table 11), the estimate of within-individual variance was significant and the model indicated that the level 1 variables accounted for 5.35% of the variance in sleep irregularity's within-individual variability. An examination of the fixed effects indicated that none of the proposed variables of interest were uniquely related to sleep irregularity. The estimate of the between-group variance was significant and the estimate of between-group variance was higher than in the intercept only model. Also, the estimate of the autocorrelated effect was significant, indicating that the autocorrelated structure of the data was not accounted for by the level 1 factors in the model.

Multilevel Random Effects Model Predicting Pain

A multilevel random effects model was calculated to examine the reciprocal relationship between sleep during the night (e.g., sleep quality, sleep duration, sleep irregularity) and pain that day (Table 12). Level 1 predictors in this model consisted of sleep quality, sleep duration, sleep irregularity, stress, and the various interaction terms representing the association between sleep and stress. Level 2 covariates in this 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 estimate of within-

individual variance was significant and the model indicated that the level 1 variables in the model accounted for 14.76% of the variance in pain's within-individual variability. Age was the only level 2 covariate that was significantly related to pain severity (Beta = 4.72, p = .05), indicating that older children experienced higher daily pain severity. Also, on a day-to-day basis, poor sleep quality during the night (Beta = -6.04, p < .01) and high stress that day (Beta = 1.93, p = .02) were uniquely related to high pain severity that day. The estimate of the between-individual variance was significant and the estimate of the autocorrelated effect was significant.

CHAPTER 5

DISCUSSION

This study investigated the temporal relationship between SCD pain and sleep and examined the influence of additional stressors and pain medication practices on this relationship. To accomplish the goals of the study, daily diaries were completed by a group of children with SCD and analyzed using multilevel models. Results are consistent with the hypothesis that there is a cyclic relationship between high SCD pain and poor sleep. Specifically, high levels of daily SCD pain were significantly related to poor sleep quality that night. Also, poor sleep quality during the night was significantly related to high SCD pain that day. However, contrary to hypotheses, results were more consistent with the hypothesis that poor sleep quality is the more powerful factor in the pain-sleep cycle. This was evidenced by the relative magnitude of the effect of sleep quality during the night on pain that day versus the magnitude of the effect of pain during the day to sleep quality that night.

One explanation for why poor sleep quality during the night may impact the pain experience that day is by lowering one's pain threshold (Onen et al., 2005). In addition, the mood dis-regulation that has been connected to poor subjective sleep quality may be the mechanism by which poor sleep quality influences the pain threshold (Kirmil-Gray et al., 1984; Manni et al., 1997; Meijer & van den Wittenboer, 2004). Previous diary research has linked daily reports of low positive mood and high negative mood to high same day pain in adults and adolescents with SCD (Gil et al., 2003; Gil et al., 2004). Also, reports of low

positive mood and high negative mood have been connected to high same-day health-care use and reductions in activity participation (e.g., work in adults, school and social activities in adolescents) above and beyond the influence of pain. Thus, through daily mood as a mediating factor, the influence of poor sleep quality may also be seen in the way children and their families behaviorally respond to the pain experienced by the child.

Another possible explanation for the relationship between sleep quality during the night and pain that day may be that poor subjective sleep quality is an indicator of some underlying biological precursor to a pain episode. This finding would be meaningful information given that though a number of factors have been put forth as preceding events, such as dehydration, infection, physical overexertion, cold weather, and daily fluctuations in stress, research still indicates that the majority of pain episodes are not preceded by any obvious factor (Ballas, 1998; Gil et al., 2003). However, it could also be a sign that the child is experiencing sleep fragmentation due to the experience of either the onset or the continuation of a pain episode that he/she is not properly managing.

An alternative explanation to the three presented for the relationship between sleep quality during the night and pain that day may be method variance. As noted by Dampier and associates (2002), proper daily compliance of paper diaries is hard to verify without simultaneous independent information. Thus, the possibility that the children completed both the sleep information and the pain severity information on the same diary at the same time cannot be discounted.

As for the relation between high SCD pain during the day and poor sleep quality that night, this is consistent with findings that high pain is linked to factors related to subjective reports of poor sleep quality, such as decreased sleep efficiency and fragmented sleep (Onen

45

et al., 2005). Possible mechanisms of influence include the experience of pain during the night and the disturbance of underlying sleep processes by the biological condition causing the pain. Another explanation offered for the link between pain and poor sleep patterns is the influence of pain medication on sleep. However, results from the current study indicate that pain is related to poor sleep above and beyond the effects of pain medication. Notably, the relationship between pain during the day and poor sleep quality that night may help to explain the prolonged effect of SCD pain on functioning days later. Results from adult and adolescent diary studies indicate that high SCD pain is related to low positive mood and high stress the next day and two days later, and that in adults with SCD, high SCD pain is related to high negative mood the next day and two days later (Gil et al., 2003; Gil et al., 2004). Given the link between poor sleep quality and mood dis-regulation, poor sleep may act as a mediating factor connecting pain one day to mood and stress the following days.

Lastly, results did not support the hypothesis that high SCD pain is related to less sleep that night. This finding is inconsistent with literature that indicates that pain is associated with sleep loss (Onen et al., 2005). However, this result may be explained by the inclusion of stress in the model predicting sleep duration. Findings from the interview data (Valrie et al., 2005) suggested that the relationship between pain and sleep duration may be masked by the effects of stress on sleep duration. Specifically, results indicated that the negative relationship between pain and sleep duration is only evident at low levels of stress. As for sleep irregularity, results did not support the hypothesis that high SCD pain is related to high sleep irregularity. The majority of researchers examining sleep irregularity have focused on the phenomenon in the adolescent population and thus, have proposed factors that are more relevant to that population, such as the social, school, and biological changes

associated with the onset of puberty (Carskadon, 2002; National Sleep Foundation, 2000). In addition, most of studies have focused more on discrepancies between week day and weekend sleep patterns; substantially more research is needed to elucidate what factors may influence the variability noted in daily sleep patterns in children, specifically children with SCD, and the effects of this irregularity.

Clinical Implications and Future Directions. In conclusion, these findings suggest possible clinical implications and highlight specific strategies for future research. Clinically, this information suggests that patients, their families, and health care providers may benefit from taking into account the role that sleep plays in the child's experience of pain. This information may help patients and their families better manage the child's pain at home by making parents and children with SCD aware that poor sleep may be a precursor to pain episodes, that good sleep hygiene may help in the management of pain episodes, and that pain during the night may interfere with normal sleep processes. Also, behavioral pain interventions, such as those designed by Gil and associates (1997) for children and adolescent with SCD, may be improved by the inclusion of strategies to encourage proper sleep hygiene and address sleep issues.

Hypotheses examined by the current research indicate that a mediational framework, as offered by structural equation modeling, may be more appropriate to properly model the relationship between pain and sleep. Specifically, results suggest that the child's experience of pain leads to poor sleep quality that night and that this poor sleep quality leads to a higher pain experience the following day, possibly through changes in the child's mood. In addition, the child's poor sleep quality, as possibly mediated by the child's mood, may influence other behavioral activities associated with responding to the pain experience, such

47

as health care use and reductions in activities. Lastly, future research in this area could be improved by either parental monitoring of diary completion, the use of more objective measures to assess diary variables, or the use of electronic daily diaries that could record specific times that information is entered. This procedure would help to address concerns about the validity of the information provided by the diaries.

The Influence of Additional Stressors and Pain Medication Use

It was also proposed that stress unrelated to SCD pain would intensify the relationship between high SCD pain and sleep that night and between poor sleep during the night and high SCD pain during the day. In addition, it was proposed that pain medication use would attenuate the association between high SCD pain and sleep that night and that the strength of this effect would be stronger for narcotic medication in comparison to analgesic medication. Inconsistent with this second set of hypotheses, additional stress and pain medication use did not evidence a substantial impact on the relationship between SCD pain and sleep, but instead evidenced more direct influences on SCD pain and sleep aspects.

Although results did not support the hypothesis that stress influences the pain-sleep relationship, the findings were consistent with the majority of other research that indicates that stress is related to shorter sleep duration (Sadeh, 1996). Also, this finding and results from the interview data (see Valrie et al., 2005) that suggests that high chronic stress is related to longer average sleep durations lend support to Sadeh's (1996) theory of two adaptive sleep responses to stress: the "turn-on" and "shut-off" responses, respectively. However, high daily stress was not related to sleep quality or sleep irregularity. This finding may indicate that the theory is only useful when examining sleep duration in response to stress. Alternatively, the influence of stress on sleep quality may be mediated in this

population by the pain experience. The finding that high stress is related to high same-day pain in children with SCD is consistent with research examining this relationship in adults and adolescents with SCD (Gil et al., 2003; Gil et al., 2004). The stress-pain relationship, in conjunction with the fact that high SCD pain is related to poor sleep quality that night supports the hypothesis that stress may influence sleep quality through its effect on SCD pain.

As for pain medication use, results do support the hypothesis that pain medication use has a buffering effect on the impact of SCD pain on sleep that night and that the magnitude of the effect is different given the type of medication. However, the nature of that difference was opposite to what was expected and the influence of pain medication on the pain-sleep relationship appeared to be overshadowed by the direct influence of pain medication on sleep. Specifically, taking an analgesic weakened the relationship between high SCD pain and poor sleep quality that night. However, taking an analgesic or a narcotic was related to poor sleep quality that night regardless of pain severity, and it appeared that the positive benefits of taking an analgesic on the pain-sleep relationship was offset by the negative effect of taking an analgesic on sleep quality.

Inconsistent with past research, pain medication use was not related to daily sleep duration. This finding may be due to the fact that the current study was only assessing sleep during the night. Possibly the child was taking naps during the day in response to the sedative effects of taking a pain medication. Pain medication use was also not related to sleep irregularity. As noted earlier, there is a lack of research on factors related to daily sleep irregularity in children.

The above results must be qualified by the fact that there were marked individual differences in pain medication practices. Of the 18 children who reported on medication use, 10 did not take a pain medication during the course of the study. For the entire reporting sample, pain medication was taken on less than half of the pain days reported (e.g., 41.54% of pain days). In contrast, when the analysis was restricted to children who reported taking a pain medication, a pain medication was taken on the majority of pain days reported (e.g., 71.05% of pain days). Similar individual differences were noted in a diary study where parents of 34 children and adolescents with SCD aged 6 to 17 years reported on their children's pain and health-care use (Gil et al., 2000). Results indicated that 62% of their sample reported pain medication use on all of their pain days, while 29% reported no pain medication use despite the fact that they experienced pain.

Notably, these individual differences may help to explain the fact that estimates of pain medication use on pain days in children and adolescents with SCD vary widely across studies. For example, while one diary study of children with SCD reported pain medication use on 86% of pain days for children aged 5 to 13 years (Dampier et al., 2002), another reported pain medication use on only 9% of pain days for children aged 6 to 13 years (Maikler et al., 2001). These same two studies reported pain medication use on 94.3% to 100% of pain days for adolescents with SCD. In contrast, the adolescent sample of Gil et al.'s (2003) study used analgesics on 26% of pain days and narcotics on 19% of pain days. Taken together, it appears that there are marked differences in rates of pain medication use in children and adolescents with SCD and there is a need to understand what factors might be related to these differences.

Research has primarily focused on attitudes of health-care providers and parents as the reason for differential patterns of pain management in children who experience pain. Health-care providers are seen as providing access and basic knowledge to patients and their families, while parents controll their children's pain medication use at home. In a 2002 report, the Institute of Medicine noted disparities in pain management for vulnerable populations (e.g., children and minorities). Primary factors linked to these disparities include communication problems between patients and health care providers (specifically related to pain assessment) and concerns about pain medication addiction and abuse (Sullivan & Eagel, 2005). These findings are consistent with a review of factors affecting pain management in individuals with SCD by Elander and Midence (1996).

Research has also investigated behaviors and attitudes toward pain medication of parents of children who experience cancer, "minor" surgery, and common childhood pains (Ferrell, Rhiner, Shapiro, & Strause, 1994; Finley, McGrath, Forward, McNeill, & Fitzgerald, 1996; Forward, Brown, & McGrath, 1996; Gedaly-Duff & Ziebarth, 1994). Results indicate that parents are concerned that their children may become addicted to pain medication. In addition, they are concerned with side-effects of the medication (specifically respiratory depression) and drug tolerance. A common parental attitude noted across the studies was the desire to give the least amount of pain medication sufficient to address the child's pain to either save pain medications for worse pain or to avoid negative side-effects of medication. This reluctance to give pain medication was evidenced in the current study by the parent of a child who experienced a large amount of pain, but took no pain medication. In addition, the high incidence of narcotic use relative to analgesic use may also be evidence that parents in the current study are reluctant to give their children pain medication and thus

often wait until the pain is severe enough to be treated with a narcotic. Notably, no research has examined parental attitudes toward pain medication use in parents of children with SCD.

Characteristics of individuals are also likely to shape individual differences in medication use. For example, in a recent investigation adolescents with SCD who were more optimistic were better able to match their pain medication use to their SCD pain severity (Pence, Valrie, Gil, Redding-Lallinger, & Daeschner, 2006). Additionally, low stress, low negative affect, and high positive affect in adults with SCD were linked to a stronger relationship between SCD pain severity and narcotic medication use (Porter et al., 2000). In the same study, high stress and high negative affect were related to high analgesic use. Taken together, these results suggest that individuals who experience more positive emotions (e.g., optimism, positive affect) and less negative emotions (e.g., negative affect, stress) are better able to match their pain medication use to the level of their SCD pain.

Non-pain medications were used on approximately half of the diary days (44.59% of diary days) with 6 of the 10 children who reported using a non-pain medication using it throughout the entire study period. Correlations indicated that non-pain medication use may be related to poor sleep quality that night, and non-pain, sedating medication use may also be related to high same-day pain severity and low sleep irregularity that night. These findings are particularly noteworthy due to the dearth of information on non-pain medication use in children and adolescents with SCD.

Clinical Implications and Future Directions. Overall, these results concerning the influences of stress and pain medication use on sleep and SCD pain suggest possible clinical implications and emphasize vital areas for further study. Specifically, these results highlight possible indirect and prolonged effects of stress and pain medication use for patients, their

families, and health care providers. This information suggests to patients and their families the possible benefits of prioritizing stress management as a part of learning to adapt and the possible need to augment or offset the use of pain medications with alternative pain coping strategies. In addition, these results suggest that existing programs for children with SCD and their families may be improved by including stress management information.

As for future research, the utilization of more time-sensitive and frequent measure methodologies would enable researchers to disentangle the role of factors that vary throughout the day, such as stress and medication use, on fluctuations in pain and sleep. For example, a study that incorporated multiple measurements of SCD pain and stress throughout the day with sleep measurements at night would allow researchers to more effectively investigate the possible indirect effects of stress on sleep as mediated by SCD pain. Also, research is needed to investigate specific family and child level factors, beyond pain, that might account for the marked individual differences in pain medication practices in children with SCD and the differences in rates noted across studies. And, given the high incidence of non-pain medication use noted in the current study, additional research is needed to investigate the role that pain and non-pain medications may play in the adaptation of children with SCD. Results from the current study indicate that pain medications negatively impact sleep quality. In addition, narcotics have been found to cause concentration difficulties, and "mental cloudiness" in children (Schecter, 1985; Yaster & Deshpande, 1988). However, research examining the short- and long-term effects of pain medications on sleep, cognition, and school performance in children who experience chronic pain, including children with SCD, is limited (Hander & DuPaul, 1999).

<u>Limitations of the Current Study</u>

Limitations of the present study should be addressed when interpreting the results and designing future research. First, all of the measures were self-report. As mentioned previously, time of assessment could not be verified, thus limiting the validity of the diary information, specifically the sleep information, which is limited by the child's own knowledge and awareness of his/her own sleep and may be biased by other factors (Sadeh, 1996). The use of more objective, time-sensitive measurement would be appropriate to validate and augment information provided by paper and pencil diaries. Daily electronic diaries are one methodology to be considered to replace or augment existing paper diaries. Palermo, Valenzuela, and Stork (2004) compared electronic diaries (e-diaries) and paper diaries assessing pain in 60 children with headaches or juvenile arthritis. Results indicated that though children found both strategies easy to use, the e-diaries produced higher completion, compliance, and accuracy rates than the paper diaries. In addition, compliance was particularly improved for the boys in the study, a notable finding for the current study given that boys were more likely not to complete diaries. However, as with the paper and pencil diary, this method would still not fully address issues of validity of information on the diary or the scope of the information.

In contrast, the use of actigraphy to measure sleep would nicely augment either the current paper and pencil diary or an e-diary. Actigraphy is designed to electronically monitor movement, which is then recorded and interpreted using computer algorithms developed to detect the difference between sleep and waking times (Richards, 2002). It is generally inexpensive, unobtrusive, as the devices are generally about the size of a wristwatch, and able to record continuous information throughout the day. It would allow for objective, time-

sensitive assessment of sleep aspects and even would allow for measurement of sleep during the day, an aspect of sleep not measured as part of the current study. Measurement of daytime sleep may be particularly important as it may be a sign that children are using sleep as a coping strategy. Results from Dampier and associates' (2004) and Maikler et al.'s (2001) diary studies of children and adolescents with SCD indicated that sleep is the most common physical and/or cognitive-behavioral activity used to relieve pain. Also, as suggested by the current study, sleep during the day is possibly related bi-directionally to same-day pain and sleep that night.

Another limitation related to the method of assessment is the uni-dimensional methods of assessing each of the key variables. For example, pain is viewed as a multi-faceted phenomenon and comprehensive approaches to assessing pain are advocated to fully understand and design interventions to treat it (Graumlich et al., 2001; Varni, Thompson, & Hanson, 1987; Walco & Dampier, 1990). However, consistent with similar diary research, the current study utilized only a VAS assessing "average" daily pain. Future studies utilizing daily diaries to assess pain in children may be improved by evaluating multiple dimensions to quantify pain. For example, future studies can utilize a color-coded pain rating scale or assess "present" and "worse" pain during the day (Varni et al., 1987).

Also, as mentioned in the introduction, the conceptualization of stress in the current study was consistent with the environmental perspective, which focuses on stressful events as they uniformly relate to adaptive strain (Cohen et al., 1995). Thus, stress was measured by having the child endorse stressful events he/she experienced during a given day from a checklist of common daily stressors. This strategy was seen as particularly appropriate given the age range of the children in the current study and this method's focus on recognition

55

versus recall. However, alternative dimensions of stress not examined in the current study may be related to the pain-sleep relationship. For example, another dimension of stress is the individual's subjective perception and appraisal of stressors in his or her environment (Lazarus and Folkman, 1984). This dimension of stress captures both the individual's exposure to stressors and the individual's evaluation of their own ability to cope with the demands associated with these stressors. Notably, this dimension has been assessed on daily diaries for adolescents with SCD and has been positively related to same-day pain, health care use, and reductions in school and social activities (Gil et al, 2004). Another dimension of stress not assessed in the current study is the individual's psycho-physiological response to the stressor. When assessing this dimension of stress, which is advocated as a more objective measurement of stress, the focus is on the activation of physiological systems that have been linked to responding to psychological and physiological strain, such as the hypothalamic-pituitary-adrenocortical axis (Cohen et al., 1995). Additional research is needed to examine how perceived stress and the child's psycho-physiological response to stress may influence the pain-sleep relationship in children with SCD.

Even within the environmental perspective, additional stressors beyond traditional daily hassles should be researched to indicate how they may impact pain and sleep in pediatric populations. Maternal stress, maternal psychological distress, and economic stress as reported by the adolescent and the parent have been related to high SCD pain in adolescents with SCD (Ready, 2001). In addition, given the racial make-up of the majority of children with SCD, contextual stressors associated with the African American experience within the United States should be considered. For example, recent research indicates the majority of pre-adolescent African American children have encountered perceived racial

discrimination in their environments (Simons et al., 2002). Racial discrimination is believed to lead to an "exaggerated psychological and physiological stress response" and has been linked to negative physical and psychological outcomes in African American adults (Clark, Anderson, Clark, & Williams, 1999). Research has also linked it to a range of externalizing and internalizing disorders, such as substance use, violent behavior, anger, poor self-esteem, and depressive symptoms in African American children and adolescents (Brook, Rosenberg, Brook, Balka, & Meade, 2004; Caldwell, Kohn-Wood, Schmeelk-Cone, Chavous, & Zimmerman, 2004; Gibbons, Gerrard, Cleveland, Wills, & Brody, 2004; Wong, Eccles, & Sameroff, 2003). However, research is needed to examine how perceived discrimination is possibly related to disease symptoms in chronically ill African American children.

As for assessing medication use, the current study used an open-ended question to determine the medications that the child took. This method of assessment may have been influenced by recall bias of the child (Stone et al., 1991). An alternative strategy used by some researchers is a checklist format (Dampier et al., 2002). That strategy relies on recognition and reduces biases associated with having to recall specific medications. However, it could also limit the scope of the information assessed or significantly increase the length of the diary, thereby increasing problems related to diary completion due to fatigue. Also, dosage of the medication was not measured. Information concerning dosage amount could be used to assess if the dosage amounts of pain medication are appropriately matching up with the level of pain experienced by the child and to determine what dosages of medications may have the most deleterious effects on sleep patterns in this population. For example, it is possible that increasing amounts of pain- or non-pain medication have a more harmful effect on sleep or that at a specific threshold of dosage, medications primarily

influence sleep qualities. In addition, information concerning timing of medication (e.g., do children generally take medication when they reach a specific pain threshold) and number of times medications were taken also needs to be assessed in future research.

The small sample size of the current study may make it hard to generalize these results to the general population of children with SCD. In addition, it made it difficult to fully investigate individual differences in the variables of interest, such as those noted in pain and non-pain medication practices. However, this problem was offset by the large number of diaries completed by the 20 children and the focus of the current study, which was to examine the relationship between daily pain and daily sleep. Future research focused on individual differences should use larger samples that are representative of the SCD population. An additional limitation is the age range of the sample. This age range was chosen to optimize the ability to detect the effects of pain on sleep processes due to the low incidence of sleep problems (Lin-Dyken & Dyken, 1996). However, research needs to be done to assess the influence of pain in infants and adolescents with SCD above and beyond the influence of other factors known to disrupt sleep.

Other limitations include missing data and variability in the number of diaries completed. Since these are common issues when assessing information using frequent monitoring techniques, such as daily diaries (Porter et al., 2000), strategies recommended by Butz and Alexander (1991) to improve diary completion in chronically ill children were employed. For example, the study period was limited to 8 weeks to reduce fatigue, the children were contacted weekly, and the children were rewarded every week they returned diaries. In addition, these issues were handled statistically through the use of multilevel models and the SAS Proc Mixed program, which deletes missing cases at the observation

versus the individual level. After investigation of possible factors that may have influenced diary completion, gender appeared to be the only substantial one of interest. Specifically, girls were more likely to complete the diaries than boys. However, the possibility that there were other systematic differences in the rates of diary completion can not be discounted. Additional research needs to be done to investigate what factors may influence diary completion in this and other pediatric populations.

Additional Areas of Interest

Related to the current study, three additional areas can be highlighted for future research. First is the area of sleep in healthy or non-chronically ill children. Of particular note is the limited amount of systematic research in children concerning normative sleep patterns and factors that may cause sleep disruption in this population (NCSDR, 2003). Possible factors that should be examined are highlighted by some of the primary tasks associated with this developmental period. For example, children aged 8 to 12 years are commonly dealing with issues related to skill development associated with schooling of some form and comparisons of their ability to acquire and master these skills to their same-age peers (Erickson, 1963). Thus, factors related to self and external evaluations of one's ability, such as those made by teachers, family members, and peers, may impact children's sleep patterns. As the field of sleep research in children advances, it will significantly increase the understanding of the complex role that sleep has to play in the functioning of chronically ill children.

Second, there is a need for additional research examining the mechanisms connecting chronic illness symptoms to poor sleep patterns in children, adolescents, and adults as well as examining how these mechanisms may be influenced by specific features associated with

each of these developmental periods and the disease progression (NCSDR, 2003). For example, SCD is a progressive disorder that leads to more frequent and higher intensity pain episodes over the course of the lifespan (Baum et al., 1987; Platt et al., 1991). The current study indicates that within-child, as pain escalates it more adversely impacts sleep quality. However, the study period was only 8 weeks and research is needed to examine how longer and more stable changes in pain patterns may impact sleep patterns over the course of the lifespan.

Lastly, given the negative effects associated with medication use and other barriers leading to varying amounts of use, research on pain coping strategies that can either augment or replace pain medication use and the effectiveness of these strategies is vital to understanding the functioning of chronically ill children. Results from Maikler et al's (2001) diary study indicated that children with SCD used non-pharmacological strategies to manage their pain on 51% of pain days and that adolescents with SCD used non-pharmacological strategies on 86% of their pain days. The adolescent estimate was comparable to results from Dampier and associates' (2004) diary study that indicated that children with SCD aged 5 to 21 years used non-pharmacological strategies on 84.6% of their pain days. Common strategies across the two studies included sleep/rest, applying heat, distraction (e.g., watching TV, listening to music, and reading), massage, and prayer. These were consistent with categories of non-pharmacologic strategies used by parents of children with SCD in Beyer and Simmons' (2004) ethnographic study.

As for the effectiveness of these strategies, Gil and associates are one of the few research teams to systematically examine the effectiveness of cognitive and behavioral strategies to manage SCD pain and their findings support the effectiveness of utilizing active

coping strategies (e.g, diverting attention and re-interpreting pain) versus passive coping strategies (e.g., negative thinking and passive adherence) to manage pain (Gil et al., 1993; Gil et al., 1991, Gil et al., 1997). Results from Gil et al.'s (1991) study indicated that children who use active cognitive and behavioral strategies versus passive strategies to manage their pain are more active and require less health care service when in pain. These results were replicated in a follow-up study conducted 9-months later (Gil et al., 1993) that also suggested that cognitive strategies are un-stable over time in children and adolescents with SCD, suggesting a certain degree of malleability. This prompted Gil and associates (1997) to develop and implement a pain coping skills intervention for children and adolescents with SCD. This intervention has been found to be related to decreased negative thinking and lower pain ratings during a laboratory pain simulation immediately after the intervention, and to increased active coping at 1-month follow-up. Diary results from the intervention group also indicated that on days when children practiced their coping strategies to deal with their pain, they were more active, missed less school, and had fewer health care contacts than days they did not. Related, Beyer and Simmons (2004) had parents rate the perceived effectiveness of various cognitive and behavior strategies and how satisfied their child was with the strategy. On 100 point scales, effectiveness scores ranged from 40 to 95 and satisfaction ranged from 50 to 100.

Taken together, these results indicate that children with SCD and their families are using several cognitive and behavioral strategies in conjunction with or instead of pain medication. However, there is a need for additional research addressing the effectiveness of specific pain coping strategies in children and adolescents with SCD and how they influence

other outcomes, such as sleep. Also, additional research on factors that may be related to the use and effectiveness of coping strategies in this population is needed.

Conclusions

Within the larger context of research addressing adaptation in children with a chronic illness, the current study helps to elucidate how sleep plays a role in the functioning of children who experience chronic pain. In addition, the importance of additional stress and disease management strategies on adaptation in these populations has been highlighted. Clinical/policy implications include the need to raise awareness among clinicians, policymakers, patients, and their parents about the interaction between the child's symptoms and sleep aspects. Additional research should study how other disease symptoms may influence sleep and how sleep may influence other disease symptoms. In addition, this research should examine the role of disease management strategies implemented by the child and his/her family on these relationships.

[1]All medications were classified using information from Medline Plus <http://medlineplus.gov>, a service of the US National Library of Medicine and the National Institutes of Health.

[2]Non-pain medications taken include medications taken for cold/allergy symptoms (e.g., Claritin, cold medicine, Zyrtec), asthma (e.g., Flovent), stomach acid (e.g., Prilosec, Tums), infection (e.g., Penicillin, urinary tract infection medicine), and seizures (e.g., Lamictal). Also, two non-pain medications are taken to reduce disease symptoms associated with SCD (e.g., Hydroxyurea is taken to in decrease sickling of red blood cells and Folic acid is taken to help the body manufacture new red blood cells).

[3]When included in the sleep quality model, the estimates for non-pain, sedating medication use and the interaction between non-pain, sedating medication use and pain severity were significant (Beta = -8.55, $p < .01$ and Beta = -32.28, $p < .01$, respectively). However, results from statistically probing these effects suggested that non-pain, sedating medication use and the interaction between non-pain, sedating medication use and pain severity were not significant in predicting sleep quality. Further examination revealed that 3 of the 6 individuals who reported using a non-pain, sedating medication took the medication on 100% of their diary days and 1 of the 6 used the medication on 91% of his/her diary days. These 4 children accounted for 92.42% of the 211 days of reported non-pain, sedating medication use. Non-pain, sedating medication use was not predictive of sleep duration or sleep irregularity and other medication use was not predictive of any of the sleep variables; thus non-pain medications were excluded from the final multilevel models predicting sleep.

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Table 1

Comparison of Child Baseline and Diary Reports

	Baseline Report		Daily Diary			
	M	SD	M	SD	df	t
Sleep Quality	69.58	25.07	81.67	13.96	19	-2.62*
Sleep Duration (hrs)	9.12	1.12	8.8	1.65	19	0.77
Pain Frequency (% of days)	6.32%	11.87%	21.31%	23.16%	19	-2.66*
Pain Severity[a]	7.73	2.05	52.59	14.54	15	-1.33
Pain Duration (days)	3.25	3.71	-	-		
Stress[a]	40.21	9.4	1.69	1.41	19	-0.00

Note: The (-) indicates that data was not obtained.
[a]Scales for the baseline and diary reports are different for these variables. Thus, variables were rescaled prior to the analysis.
*p<.05

Table 2a

Comparison of Diary Completers versus Diary Non-Completers on Baseline Characteristics

| | Diary Completers | | Diary Non-Completers | | | |
	M	SD	M	SD	df	t
Demographic Variables						
Age (yrs)	10.10	1.07	10.25	1.71	22	0.23
Maternal Education (yrs)	12.70	2.10	12.75	2.22	22	0.04
CDI[a]	46.12	5.38	44.33	10.69	18	-0.46
Puberty[b]	2.54	1.05	1.50	.71	13	-1.33
Study Variables						
Sleep Quality[c]	69.00	19.89	72.5	47.95	3.21	0.14
Sleep Duration (hrs)	9.14	1.29	9.92	.38	21	1.02
Pain Frequency[d] (per yr)	9.03	8.97	4.63	5.44	19	-0.93
Pain Duration (days)	3.45	3.98	2.25	1.89	22	-0.58
Pain Severity	7.48	2.01	9.00	2.00	22	1.39
Stress	40.2	9.29	40.25	11.44	22	0.01

Note: Results may have been affected by the small sample sizes used for analysis. $N = 20$.
[a]N = 17 due to missing data.
[b]N=13 due to missing data.
[c]Analysis indicated assumption of equal variances may have been violated for these variables, so the t-statistic calculated using the Satterthwaite method was reported.
[d]Three children were identified as outliers (two children reported pain frequency of 100 pain episodes a year and one child reported pain frequency of 182 episodes a year). Once removed, pain frequency reports ranged from 1 to 30 episodes per year.
*p < .05.

Table 2b

Comparison of Diary Completers versus Diary Non-Completers on Baseline Characteristics

	Diary Completers	Diary Non-Completers	x^2
Gender (% Female)	65%	0%	5.67*
SCD Type	70%	75%	0.04
Analgesic Use	75%	50%	1.01
Narcotic Use	85%	50%	2.48

Note: Results may have been affected by the small sample sizes used for analysis. N = 20
*p < .05, **p<.01.

Table 3

Correlations between Number of Diaries Completed and Baseline Characteristics

	Number of Diaries Completed
Age	-.29
Gender	-.15
Maternal Education	.31
SCD Type	-.19
CDI[a]	.28
Puberty [b]	-.60**
Sleep Quality	.08
Sleep Duration	-.07
Pain Frequency	-.26
Pain Duration	-.27
Pain Severity	-.20
Stress	-.37
Analgesic Use	.09
Narcotic Use	.53**

Note: Results may have been affected by the small sample sizes used for analysis. N = 20.
[a]N = 17 due to missing data.
[b]N=13 due to missing data.
*p < .05, **p<.01.

Table 4

Daily Stress Checklist: A Comparison of Item Endorsement on Pain versus Non-Pain Days

	% of Pain Day	% of Non-Pain Days	x^2
1. Had too much homework	12.34%	12.61%	0.01
2. Didn't get along with other kids	2.60%	6.86%	3.92*
3. Didn't have anyone to play with	22.08%	9.28%	18.43**
4. Was made fun of	15.58%	11.13%	2.23
5. Was unable to do things my friends did	12.34%	4.08%	14.67**
6. Didn't have money to buy things	27.27%	19.85%	3.91*
7. Nothing fun to do	37.01%	19.85%	19.53**
8. Argued with parents	20.78%	24.30%	0.83
9. Had too much to do around the house	15.58%	5.75%	15.85**
10. Got in trouble	16.23%	2.60%	41.94**
11. Other people at home didn't get along	16.88%	3.71%	33.54**
12. Didn't like the way I looked	5.19%	0.93%	11.85**
13. Parent was away from home	19.48%	10.02%	10.07**
14. Got a bad grade at school	9.74%	8.53%	0.22
15. Too many people told me what to do	11.69%	7.24%	3.15
16. Felt pressured or bossed around by friends	6.49%	7.42%	0.15
17. Not allowed to do things	4.55%	3.71%	0.22

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

Table 5a

Drugs Taken by Participants during the Course of the Study

Drug Type	Drug Name
Analgesic	Aspirin
	Ibuprofen
	Motrin
	Tylenol
Narcotic	Amitriptyline[a]
	Morphine
	Oxycodone
	Oxycontin
	Tylenol with Codeine
Non-Pain, Sedating Medication	Claritin
	Cold Medicine[b]
	Flovent
	Hydroxyurea
	Lamictal
	Zyrtec
Other Medication	Folic Acid
	Penicillin
	Prilosec
	Tums
	Urinary Tract Infection Medication[c]

[a]Amitriptyline is not a narcotic, it is a tricyclic antidepressant. It was coded as a narcotic due to its similarities to the properties of narcotics in the present study. In particular, it can be prescribed for chronic pain and has a sedative effect. The study analyses were run with amitriptyline not coded as a narcotic and coded as a narcotic. The results were not significantly different, so it was decided to present the analysis with amitriptyline coded as a narcotic.
[b]Cold medicine was classified as a non-pain, sedating medication due to the sedative effects of most cold medicines.
[c]Since the exact medication taken for the urinary tract infection could not be determined, it was classified in the "other" category.

Table 5b

Descriptive Information on Medication Use Data

	Across All Diaries		
	% of Diary Days	% of Pain Days	% of Non-Pain Days
Pain Medication Use			
Analgesic Use	3.28%	15.38%	0.00%
Narcotic Use	7.22%	32.31%	0.00%
Combination of Analgesic and Narcotic	1.31%	6.15%	0.00%
Non-Pain Medication Use			
Sedating Medication Use	34.59%	30.59%	40.30%
Other Medication Use	43.11%	46.92%	51.54%
Sub-Sample of Children who Reported Using a Pain Medication			
	% of Diary Days	% of Pain Days	% of Non-Pain Days
Pain Medication Use			
Analgesic Use	6.37%	26.31%	0.00%
Narcotic Use	14.01%	55.26%	0.01%
Combination of Analgesic and Narcotic	2.55%	10.53%	0.01%

Table 6

Correlations Between Diary Variables

	1	2	3	4	5	6	7	8	9
1. Sleep Quality	-								
2. Sleep Duration	.04	-							
3. Sleep Irregularity	-.07	-.46	-						
4. Pain Severity	-.32	-.07	.13	-					
5. Stress	-.06	-.08	.19	.15	-				
6. Analgesic Use	-.13	-.02	.07	.38	.08	-			
7. Narcotic Use	-.29	-.07	.23	.53	.34	.23	-		
8. Sedating Med Use	-.18	.06	-.11	.09	.15	-.02	.14	-	
9. Other Med Use	-.25	.07	-.06	.04	.03	-.05	.10	.77	-

Table 7

Intercept-Only Multilevel Models Predicting Sleep

	Model 1: Sleep Quality (n=702)		
	Variance	SE	Z value
Between Individuals	171.35	62.70	2.73**
Within Individuals	514.77	27.88	18.47**
Total	686.12		
ICC	.25		
	Model 2: Sleep Duration (n=668)		
	Variance	SE	Z value
Between Individuals	.97	.35	2.75**
Within Individuals	2.08	.12	17.99**
Total	3.05		
ICC	.32		
	Model 3: Sleep Irregularity (n=701)		
	Variance	SE	Z value
Between Individuals	2775.74	979.14	2.83**
Within Individuals	5858.58	317.44	18.46**
Total	8634.32		
ICC	.32		

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

Table 8

Intercept-Only Multilevel Model Predicting Pain.

	Model 3: Pain Severity (n=704)		
	Variance	SE	Z value
Between Individuals	106.02	41.91	2.53**
Within Individuals	487.09	26.35	18.48**
Total	593.11		
ICC	.18		

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

Table 9

Multilevel Random Effects Analyses Predicting Sleep Quality

	Variance	SE	Z value
Random Effects	(Conditional error variance components)		
Between Individuals	93.26	58.27	1.60*
Autocorrelated Effect	.18	.05	3.68**
Within Individuals	472.35	30.41	15.53**

	Beta	SE	t value
Fixed Effects			
Intercept	89.27	13.56	6.58**
Pain	-3.72	1.28	-2.91**
Stress	0.53	.99	0.53
Analgesic Use	-6.96	2.68	-2.59**
Narcotic Use	-6.02	2.69	-2.24*
Pain*Stress	-0.32	1.22	0.26
Pain*Analgesic Use	2.81	1.23	2.29*
Pain*Narcotic Use	0.14	0.92	0.16

Note: Only fixed effects related to the intercept and level 1 predictors were reported. Level 2 predictors included age, gender, level of maternal education, SCD type, and person-means for diary variables. No level 2 predictors significantly predicted sleep quality. Total N = 561. N for individuals = 18.
*p<.05, **p<.01

Table 10

Multilevel Random Effects Analyses Predicting Sleep Duration

	Variance	SE	Z value
Random Effects	(Conditional error variance components)		
Between Individuals	1.62	.87	1.87*
Autocorrelated Effect	.09	.05	1.85
Within Individuals	1.94	.12	15.75**

	Beta	SE	t value
Fixed Effects			
Intercept	9.03	1.61	5.62**
Week vs. Weekend	.35	.14	2.49*
Pain	-.08	.08	-1.00
Stress	-.13	.06	-2.07*
Analgesic Use	.08	.18	0.44
Narcotic Use	.27	.17	1.58
Pain*Stress	.05	.08	0.64
Pain*Analgesic Use	-.02	.08	-0.22
Pain*Narcotic Use	-.08	.06	-1.40

Note: Only fixed effects related to the intercept and level 1 predictors were reported. Level 2 predictors included age, gender, level of maternal education, SCD type, and person-means for diary variables. No level 2 predictors significantly predicted sleep duration. Total N = 540. N for individuals = 18.
*p<.05, **p<.01

Table 11

Multilevel Random Effects Analyses Predicting Sleep Irregularity

	Variance	SE	Z value
Random Effects	(Conditional error variance components)		
Between Individuals	4740.54	2663.50	1.78*
Autocorrelated Effect	.25	.05	5.24**
Within Individuals	5545.12	370.47	14.97**
	Beta	SE	t value
Fixed Effects			
Intercept	-63.18	87.35	-0.72
Pain	-1.19	4.31	-0.28
Stress	1.81	3.32	0.54
Analgesic Use	5.90	8.92	0.66
Narcotic Use	6.44	9.26	0.70
Pain*Stress	-2.64	3.80	-0.69
Pain*Analgesic Use	-0.15	4.06	-0.04
Pain*Narcotic Use	3.55	3.17	1.12

Note: Only fixed effects related to the intercept and level 1 predictors were reported. Level 2 predictors included age, gender, level of maternal education, SCD type, and person-means for diary variables. No level 2 predictors significantly predicted sleep irregularity. Total N = 564. N for individuals = 18.
*p<.05, **p<.01

Table 12

Multilevel Random Effects Analyses Predicting Pain Severity

	Variance	SE	Z value
Random Effects	(Conditional error variance components)		
Between Individuals	47.09	30.84	1.53
Autocorrelated Effect	0.25	0.05	5.37**
Within Individuals	415.21	25.87	16.05**
	Beta	SE	t value
Fixed Effects			
Intercept	35.89	33.13	1.08
Sleep Quality	-6.04	0.81	-7.46**
Sleep Duration	1.08	0.95	1.13
Sleep Irregularity	0.29	0.99	0.29
Stress	1.93	0.85	2.27*
Sleep Quality*Stress	0.63	0.62	1.01
Sleep Duration*Stress	-0.05	1.00	-0.05
Sleep Irregularity*Stress	0.53	0.96	0.55

Note: Only fixed effects related to the intercept and level 1 predictors were reported. Level 2 predictors included age, gender, level of maternal education, SCD type, and person-means for diary variables. Age was the only level 2 predictor that significantly predicted pain severity (Beta = 4.72, SE = 2.17, t(12) = 2.18, p = .05). Total N = 645. N for individuals = 20.
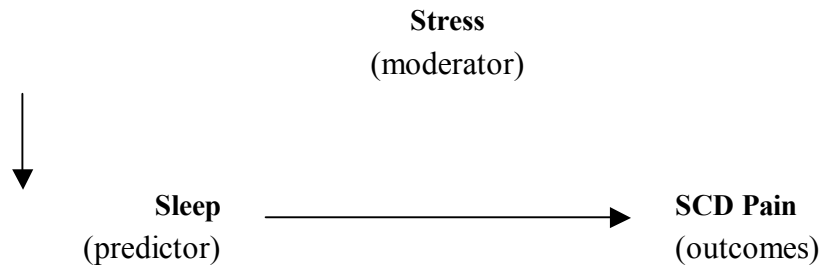*p<.05, **p<.01

Figure 1. Proposed Moderation Hypotheses: (1) Stress moderating the relationship between SCD Pain and Sleep, and (2) Medication Use moderating the relationship between SCD Pain and Sleep.
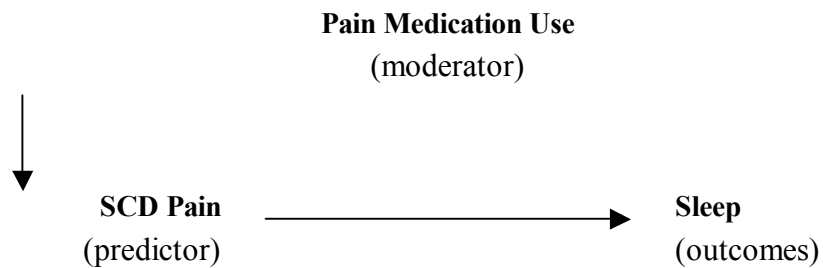
(1a)
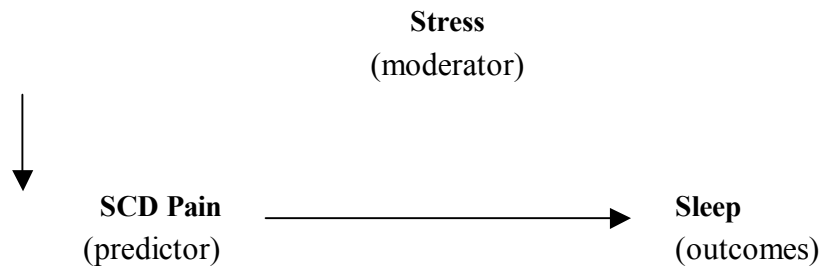
(1b)

(2)

Figure 2. Interaction of Pain Severity and Analgesic Use Predicting Sleep Quality