Sleep-Disordered Breathing in Children and Adolescents with Systemic Lupus Erythematosus and its Association with Executive Functioning

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ABSTRACT

Sleep-Disordered Breathing in Children and Adolescents with
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The relationship between sleep-disordered breathing and executive functioning in children and adolescents with Systemic Lupus Erythematosus (SLE) has not been well-studied, despite literature referring to sleep problems in individuals with SLE. The goals of this study were to examine whether sleep-disordered breathing was more prevalent in children and adolescents with SLE compared to controls, whether there was an association between sleep-disordered breathing and executive functioning, and whether certain risk factors moderated or mediated this relationship.

The SLE group consisted of 22 participants whose parents completed the study questionnaires (*M* age = 15.5, *SD* = 2.70, *range* = 9 - 18) and of which 17 completed the cognitive testing. Twenty-four controls from an attempted demographically matched population completed a subset of the questionnaires (*M* age = 14.2, *SD* = 1.96, *range* = 9 - 17). Parents of those with and without SLE completed the Sleep Disorders Inventory for Students (SDIS). Parents of those with SLE also completed the Behavior Rating Inventory of Executive Function (BRIEF) and Depression and Anxiety in Youth Scale (DAYS). Participants with SLE completed the Delis-Kaplan Executive Function System Trail Making and Verbal Fluency tests and the Wechsler Intelligence Scale for Children-IV/Wechsler Adult Intelligence Scale-III Digit Span test. Disease activity and disease severity variables were collected by chart review.

Results from an independent samples t-test indicated that the SLE sample did not exhibit more sleep-disordered breathing symptoms than controls. For the SLE group, correlation analyses indicated that sleep-disordered breathing symptoms were positively associated with the BRIEF Global Executive Composite score. Multiple regression analyses to determine moderation and mediation in the relationship between sleep-disordered breathing and executive dysfunction were not conducted because of a small sample size.

This study suggests that sleep-disordered breathing is not a major health concern for children and adolescents with SLE, but those with more symptoms of sleep-disordered breathing may exhibit more executive functioning difficulties. This study also suggests that the BRIEF, SDIS, and DAYS questionnaires may be useful screening measures for use with this population. Given several methodological limitations, findings are preliminary. Further research is needed that incorporates larger samples.

CHAPTER 1: INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic inflammatory multi-system autoimmune disease (Jump et al., 2005; McGhee, Kickingbird, & Jarvis, 2004). Immunoregulatory proteins are thought to regulate this inflammation process in SLE (Gabay et al., 1997; Lacki, Samborsi, & Mackiewicz, 1997). Similar immunoregulatory proteins regulate the inflammation process in sleep-disordered breathing (Alberti et al., 2003; Tauman, Ivanenko, O'Brien, & Gozal, 2004). Despite this knowledge, scant research has investigated sleep-disordered breathing in detail in SLE (Cruz et al., 2007; Valencia-Flores et al., 1999).

In a review article by Sweet, Doninger, Zee, and Wagner (2004), the authors recommended future studies to investigate the relationship between sleep disturbance and cognition in SLE in order to better inform clinical practice. The general pediatric literature and heuristic models indicate an association between sleep-disordered breathing and executive dysfunction (Archbold, Girodani, Ruzicka, & Chervin, 2004; Beebe, 2005; Beebe et al., 2004). Although research suggests mild cognitive difficulties in children and adolescents with SLE (Papero, Bluestein, White, & Lipnick, 1990; Wyckoff, Miller, Tucker, & Schaller, 1995), no studies have examined the relationship between sleep-disordered breathing and executive dysfunction in this population. Executive dysfunction imposes a serious risk to children and adolescents with SLE during their critical years of cognitive and educational development. These pediatric sleep speculative models also suggest that risk and resilience factors may contribute to the relationship between sleep-

disordered breathing and executive dysfunction (Beebe, 2005). In SLE, different illness-related risk factors may contribute to this relationship.

The purpose of this study was to conduct a multi-site project to investigate sleep-disordered breathing in SLE. This study attempted to examine a broad developmental age range of children and adolescents with SLE between the ages of 8:0 to 18:11 years old. This study was designed to use a control group and a reliable sleep functioning measure. The first aim was to determine if symptoms of sleep-disordered breathing occurred more in children and adolescents with SLE compared to a control group. The second aim was to determine if there was an association between symptoms of sleep-disordered breathing and executive dysfunction in those with SLE. The third aim was to determine if certain risk factors moderated (i.e., disease severity, disease activity) and/or mediated (i.e., depression) the relationship between sleep-disordered breathing and executive dysfunction in those with SLE.

The following literature review includes a description of SLE and a review of the literature regarding sleep-disordered breathing. This review will also discuss the heuristic models that propose explanations for the association between sleep-disordered breathing and executive dysfunction.

CHAPTER 2: LITERATURE REVIEW

2.1 Systemic Lupus Erythematosus (SLE)

2.1.1 Description

Pierre Cazenave and Henri Schedel provided the first detailed description of SLE in 1851 (Wallace & Lyon, 1999). Today, SLE is described as a disorder of the immune system that is systemic, in that it attacks multiple organs (Jump et al., 2005). These systems may include the skin, blood, joints, lungs, heart, kidneys, liver, brain, and the nervous system (Lash, 1998). Seventy percent of SLE cases are systemic and 50% of those cases will affect a major organ (Lupus Foundation of America, 2006). There are two other forms of lupus including discoid lupus and drug induced lupus (Lupus Foundation of America, 2006). Discoid lupus is limited to a skin rash. Drug induced lupus is a reversible condition resulting in symptoms similar to SLE. It can reportedly develop from the use of some 38 drugs, but most commonly from the use of procainamide, hydralazine, and quinidine. The current study focuses on SLE.

The exact prevalence of SLE is difficult to estimate from the epidemiological literature (Kardestuncer & Frumkin, 1997; McCarty et al, 1995; Michet, McKenna, Elveback, Kaslow, & Kurland, 1985; Siegel & Lee, 1973; Uramoto et al., 1999). In the United States, a study from 1998 estimated that about 40 to 50 people in the United States out of every 100,000 have SLE (Lawrence et al., 1998). A study from 1985, in Sweden, indicated that 39 people out of every 100,000 individuals in Sweden have SLE (Nived, Sturfelt, & Wollheim, 1985). Another study from 1994 reported that in the United Kingdom the prevalence of SLE was 24.7 out of every 100,000 in the population

(Hopkinson, Doherty, & Powell, 1994). In this same study, SLE occurred in 207.0 out of 100,000 Afro-Caribbean females, 48.8 out of 100,000 Asian females, and 20.3 out of 100,000 Caucasian females (Hopkinson et al., 1994). This study highlights that SLE is generally more common in females and ethnic minorities. In a study by Anstey, Bastian, Dunckley, and Currie (1993), the authors concluded there was a prevalence of SLE in 1 out of every 1,900 Australian aborigines, which is twice that estimated in non-aboriginal Australians.

Currently, no known single gene causes SLE; however, there is an association between some genes and the disease. An association exists between a gene on chromosome one and the occurrence of SLE in some families (Tsao et al., 1997). There is also an association between the gene on chromosome six, called the immune response gene, and the occurrence of the disease (van der Linden et al., 2001). Some individuals with SLE have an altered Runx-1 binding site (Prokunina et al., 2002). Approximately 20% of SLE patients have a close relative, including a parent or sibling with the disease. However, only 5% of the children born to individuals with SLE will develop the disease (Lupus Foundation of America, 2006), suggesting environmental contributions. Some environmental factors may trigger disease onset and/or exacerbate SLE symptoms. These factors include infections, antibiotics, ultraviolet light, extreme stress, certain drugs, and hormones (Lupus Foundation of America, 2006).

The body's immune system normally makes proteins called antibodies to protect it against exogenous antigens such as viruses and bacteria. In an autoimmune disorder such as SLE, the immune system loses its ability to tell the difference between exogenous antigens and its own cells and tissues. In response, the immune system makes antibodies

directed against the self, called autoantibodies. The autoantibodies react with the body's own cells and tissues to form immune complexes. These immune complexes build up in the tissue and cause inflammation, injury to the tissue, and pain.

SLE is different from other autoimmune disorders because it affects many tissues and organs. In contrast, for example, in multiple sclerosis, the autoimmune reaction is directed against the brain and spinal cord. The autoimmune reaction in rheumatoid arthritis attacks bone joints. In Graves' disease, anti-thyroid antibodies stimulate an overproduction of hormones. Hashimoto's thyroiditis, also affecting the thyroid by an autoimmune reaction, causes inflammation and later dysfunction of the thyroid. The autoimmune reaction in Crohn's disease is directed against the gut and intestinal tract. Finally, in Type 1 diabetes mellitus, the autoimmune reaction attacks the islet cells of the pancreas.

2.1.2 Clinical manifestations

The course of SLE involves intense flares and periods of remission. The major reported symptoms include the following: achy joints, fever, swollen joints, extreme fatigue, skin rashes, anemia, kidney involvement, chest pain, butterfly-shaped rash across cheeks and nose, sun sensitivity, hair loss, Raynaud's phenomenon (i.e., a condition affecting blood flow to the extremities when exposed to temperature changes or vibrations), seizures, and mouth or nose ulcers (Kotzin, 1996). For females, an increase in disease symptoms sometimes occurs before menstruation and/or during pregnancy (Kotzin, 1996).

Some individuals with SLE have central nervous system involvement, characterized by neuropsychiatric symptoms (Arkachaisri & Lehman, 1999; Klein-Gitelman, Reiff, & Silverman, 2002). These symptoms usually manifest within the first year of diagnosis of SLE. According to the American College of Rheumatology nomenclature and case definitions, there are 19 neuropsychiatric symptoms associated with SLE (American College of Rheumatology Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature, 1999). Symptoms associated with central nervous system involvement include aseptic meningitis, cerebrovascular disease, demyelinating syndrome, headaches, movement disorder, myelopathy, seizure disorders, acute confusional state, anxiety disorder, cognitive dysfunction, mood disorder, and psychosis. Symptoms associated with peripheral nervous system involvement include acute inflammatory demyelinating polyradiculoneuropathy, autonomic disorder, single/multiplex mononeuropathy, myasthenia gravis, cranial neuropathy, plexopathy, and polyneuropathy. There are inconsistent reports of the prevalence of neuropsychiatric symptoms in SLE in children, with statistics ranging from 48% to 95% (Sibbitt et al., 2002; Steinlin et al., 1995). Less formal chart review studies indicate that between 36% and 48% of children from SLE samples demonstrated depressive symptoms (Parikh, Swalman, & Kim, 1995; Steinlin et al., 1995).

Neuropsychiatric symptoms in SLE are thought to be caused by antibodies attacking blood vessels in the body, causing these blood vessels to be ineffective in delivering nutrients and oxygen to the central nervous system (Lupus Foundation of America, 2006). Nerve tissue damage occurs when nerves lack these vital elements. Imaging studies in adults with SLE with central nervous system involvement have

identified focal deficits, diffuse bitemporal-parietal patterns, structural changes including atrophy, and volumetric changes (Chinn et al., 1997; Rogers et al., 1992).

2.1.3 Diagnosis

Diagnosis of SLE occurs between the age of 15 and 45 in approximately 80% of individuals, with diagnosis in childhood occurring in approximately 15% to 20% of cases (McGhee et al., 2004; Stichweh, Arce, & Pascual, 2004). No single laboratory test can confirm the presence of SLE (Lupus Foundation of America, 2006); however, several laboratory tests help to identify the disease. A diagnosis of SLE occurs after a review of the patient's medical history, a physical examination, and the results of laboratory tests related to immune status. The lupus erythematosus (LE) cell test was the first laboratory test developed to help diagnose SLE (Dubois, 1953). The administration of this test is rarely used today because it is not specific to SLE and can be positive in other disorders (i.e., such as rheumatoid arthritis, Sjogren's syndrome, scleroderma, patients with liver disease, and in people taking certain drugs).

Currently, three categories of diagnostic tests help to diagnose SLE (National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2001). The three types of tests assess the following: blood cell abnormalities (i.e., tests for anemia, leucopenia, and thrombocytopenia), autoimmunity (i.e., antinuclear antibody [ANA], anti-Sm, anti-nDNA, anti-Ro [SSA], anti-La [SSB], complement, erythrocyte sedimentation rate (ESR), C-reactive protein [CRP], antiphospholipid antibodies [APL's], syphilis serology, anticardiolipin antibody [ACA], and lupus anticoagulant) and kidney function (i.e., glumerular filtration rate, urinalysis, serum creatinine concentration, and kidney biopsy).

The American College of Rheumatology devised 11 criteria, of which 4 should be present, to help diagnose SLE (Hochberg, 1997; Tan et al., 1982). The SLE criteria include symptoms of malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorder, neurological disorder, hematologic disorder, immunologic disorder, and abnormal ANA titer (Tan et al., 1982). Physicians apply these diagnostic criteria to both adults and children.

2.1.4 Treatment

There is no cure for SLE; however, medication and lifestyle choices help to control symptoms and prevent flares. For photosensitive individuals with SLE, avoidance of excessive sun exposure and use of regular sunscreen helps prevent rashes (Lupus Foundation of America, 2006). Regular exercise assists in preventing muscle weakness and fatigue. Immunizations protect against some infections. Emotional rest, social support, and counseling help to relieve stress (National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2001). A healthy well-balanced diet and physical rest also help to alleviate symptoms. Smoking, excessive consumption of alcohol, too much or too little of a prescribed medication, or postponing regular medical checkups can result in an increase in flare-ups and disease activity. Medication for symptom management depends on symptoms and organ involvement. Medications commonly used include non-steroidal anti-inflammatory drugs, acetaminophen, corticosteroids, antimalarials, immunomodulating drugs, and anticoagulants.

2.1.5 Mortality and morbidity

Mortality rates in SLE are associated with socioeconomic status, individual access to health care, educational background, ethnicity due to low socioeconomic status and reduced access to healthcare, endemic infection rates, disease activity, renal involvement, and central nervous system symptoms (Cook, Gladman, Pericak, & Urowitz, 2000). Cardiac disease is a significant cause of morbidity and mortality in children and adults with SLE. Pulmonary function is abnormal in a majority of children with SLE. When it occurs, mortality is 90% even with treatment by corticosteroids and other immunosuppressive agents (Ciftci et al., 2004; Paran, Fireman & Elkayam, 2004). In the past, Lupus nephritis led to increased morbidity and mortality in SLE; however, because of successful treatment with cyclophosphamide or azathioprine, prognosis has increased to a survival rate of 94% (Hagelberg et al., 2002). In children, neuropsychiatric symptom involvement is associated with significantly higher rates of morbidity and mortality (Vyas, Hidalgo, Baqi, Von Gizyki, & Singh, 2002).

The survival rate of individuals with SLE has drastically improved because of earlier diagnosis and better approaches to therapy. These advancements in treatment help to control acute organ attack and inflammatory response. In 1955, the 5-year survival rate for those with SLE was less than 50% (Merrel & Shulman, 1955). In the 1960's, physicians began prescribing glucocorticosteroids, which prolonged the lives of these individuals. In 1995, the 5-year survival rate rose to 93% and the 20-year survival rate was 68% (Abu-Shakra, Urowitz, Gladman, & Gough, 1995). A report from 2004 indicated that the 5-year survival rate for pediatric onset SLE was 100% and the 10-year survival rate was 86% (Miettunen et al., 2004).

2.1.6 Cognitive functioning

A literature review uncovered only two studies examining cognitive functioning in children with SLE. A study by Papero and colleagues (1990) compared 21 children with SLE with a mean age of 15 years old who had no overt central nervous system involvement to 11 children with juvenile rheumatoid arthritis. The participants constituted a middle class sample, with 86% being female and 71% being African American. The participants were administered a battery of neuropsychological tests (i.e., Wechsler Intelligence Scale for Children-Revised, Wisconsin Card Sorting Test, Category Test, Seashore Rhythm, Speech Sounds Perception, Finger Tapping, Hand Dynamometer, Reitan-Klöve Sensory Perceptual Exam, and Trail Making tests). The SLE group had average intellectual abilities (Full Scale IQ, $M = 95.8$, $SD = 20.2$). They displayed a statistically but not clinically significant lower score on a complex problem solving task compared to those with arthritis, with the score in the low end of the average range ($M = 90$, $SD = 14.4$). A longer duration of SLE was associated with more cognitive difficulties. In this study, 43% of the children with SLE had neuropsychological difficulties compared to only 18% of those with juvenile rheumatoid arthritis. Cognitive difficulties were defined by a score two or more standard deviations below the individual's FSIQ.

Another study compared 8 children with SLE ranging in age from 9 to 17 years old to neuropsychological test normative data, but not to a healthy control group (Wyckoff et al., 1995). Females comprised 75% of the participants. Ethnicity of the sample was not reported. The participants were administered a battery of cognitive tests (i.e., Wechsler Intelligence Scale for Children-Revised, Wechsler Adult Intelligence

Scale-Revised, Wide Range Achievement Test, Gates Comprehension, Trails A and B, Finger Oscillation Test, Wechsler Memory Scale, Stanford Binet Intelligence Scale-Fourth Edition Memory Scale, Achenbach Child Behavior Checklist, and Achenbach Youth Self Report). Performances were below the normal range on the Wechsler Memory Scale (M = 70.0, SD = 8.4) and Stanford Binet Memory scale (M = 74.4, SD = 25.8), and were low average on the measures of intelligence (Full Scale IQ, M = 85.2, SD 13.9). The authors described slow sequential processing speed on Trails B; however, a standardized score was unavailable for verification. Despite the small sample size and possible low power in these studies, results suggest the presence of mild cognitive difficulties in small samples of children and adolescents with SLE.

2.1.7 Summary of SLE

In summary, SLE is a chronic inflammatory multi-system autoimmune disease. In the U.S., SLE occurs in 40 to 50 people out of every 100,000, with 15% to 20% of all SLE cases being children (McGhee et al., 2004; Stichweh et al., 2004). Although children with SLE have the same disease symptoms as adults, SLE can be even more devastating for children. Children have higher rates of organ involvement and a more aggressive clinical course compared to adults (Rood et al., 1999). Since 80% of individuals with SLE develop the disease between the age of 15 and 45 (Lupus Foundation of America, 2006), there are a limited number of children with SLE. Therefore, few research studies have investigated functioning in these children. The two studies that investigated cognitive functioning in children with SLE suggest mild

cognitive difficulties. The current study aims to provide more detailed information into the area of executive function in children and adolescents with SLE.

2.2 Sleep-Disordered Breathing

2.2.1 Description

William Hill (1889) provided the first description of sleep-disordered breathing, explaining that symptoms caused "backwardness and stupidity" in children. He described this impaired daytime functioning as secondary to impairment in cerebral functions. Recent research suggests that children with sleep-disordered breathing have executive functioning, academic, and behavioral difficulties (Archbold et al., 2004; Beebe et al., 2004; Lewin, Rosen, England, & Dahl, 2002). Together these deficits are termed "neurobehavioral dysfunction" because of their presumed association with impaired brain functioning.

Sleep-disordered breathing is the overarching term referring to a spectrum of severities of upper airway resistance problems. The spectrum ranges in severity in the following order from mild to severe: primary snoring, upper airway resistance syndrome, partial obstructive hypoventilation hypopneas, and obstructive sleep apnea (Anstead, 2000). Sleep-disordered breathing can be caused by adenotonsillar hypertrophy, over-relaxed muscles in the throat, fat deposits in the throat, and nasal deformities (Ali, Pitson, & Stradling, 1996; Ward & Marcus, 1996).

At the mild end of the spectrum, individuals have increased difficulty in breathing because of airway resistance and have minimal arousals, but no apnea (complete pause in breathing), hypopnea (partial pause in breathing), or hypoxemia (insufficient oxygenation

of the blood; Anstead, 2000). At the more severe end of the spectrum, the common nighttime symptoms include loud snoring, breathing pauses, struggling to breathe, restless sleep, sweating, and odd sleeping positions. Furthermore, the upper airway collapses causing hypopnea or apnea, resulting in recurrent arousals from sleep and leading to sleep deprivation and waking hypersomnolence. Individuals with the more severe forms experience decreased blood oxygenation saturation levels, producing hypoxemia in surrounding tissue and in the brain (Dahl, 1996; Marcus & Loughlin, 1996). These repeated hypoxic episodes return to normal blood oxygenation saturation levels throughout the night. Symptoms including respiratory disturbance, increased rates of arousal, and repeated fragmentation of sleep occurring during the night are related to a decrease in optimal daytime functioning (Greenberg, Watson, & Deptula, 1987; Randazzo, Muehlbach, Schweitzer, & Walsh, 1998).

Research indicates that sleep-disordered breathing is related to underlying inflammation (Alberti et al., 2003; Tauman et al., 2004). Immunoregulatory proteins (i.e., also called cytokines) mediate and regulate immunity, inflammation, and hematopoiesis and there are many different types of these proteins involved in this process (i.e., interleukins, interferon gamma, transforming growth factor, tumor necrosis factor, and c-reactive protein). In this research area, a literature review only found one study investigating immunoregulatory proteins in children. This study investigated sleep-disordered breathing in 81 children ranging in age from 3 to 18 years and indicated an increase in c-reactive protein (Tauman et al., 2004) in this group. Other literature has investigated immunoregulatory proteins in adults with sleep-disordered breathing. For example, a study by Alberti and colleagues (2003) examined immunoregulatory proteins

in a subset of 18 adults with obstructive sleep apnea and 20 controls. Results from this study indicated higher levels of tumor necrosis factor, an increase in interleukin 6, and a significant decrease in the levels of interleukin 10 among those with obstructive sleep apnea compared to the control group. In a study by Shamsuzzaman and colleagues (2002), the authors compared 22 adults with obstructive sleep apnea to 20 controls matched for age and body mass index. In this study, c-reactive protein levels were higher in those with obstructive sleep apnea than in controls.

Research indicates that demographic factors such as socioeconomic status, ethnicity via socioeconomic status, and body mass index are related to sleep-disordered breathing. A study by Chervin and colleagues (2003) investigated sleep-disordered breathing in 145 children from 8 to 11 years old, of which 40% were male. In this sample, 58% were non-African American and 42% were African American. Parents completed the Pediatric Sleep Questionnaire. The results indicated there was an association between the existence of sleep-disordered breathing and lower socioeconomic status, when controlling for ethnicity (Chervin et al., 2003). Another study by Urschitz and colleagues (2004), evaluated 1,144 children in third grade for primary snoring. In this group, there was an association between snoring and lower socioeconomic status. A study by Beebe and colleagues (2006) investigated the relationship between obesity and sleep-disordered breathing in 60 overweight adolescents ranging in age from 10 to 16.9 years old. The overweight group was comprised of 67% females and 97% African Americans. These participants were compared to 22 healthy children. Procedures included a polysomnography study, actigraphy, and a parent-report questionnaire called the Children's Sleep Habits Questionnaire. The overweight children exhibited more

sleep-disordered breathing than the healthy controls. Other studies evaluating overweight children indicate 24% (Mallory, Fiser, & Jackson, 1989) to 36% (Marcus & Loughlin, 1996) of the sample groups had sleep-disordered breathing.

2.2.2 Sleep-disordered breathing in children and adolescents

The most recent national studies of sleep problems were conducted with children and adolescents in 2004 and 2006 by the National Sleep Foundation (2004, 2006). Two studies were conducted examining sleep functioning in a sample of 646 school age children ranging in age from 6 to 10 years old and a group of 1,602 adolescents ranging in age from 11 to 17 years old. Results from these parent-report surveys indicated that snoring occurred in 18% of children and adolescents. A study by Johnson and Roth (2006) examined sleep-disordered breathing by parent and adolescent report in 1,014 adolescents between the age of 13 and 16. Results of this study suggested that approximately 20% snored and 3% to 6% of adolescents had obstructive sleep apnea symptoms. Sanchez-Armengol and colleagues (2001) examined sleep-disordered breathing in a sample of 101 adolescents from 12 to 16 years old. In this study, results from a cardiorespiratory polygraphy study indicated 29% of these individuals snored and sleep apnea occurred in 3% of the adolescents.

Sleep-disordered breathing is common in children with chronic medical illness, including children with diabetes and sickle cell disease (SCD). In SCD, research indicates that obstructive sleep apnea and nighttime oxygen desaturation occurs in up to 40% of these children and adolescents (Castele, Stohl, Chester, Brittenham, & Harris, 1988; Franco et al., 1996). In this population, there is an association between low oxygen

saturation and high rates of painful crises. One study investigated sleep-disordered breathing in a sample of 35 children with SCD ranging in age from 4 to18 years old, with 74% of the sample being male (Kothare, Grant, Coleman, & Dampier, 2005). Ethnicity information was unavailable, although a majority of individuals with SCD are African American. Results indicated that these children had sleep disruption problems, as indicated by a higher prevalence of excessive daytime sleepiness and sleep-disordered breathing. Research also suggests children with diabetes have co-occurring obstructive sleep apnea (Villa et al., 2000). A study by Villa and colleagues (2000) investigated obstructive sleep apnea in 25 children with insulin-dependent diabetes mellitus. These children ranged in age from 5 to 11 years old, were mostly male (76%), and were of average weight. Information regarding ethnicity was unavailable. The children with diabetes had a higher prevalence of obstructive sleep apnea than 20 age-matched controls. Specifically, sleep-disordered breathing was associated with duration of diabetes and to their glycaemic control.

Children with neurodevelopmental disorders are also reported to have a high incidence of sleep-disordered breathing. In a clinic based questionnaire study, approximately 20% of the 83 children with spina bifida had moderate to severe sleep-disordered breathing (Kirk, Morielli, & Brouillette, 1999). Another research study investigated sleep-disordered breathing in 46 children diagnosed with Attention-Deficit Hyperactivity Disorder (ADHD) ranging in age from 5 to 9 years of age, of which 79% were male (Owens, Maxim, Nobile, McGuinn, & Msall, 2000). Information on ethnicity was unavailable. This study revealed that children with ADHD had more symptoms of sleep-disordered breathing than 46 healthy controls. A study that examined sleep-

disordered breathing among 23 children with Down Syndrome reported an increase in sleep-disordered breathing in this population, including more nighttime movements and arousals than a healthy control group (Levanson, Tarasiuk, & Tal, 1999).

2.2.3 Executive dysfunction and sleep-disordered breathing

One consequence of sleep-disordered breathing may be problems in executive function. Executive functions are cognitive abilities used to control and regulate one's behaviors, and are higher-level abilities that involve attention, problem-solving, working memory, mental flexibility, and abstract reasoning. Beebe and Gozal (2002) offer a provisional prefrontal cortex model (see Figure 1) of sleep-disordered breathing describing the daytime impairments first described by Hill (1889). In this causal model, sleep disruption, hypoxemia (insufficient oxygenation of the blood), and hypercarbia (presence of high levels of carbon dioxide in the blood) alter restorative processes that occur during sleep. These disruptions interrupt the functional homeostasis and neuronal viability within the prefrontal cortical areas, leading to dysfunction of the brain's cognitive executive system. Subsequently, this disruption results in adverse day time effects including difficulties with mental manipulation, poor judgment/planning, disorganization, and impulsivity. Furthermore, a neurobehavioral functioning heuristic model of sleep-disordered breathing by Beebe (2005) proposes that certain risk and resilience factors may contribute to the relationship between sleep-disordered breathing and executive dysfunction in the pediatric population (see Figure 2). In this model, illness-related (i.e., disease duration, disease activity, disease severity), demographic (i.e., age, gender, socioeconomic status, cognitive reserve, body mass index), and comorbid

(i.e., depression) factors are proposed to potentially moderate the relationship between sleep-disordered breathing and executive dysfunction.

Several research studies have investigated executive functioning in children with sleep-disordered breathing. Beebe and colleagues (2004) investigated cognitive performance among the spectrum of severity of sleep-disordered breathing (i.e., primary snoring, mild OSA, and moderate-severe OSA) in 32 children ranging in age from 6 to 12 years old compared to controls. From the overall sleep-disordered breathing group, 59% were males and 37% were reported to be from a minority population. Procedures included a polysomnography study, cognitive testing (i.e., Wechsler Intelligence Scale for Children-Third Edition, Wide Range Assessment of Memory and Learning, Stroop Test, Gordon Diagnostic System, NEPSY, and Wisconsin Card Sorting Test) and parent-report measures including the Children's Sleep Habits Questionnaire, the Behavioral Assessment Scale for Children (BASC), and the Behavior Rating Inventory of Executive Function (BRIEF). The authors concluded that some subgroups of these children displayed clinically and statistically significant elevated scores on the BRIEF and BASC on measures of impulsivity (i.e., primary snoring group), emotional control (i.e., primary snoring group, moderate-severe OSA group), working memory (i.e., primary snoring group, moderate-severe OSA group), planning (i.e., primary snoring group), and self-monitoring (i.e., primary snoring group) compared to 17 controls. In addition, the authors concluded that some subgroups displayed only statistically significant elevated scores on the BRIEF and BASC on measures of impulsivity (i.e., mild OSA group, moderate-severe OSA group), emotional control (i.e., mild OSA group), self-initiation of activities (i.e., primary snoring group, mild OSA group, Moderate-Severe OSA group),

working memory (i.e., mild OSA group), organization (i.e., primary snoring group, moderate-severe OSA group), and self-monitoring (i.e., mild OSA group, moderate-severe OSA group). The authors also reported that all groups exhibited mildly decreased verbal fluency (low end of average) and visual attention skills (low average).

Some studies investigated cognitive functioning in individuals with sleep-disordered breathing of different levels of severity, such as in those with moderate to severe obstructive sleep apnea. One study investigated cognitive functioning in 28 children ranging in age from 4 to 12 years-old, with 69% of the sample being female (Lewin et al., 2002). Information on ethnicity was unavailable. These individuals were at the severe end of the sleep-disordered breathing spectrum with moderate to severe obstructive sleep apnea. Procedures included a polysomnography study, administration of the Differential Abilities Scale, and parent-report questionnaires including the Brouillette Apnea Symptom Scale and Achenbach Child Behavior Checklist. Compared to an age-matched comparison group of 10 children, the children with obstructive sleep apnea had statistically but not clinically significant more behavioral problems and they demonstrated mild difficulty on a task involving visual processing speed and sustained attention.

Some studies have investigated cognitive functioning in individuals with mild levels of sleep-disordered breathing. A study by Archbold and colleagues (2004) examined cognitive functioning in 12 children from 8 to 11 years old with only mild levels of sleep-disordered breathing. Procedures included a polysomnography study, sleep latency test, and administration of cognitive testing (i.e., Integrated Visual and Auditory Continuous Performance Test, Children's Memory Scale, Children's Category

Test, Wechsler Abbreviated Scale of Intelligence, and Wechsler Individual Achievement Test). These children had significant deficits, scoring in the borderline range, in areas of executive functioning including sustained attention, vigilance, and mental flexibility, but had no impairment in general intelligence. In this study, there was an association between a higher arousal index from a polysomnography study and low mental flexibility on a problem solving task.

Research that has investigated primary snoring in children indicates a decrease in executive functioning abilities in this group as well. For example, a study by Kennedy and colleagues (2004) evaluated 13 Caucasian children ranging in age from 5 to 10 years old who snored compared to 13 children who did not snore. Procedures included a polysomnography study and administration of cognitive testing (i.e., Wechsler Preschool and Primary Scale of Intelligence-Revised, Wechsler Intelligence Scale for Children-Third Edition, Wide Range Assessment of Memory and Learning, and Auditory Continuous Performance Test). Although these children had a normal obstructive respiratory disturbance index on the polysomnography study, there were some polysomnographic variables that were related to cognitive functioning. For example, there was a relationship between the severity of neurocognitive difficulties with the number of mild oxygen desaturations, obstructive hypopneas, and respiratory arousals. Specifically, the authors reported that those who snored had statistically significant lower scores on measures of intelligence and memory, but not clinically significant as these scores were in the lower end of the average range. These authors also indicated that those who snored had statistically significant lowered scores on a measure of selective and sustained attention. In another study by Blunden, Lushington, Kennedy, Martin, and

Dawson (2000), participants included 16 children who snored from 5 to 10 years old, of which 44% were male. There was no indication of ethnicity. The control group consisted of 16 individuals who did not snore. Procedures included a polysomnography study, administration of cognitive testing (i.e., Wechsler Preschool and Primary Scale of Intelligence-Revised, Wechsler Intelligence Scale for Children-Third Edition, Wide Range Assessment of Memory and Learning, and Auditory Continuous Performance Test), and parent-report questionnaires including the Achenbach Child Behavior Checklist and Sleep Disturbance Scale for Children. According to the authors, the children who snored had significantly impaired attention, and although within the normal range, lower memory and intelligence scores.

2.2.4 Sleep-disordered breathing and its relationship with executive functioning in SLE

Sleep-disordered breathing has not been extensively studied in SLE and research findings are inconsistent, despite the fact that clinicians and patients refer to sleep problems. A pilot study investigated sleep functioning assessed by the Children's Sleep Habits Questionnaires in 20 adolescents with SLE that ranged in age from 14 to 20 years old (Cruz et al., 2007). This study initially concluded that these adolescents exhibited more symptoms of sleep-disordered breathing compared to normative scores and a control group. However, through recent personal communication with the authors (M. Grant, Ph.D, M. Cruz, M.D., personal communication, April, 16, 2008), these authors indicated the study was withdrawn due to a significant design flaw. In this study, the adolescents were initially compared to a significantly younger control group. When the SLE group was then compared to a comparably aged control group there were no

significant differences in sleep problems (i.e., sleep-disordered breathing, daytime sleepiness, bedtime resistance, and sleep duration problems). The results from this study suggest that sleep problems may not be a concern for adolescents with SLE.

Valencia-Flores and colleagues (1999) also conducted a study to investigate sleep disorders in individuals with SLE; however, this study was conducted with an adult population that consisted of a small sample of 14 women ranging from 20 to 53 years old. Ethnicity information was unavailable. These researchers used polysomnography in their study and found abnormalities in respiration and movement (i.e., periodic leg movement) during sleep in these SLE patients. Fourteen percent of their sample had frequent alpha wave intrusions in their sleep EEG. The SLE group was sleepier during the day than the normal group and sleepiness in the SLE group was related to sleep fragmentation (more arousals and stage transitions). The magnitude of the difference was relatively small. Disease activity was associated with decreases in sleep efficiency and delta sleep, and with increases in sleep fragmentation. Despite being an adult study, this study suggests that sleep problems may occur in the SLE population, specifically those who are adults.

In SLE, illness-related factors (i.e., disease activity, disease severity, depression) may be the underlying variables that may make individuals with SLE more at risk for sleep-disordered breathing and executive functioning difficulties. Illness-related factors also may be the underlying variables that could contribute to the relationship between sleep-disordered breathing and executive dysfunction in SLE. Specifically, when individuals with SLE have an increase in disease activity, immunoregulatory proteins are active in the body. Some of these proteins have a crucial anti-inflammatory role by controlling the level of pro-inflammatory proteins (Xing et al., 1998). Only research

studies in the adult SLE population have examined immunoregulatory proteins in detail in SLE. One study by Lacki and colleagues (1997) investigated immunoregulatory proteins in 71 adults with SLE, of which 97% were women. In this study, there was an elevation of interleukin 10 and interleukin 6 in those with SLE compared to those with rheumatoid arthritis. Another study by Gabay and colleagues (1997) examined immunoregulatory proteins in 52 adults with SLE. These authors reported that those with SLE displayed an increase in interleukin 6 and tumor necrosis factor. In another study by ter Borg, Horst, Limburg, van Rijswijk, and Kallenberg (1990), c-reactive protein levels were higher in a group of 71 adults with SLE during disease exacerbations and infections than before or after these times. This research is important because as previously mentioned, immunoregulatory proteins are also actively involved in sleep-disordered breathing. Therefore, in SLE, illness-related factors may make some individuals more susceptible to sleep-disordered breathing and executive functioning difficulties.

2.2.5 Summary of sleep-disordered breathing

In summary, there is limited and conflicting research investigating sleep-disordered breathing in SLE (Cruz et al., 2007; Valencia-Flores et. al., 1999). Research indicates that immunoregulatory proteins are involved both in the inflammation process in SLE and sleep-disordered breathing (Alberti et al., 2003; Gabay et al., 1997; Lacki et al., 1997; Tauman et al., 2004), which suggests that those with SLE may be at risk for sleep-disordered breathing. The literature and heuristic models suggest a relationship between sleep-disordered breathing and executive dysfunction (Archbold et al., 2004; Beebe, 2005; Beebe and Gozal, 2002; Beebe et al., 2004). In addition, a heuristic model

by Beebe (2005) proposes that risk and resilience factors, such as illness-related factors, may contribute to the relationship between sleep-disordered breathing and executive dysfunction. The aim of the current study was to provide further detailed information into sleep-disordered breathing in children and adolescents with SLE.

2.3 Present Study

2.3.1 Purpose and rationale

There is scarce research on sleep-disordered breathing and its relationship with executive functioning in children and adolescents with SLE. The first goal of this study was to examine the occurrence of sleep-disordered breathing in a pediatric sample with SLE (age range = 8 to 18 years old). There are inconsistent findings in research investigating sleep-disordered breathing in this population (Cruz et al., 2007; Valencia-Flores et. al., 1999). However, a formal polysomnography study found abnormalities in respiration and movement during sleep in an adult SLE sample (Valencia-Flores et. al., 1999). The inflammation in SLE is regulated by immunoregulatory proteins (Gabay et al., 1997; Lacki et al., 1997), and immunoregulatory proteins have also been found to contribute to sleep-disordered breathing (Alberti et al., 2003; Tauman et al., 2004). Therefore, those with SLE with more disease activity or more profound disease severity may be at increased risk for developing sleep-disordered breathing. Hence, further investigation of sleep-disordered breathing in a younger sample of individuals with SLE was warranted. The present study was set forth to evaluate a broad age range of children and adolescents, recruit for an adequate sample size, use a reliable sleep questionnaire, and use a comparison control group.

Difficulties with executive functioning have been documented in pediatric samples with sleep-disordered breathing (Archbold et al., 2004; Beebe et al., 2004). Furthermore, the literature investigating cognitive functioning in children with SLE indicates mild cognitive difficulties in this population (Papero et al., 1990; Wyckoff et al., 1995). The second goal of this study was to examine whether symptoms of sleep-disordered breathing were related to executive functioning difficulties. To evaluate executive functioning, the present study was designed to use a multi-modal approach using both questionnaires and paper/pencil measures to assess executive functioning. These study measures will be discussed in relation to their usability as screening measures. Heuristic sleep models propose that certain risk and resilience factors may contribute to the relationship between sleep-disordered breathing and executive dysfunction (Beebe, 2005; Beebe & Gozal, 2002). Therefore, the third goal of this study was to investigate risk factors that may be specific to SLE and may contribute to the relationship between sleep-disordered breathing and executive dysfunction. The findings will be discussed in relation to their consistency with the heuristic sleep-disordered breathing models (Beebe, 2005; Beebe & Gozal, 2002).

The results of this study will hopefully provide a route for future research and clinical care. Identifying children and adolescents with SLE who may be at increased risk for sleep-disordered breathing and cognitive problems is important during the crucial period of cognitive, educational, and emotional development. Beginning intervention at an early stage may provide for better learning and development opportunities.

2.3.2 Hypotheses

There were three major hypotheses for this study. Hypothesis 1 examined the occurrence of sleep-disordered breathing in children and adolescents with SLE. This hypothesis was based on previous research of the involvement of immunoregulatory proteins in SLE (Gabay et al., 1997; Lacki et al., 1997) and in individuals with sleep-disordered breathing (Alberti et al., 2003; Tauman et al., 2004). Hypothesis 1 stated that the study sample of children and adolescents with SLE would have more parent-reported sleep-disordered breathing symptoms than a demographically matched control group.

Hypothesis 2 examined the association between sleep-disordered breathing and executive dysfunction in a pediatric sample with SLE. This hypothesis was based on previous pediatric literature and heuristic models that indicate there is a relationship between sleep-disordered breathing and executive dysfunction (Archbold et al., 2004; Beebe, 2005; Beebe & Gozal, 2002; Beebe et al., 2004), as well as research involving children and adolescents with SLE that suggest mild cognitive difficulties (Papero et al., 1990; Wyckoff et al., 1995). Hypothesis 2 stated that there would be an association between sleep-disordered breathing (i.e., measured by parent-report) and executive dysfunction (i.e., measured by parent-report and by a testing battery) in a sample of children and adolescents with SLE.

Hypothesis 3 examined the contribution of risk factors involved in the relationship between sleep-disordered breathing and executive dysfunction in a pediatric sample with SLE. This hypothesis was based on pediatric sleep heuristic models that speculate that certain risk and resilience factors may contribute to the relationship between sleep-disordered breathing and executive dysfunction in the general pediatric

sleep-disordered breathing population (Beebe, 2005; Beebe & Gozal, 2002). Hypothesis 3 stated that disease activity and disease severity would act as moderators, and depression would act as a mediator, in the relationship between sleep-disordered breathing and executive dysfunction in a sample of children and adolescents with SLE.

CHAPTER 3: METHOD

3.1 Participants

3.1.1 Inclusion and exclusion criteria

Eligible participants included families with children and adolescents between the ages of 8:0 and 18:11 for both the SLE and control groups. Exclusion criteria included non-English speaking parents for both groups and non-English speaking children and adolescents with SLE. Individuals with SLE were required to meet the criteria for SLE of having 4 out of 11 symptoms for a formal diagnosis (Tan et al., 1982).

3.1.2 Recruitment

Children and adolescents with SLE were recruited from two rheumatology clinics located in Philadelphia, Pennsylvania. The two hospitals included St. Christopher's Hospital for Children (SCHC) and The Children's Hospital of Philadelphia (CHOP). Of those recruited, 25 participants agreed to be in the study and completed the IRB consents. Four additional families were approached by a physician when a study recruiter was not present and agreed to be contacted about the study. Attempts to reach these four families by phone or at subsequent clinic visits were unsuccessful. Three additional families were not interested in hearing about the study because of time constraints at the clinic. Out of the 25 participants who consented to the study, 17 completed the study requirements including the questionnaires and cognitive testing. An additional 5 participants completed the questionnaires, resulting in 22 participants eligible for some of the study analyses. Five participants were from SCHC and 17 were from CHOP.

In regard to the comparison group, children/adolescents and their parents were recruited from the ambulatory care clinic at St. Christopher's Hospital for Children (SCHC). Twenty six out of the 57 initially recruited families failed to mail back their questionnaires (i.e., study dropouts). An amendment to the IRB was accepted to recruit an additional 26 families and have all the families complete the questionnaires in clinic. Over time, 9 of the original study dropout families completed the questionnaires, leaving 17 who never returned the questionnaires. This resulted in 72 participants meeting the study requirements. A total of 14 families were not recruited due to family time constraints in the clinic or because a parent was unavailable to complete the consent forms and questionnaires.

3.1.3 Selection of matched controls

To obtain a demographically matched control group, multiple demographic analyses were conducted to best match a subset of the 72 non-SLE individuals to the SLE sample. In order to be blind to the data during the selection process, only demographic information including age, income/socioeconomic status, gender, and ethnicity was viewable for the SLE and control groups. Individuals were matched in the following order of priority: 1) age, 2) income/socioeconomic status, 3) gender, and 4) ethnicity. The best matched sample included 24 controls. The selected control sample had a similar age range (SLE Group: 9 – 18 years old, Control Group: 9 – 17 years old). Mean age (SLE Group: 15.5 years old, Control Group: 14.2 years old) and gender (SLE Group: 77% female, Control Group: 63% female) did not statistically differ or show associations (i.e., using t-tests and Chi squares) between groups. Despite making the control sample

more similar in income, Hollingshead score, and ethnicity, these demographic factors continued to be statistically different between groups. Most of the 72 non-SLE individuals that completed the questionnaires were from a low socioeconomic status bracket and were Hispanic, making it difficult to match the samples without significantly reducing the control sample size. The twenty four selected controls were included in the data analyses.

3.2 Measures

The measures in this study were used to ascertain information about demographic, sleep functioning, and cognitive functioning. The following sections provide a detailed description of these measures and Table 1 provides a list of the measures used in this study.

3.2.1 Demographic measures

Parents of the children and adolescents in the SLE and control groups completed different versions of a 10 item Child Background Questionnaire (see Appendix A1 and A2). The questionnaire given to parents of individuals in the SLE group asked about duration of SLE, while the questionnaire given to parents of those in the control group asked if their child was diagnosed with SLE. The other nine questions were identical, and asked parents to report their child's current age, gender, weight, height, ethnic background, current medications, throat/ear infections, if they had an adenoidectomy/ tonsillectomy, and medical diagnoses. For both groups, a calculation of height and weight determined the child's body mass index and percentile (BMI percentile).

Statistical analyses used BMI percentile and age for descriptive and preliminary analyses, and ethnicity for descriptive analyses.

Both groups of parents completed the Parent Background Questionnaire which contained six questions (see Appendix B). One question asked whether the parent's primary language was English. The questionnaire also collected information on annual household income that was coded as follows: 1 = $0,000-$9,999; 2 = $10,000-$19,999; 3 = $20,000-$29,999; 4 = $30,000-$39,999; 5 = $40,000-$49,999; 6 = $50,000-$59,999; 7 = $60,000-$69,999; 8 = $70,000-$79,999; 9 = $80,000-$89,999; 10 = $90,000-$99,999; 11 = $100,000-$109,999; 12 = $110,000-$119,999; 13 = $120,000-$129,999; and 14 = $130,000+. Statistical analyses used the scores from 1 to 14 for descriptive and preliminary analyses.

Questions from the Hollingshead Four Factor Index of Social Status (Hollingshead, 1975) questionnaire also were included in the Parent Background Questionnaire. The Hollingshead questionnaire asked for each head of household's parental role, highest level of education (i.e., coded from one to seven), and current employment information (i.e., coded from zero to nine). The socioeconomic status (SES) score was obtained by multiplying the education score by three and the employment score by five and then adding the scores together. For two parents in a household, the SES scores for both parents were summed and then divided by two. On the Hollingshead, SES is divided into five categories: 1 = unskilled laborers/menial service workers (score of 8-19); 2 = machine operators/semi-skilled workers (score of 20-29); 3 = skilled craftsman clerical and sales workers (score of 30-39); 4 = medium business/minor professional (score of 40-54); and 5 = major business/professional (score

of 55-66). The Hollingshead is a widely used and accepted measure for measuring SES and has good validity (Deonandan, Campbell, Ostbye, Tummon, & Robertson, 2000). This study used scores for SES for descriptive and preliminary analyses.

3.2.2 Illness-related measures

A trained study investigator completed the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) for those with SLE. The SLEDAI is a valid and reliable measure to assess disease activity (Bombardier, Gladman, Urowitz, Caron, & Chi Hsing, 1992; Hawker et al., 1993). The questionnaire has 24 weighted items resulting in a total score that ranges from 0 to 105. Higher scores represent more disease activity. The weight calculation of the measure is as follows: 8 = seizure, psychosis, organic brain syndrome, visual disturbance, cranial nerve disorder, lupus headache, cerebral vascular accident, vasculitis; 4 = arthritis, myositis, urinary casts hematuria, proteinuria, pyuria; 2 = rash, alopecia, mucosal ulcers, pleurisy, pericarditis, low complement, high DNA; and 1 = fever, low platelets, low white blood cell count. This study also used the inflammatory level of sedimentation rate, which is another predictor of disease activity. Sedimentation rate was gathered from the participant's medical chart during a chart review. A higher sedimentation rate represented more disease activity. The SLEDAI and sedimentation rate were used in descriptive and primary analyses in this study.

Measures of disease severity including information about central nervous system (CNS) involvement and kidney disease were gathered from the medical chart of those with SLE. CNS involvement in SLE is defined as the occurrence of neuropsychiatric symptoms as described by the American College of Rheumatology nomenclature and

case definitions. These symptoms were discussed in the literature review section of this study (ACR, 1999). Presence of CNS involvement and/or kidney disease was used in descriptive and primary analyses.

3.2.3 Sleep functioning measure

Parents of individuals in the SLE and control groups completed the Sleep Disorders Inventory for Students (SDIS; Luginbuehl, 2006) to determine parent perceptions of their child's sleep behaviors. The SDIS is a 41-item questionnaire, but only 30 of these questions are used for the main scales. The questionnaire has two versions: one for children between the ages of 2-10 years old and another for adolescents between the ages of 11-18 years old. Some questions require a yes/no response and other questions are on a Likert scale ranging from 0 to 7. The measure calculates the following scales: Sleep Disturbance Index (SDI), Obstructive Sleep Apnea (OSA), Periodic Limb Movement (PLM), Delayed Sleep Phase Syndrome (DSPS), Excessive Daytime Sleepiness (EDS), and Narcolepsy (NAR). Scores are reported as t-scores (M = 50, SD = 10). On this measure, t-scores between 60 and 64 indicate at-risk problems. T-scores between 65 and 90 indicate clinically significant level of concerns. Therefore, higher scores reflect more sleep problems. In the current study, t-scores have been converted to standard scores for comparison purposes, with higher scores reflecting more sleep problems. Questions to gather information about tonsillectomies and adenoidectomies are also included on this questionnaire. Norming of this measure occurred with 595 parents of children and adolescents from 2 to 18 years old. According to normative data, the internal consistency reliability for the total SDI score for the child

version is .91 and for the adolescent version is .92. For the OSA scale, the internal consistency reliability for the child questionnaire is .90 and for the adolescent version is .88. The construction of the ethnic representation of the Sleep Disorders Inventory for Students was similar to the 2000 U.S. Census report. For the current study, all sleep scales were incorporated into descriptive analyses. Preliminary, primary, and exploratory data analyses used the OSA scale. Descriptive and exploratory analyses used the other sleep scales. Data on tonsillectomies and adenoidectomies were used for descriptive and preliminary analyses.

The current study analyzed the reliability of this questionnaire with both the SLE and control groups by use of Cronbach alpha reliability analyses (Cronbach, 1951) and descriptions of acceptability based on DeVellis (1991). For the SLE group, on the adolescent version, the OSA scale had respectable reliability (α = .71). For the control group, on the adolescent version, the OSA scale had undesirable reliability (α = .65). For both the SLE and control groups, only one child version of the questionnaire was filled out, so reliability analyses were not conducted. The reliability data for the other sleep scales can be found in Table 2.

3.2.4 Cognitive functioning measures

The investigator administered the cognitive measures only to the children and adolescents in the SLE group. The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was used to provide an estimate of general intellectual ability. The test is appropriate for individuals ranging in age from 6 to 89 years old. A two subtest version to calculate an estimated full scale IQ (FSIQ) was administered, which consisted

of the Vocabulary and Matrix Reasoning tests. The Vocabulary section provides a measure of expressive word knowledge and the Matrix Reasoning test provides a measure of nonverbal fluid abilities. This measure calculates the FSIQ as a standard score (M = 100, SD = 15; average range = 90 - 110), with lower scores indicating more problems. Standard scores were used in the current study. The reliability of the FSIQ for the normed WASI two subtest version is .96. The FSIQ was used in descriptive analyses.

The Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) is an 86-item parent-report questionnaire for children age 5 to 18 years old. The BRIEF provided a subjective but more ecologically based report of the child's or adolescent's daytime executive function behaviors at home. The measure has eight non-overlapping clinical scales including the following: inhibit, shift, emotional control, initiate, working memory, plan/organize, organization of materials, and monitoring. It also contains the Global Executive Composite (GEC) score that combines the sum of all eight scales and two indexes that include the Behavioral Regulation Index (BRI; 3 scales) and Metacognition Index (MCI; 5 scales). Scores are reported as t-scores (M = 50, SD = 10). On this measure, t-scores between 65 and 90 indicate clinically significant level of concerns. Therefore, higher scores reflect more sleep problems. In the current study, t-scores have been converted to standard scores for comparison purposes, with higher scores reflecting more sleep problems. Norming for the measure occurred with 1,419 parents. The BRIEF normative data reflect the 1999 U.S. Census estimates for socioeconomic status and ethnicity. The questionnaire has high internal consistency of .80 to .98, test reliability of .82, and good convergent validity with other measures. This study used the Global Executive Composite (GEC) score for the

descriptive, primary, and exploratory analyses. The Behavioral Regulation Index (BRI) and Metacognition Index (MCI) were used for descriptive and exploratory analyses. In the current study's sample of individuals with SLE, the GEC, BRI, and MCI scores were all in the excellent reliability range (α = .98, .93, .97, respectively).

The investigator administered the Trail Making test from the Delis-Kaplan Executive Function System (DKEFS; Delis, Kaplan, & Kramer, 2001). The Trail Making test is a visual motor test that consists of the following five tasks: 1) Visual Scanning (VS) requires the individual to find all the number threes on a page, 2) Number Sequencing (NS) requires the individual to trace numbers in increasing order, 3) Letter Sequencing (LS) requires the individual to trace letters in alphabetical order, 4) Letter-Number Sequencing (LNS) requires the individual to alternate between tracing numbers and letters in order, and 5) Motor Speed (MS) requires the individual to quickly trace a dotted line. An error score is also obtainable called the Letter-Number Sequencing Error (LNSE) score. These scores are reported as scaled scores (M = 10, SD = 3; average range = 8 - 12), with lower scores indicating poorer performance. In the current study, scores were converted to standard scores for comparison purposes. Descriptive, primary, and exploratory analyses used the Letter-Number Sequencing score and the Letter-Number Sequencing Error score. Descriptive and exploratory analyses examined the other Trail Making scores.

The investigator administered the Verbal Fluency test from the Delis-Kaplan Executive Function System (DKEFS; Delis et al., 2001). The Verbal Fluency test is designed to measure verbal fluency, verbal set shifting, and verbal processing speed and is composed of the following three tasks: 1) Letter Fluency (LF) requires the individual to

quickly produce words beginning with a specified letter, 2) Category Fluency (CF) requires the individual to quickly produce words from a specified category, and 3) Category Switching requires the individual to quickly switch back and forth between producing words from two categories. This Category Switching task has two scores, Category Switching Number Correct (CS#C) and Category Switching Accuracy (CSA). Error scores are also obtainable including the Verbal Fluency Set-Loss Errors (VFSLE) score and Verbal Fluency Repetition Errors (VFRE) score. These scores are reported as scaled scores (M = 10, SD = 3; average range = 8 - 12), with lower scores indicating poorer performance. In the current study, scores were converted to standard scores for comparison purposes. This study used the Category Switching Number Correct, Verbal Fluency Set-Loss Errors, and Verbal Fluency Repetition Errors scores for descriptive, primary, and exploratory analyses. Descriptive and exploratory analyses used the scores for the other scales.

The investigator administered the Digit Span (DS) task from the Wechsler Intelligence Scale for Children Fourth Edition (WISC-IV; Wechsler, 2003) and the Wechsler Adult Intelligence Scale Third Edition (WAIS-III; Wechsler, 1997). This measure provided an objective measure of immediate attention and working memory abilities. The individuals were asked to repeat increasingly lengthy digit strings verbatim or in reverse order. The subscale score is reported as a scaled score (M = 10, SD = 3; average range = 8 - 12), with lower scores indicating poorer performance. In the current study, this score was converted to a standard score for comparison purposes. For the WISC-IV, the reliability of the total digit span is .87. The descriptive, primary, and exploratory analyses used the digit span score.

3.2.5 Psychiatric functioning measure

Parents of children and adolescents with SLE completed the Depression and Anxiety in Youth Scale (DAYS; Newcomer, Barenbaum, & Bryant, 1994). This questionnaire is a 28-item parent-report questionnaire with scales for Depression, Anxiety, and Social Maladjustment for individuals from 6 to 19 years old. The parent responds to true-false questions that ask them to identify the presence or absence of a symptom. This parent-report was normed on 1,286 children from 6 to 19 years old and the internal consistency reliability for the Depression scale was .80. The DAYS normative data reflect the 1985 U.S. Census estimates for ethnicity. This study used the Depression scale for descriptive, primary, and exploratory analyses. In this study's sample, the Depression scale had very good reliability (α = .85).

3.4 Order of Administration

The investigators administered the cognitive testing to the SLE sample in two orders (see Table 3). Order A was: 1) WASI Vocabulary, 2) WASI Matrix Reasoning, 3) WISC-IV/WAIS-III Digit Span, 4) DKEFS Trail Making, and 5) DKEFS Verbal Fluency. Order B was: 1) WASI Vocabulary, 2) WASI Matrix Reasoning, 3) DKEFS Verbal Fluency, 4) DKEFS Trail Making, and 5) WISC-IV/WAIS-III Digit Span. Since parents completed the questionnaires either in the clinic or at home, and sometimes were not in front of the investigator, these questionnaires were completed in no specific order.

3.5 Procedure

Clinics from St. Christopher's Hospital for Children (SCHC) and the Children's Hospital of Philadelphia (CHOP) agreed to participate in this study. Following Institutional Review Board (IRB) approval at both hospitals, a clinic staff member from the rheumatology or ambulatory care clinic informed parents about the study during their clinic visit and a flyer was available describing the study. In both the rheumatology and ambulatory care clinics, a study investigator reviewed the consent form and provided a copy of the consent form to families who agreed to participate in the study. Parents signed the consent form, children age 8:0 to 17:11 completed an assent form, and 18 year olds completed their own consent form. The investigator answered any of the family's questions about the study. In addition, the parents were asked to sign a release if they wanted the following: 1) to be contacted for scheduling for cognitive testing (for the SLE group only) and to remind them to return the questionnaire, 2) if they wanted their child's results to be shared with the clinic team, and 3) if they wished to receive a summary by mail of the overall study results. Families from both groups received sleep education handouts. Funding was available from the Children's Hospital of Philadelphia (CHOP) for those individuals recruited from CHOP's rheumatology clinic. These participants received $10 for completion of the study.

Parents completed the questionnaires during their child's or adolescent's clinic visit, at home if parents were unable to complete the questionnaires during their clinic visit, or during a home visit (for the SLE group only). Questionnaires for the SLE group took approximately 20-35 minutes to complete and questionnaires for the control group took approximately 15 minutes to complete. At the beginning of the study, individuals

from the ambulatory care clinic were provided with self-addressed stamped envelopes in which to return the questionnaires. However, many people did not return these questionnaires. These participants were called to mail back their questionnaires, and/or complete the questionnaire over the phone. Because many questionnaires were never received, an IRB amendment was approved to recruit more participants from the ambulatory care clinic and new recruits were asked to complete the questionnaires in the clinic. When needed, the investigator provided help to parents who had difficulty reading the forms. Due to the difficulty of testing individuals in clinic because of patient no shows or time constraints, and an extremely slow data completion rate, an IRB amendment was made to conduct home visits. Testing took 60-75 minutes to administer to participants. Recruitment was ongoing as testing procedures were conducted with other participants. Chart reviews were conducted to gather additional medical information. An investigator was trained by a rheumatology medical resident and nurse on how to complete the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and where to look for disease severity and activity information in the individual's medical chart.

3.6 Approach to Data Analyses

Data analyses were completed using the Statistical Package for Social Science (SPSS) version 16.0. Power was calculated by G-Power ^{TM} version 3.0.10 (Faul, Erdfelder, Lang, & Buchner, 2007) and by Cohen's power tables (1988). All scores from the cognitive testing measures and questionnaires were changed to standard scores for comparison purposes.

Initial analyses were conducted to prepare for an appropriate sample size and comparison group, and to understand the meaning of the data. Some of the pediatric sleep-disordered breathing and SLE literature indicates moderate to large effect sizes with small sample sizes (Beebe et al., 2004; Beebe et al., 2006; O'Brien et al., 2004; Owens, Maxim, et al., 2000; Papero et al., 1990; Wyckoff et al., 1995). Therefore, power was calculated with a medium effect size and a probability level of .05 as the measure of significance. Power for Hypothesis 1 was detected to be .36 and for Hypothesis 2 was detected to be .28. From the non-SLE recruited sample, a group of individuals were selected that made for the best demographically matched control group to compare to the SLE group. Since a review of the literature did not indicate that the questionnaires used in this study were used on a pediatric population with SLE, reliability analyses for both the SLE and control samples were conducted by use of Cronbach alpha statistical analyses (Cronbach, 1951; see Methods section and Table 2). Descriptive statistics for different variables described both the SLE and control groups. Data were examined for equality of groups, sample representativeness, reliability of the testing procedures, and normal distribution.

Preliminary analyses for Hypothesis 1 used correlation analyses. These analyses investigated possible covariates of variables known for being related to sleep-disordered breathing, including body mass index percentile, age, socioeconomic status (income, Hollingshead), tonsillectomies, and adenoidectomies.

To test Hypothesis 1, an independent samples t-test examined the difference in the average score for the obstructive sleep apnea (OSA) scale between the SLE sample and control sample. If necessary, an ANCOVA would be used to covary for possible

covariates found to be associated with the OSA scale from preliminary analyses. This analysis used a p-value of .05, and to be conservative, a two-tailed test.

To test Hypothesis 2, correlation analyses examined the association between the obstructive sleep apnea (OSA) scale and the primary executive functioning variables (i.e., Global Executive Composite, Category Switching Number Correct, Verbal Fluency Set-Loss Errors, Verbal Fluency Repetition Errors, Letter-Number Sequencing, Letter-Number Sequencing Errors, and Digit Span) in the SLE sample. This analysis used a p-value of .05 and a two-tailed test.

To test Hypothesis 3, multiple regression analyses were planned to be used for only those executive functioning measures found to be associated with the obstructive sleep apnea (OSA) scale from Hypothesis 2. Hypothesis 3 examined which variables moderate (i.e., Systemic Lupus Erythematosus Disease Activity Index, sedimentation rate, central nervous system involvement, kidney disease) and mediate (i.e., Depression scale) the relationship between the OSA scale and the executive functioning measures in those with SLE. For moderation, the OSA scale would be regressed on the two main effects and the interaction term. To examine mediation, the predictor variable must be related to both the outcome variable and mediator variable. Then the mediator must be related to the outcome variable, when the predictor and mediator are entered into a multiple regression analysis. In this same multiple regression analysis, the relationship between the predictor and the outcome variable must no longer be significant or must decrease in significance.

CHAPTER 4: RESULTS

4.1 Summary of data

4.1.1 Characteristics and equality of groups

Table 4 lists the demographic characteristics for the SLE group. Not all data were available for all participants; therefore, averages were calculated for the available data. The average age of the 22 participants was 15.5 years old (*SD* = 2.70, *range* = 9 - 18). Seventeen (77%) were female and five (23%) were male. Ten (45%) were African American, one (4.5%) was Asian, seven (32%) were Caucasian, three (14%) were Hispanic, and one (4.5%) was identified as other indicating a different ethnicity. Out of 19 participants, results from the Hollingshead Four Factor Index of Social Status indicated an average social class rating of 4 out of 5 (*range* = 2 - 5), which is the second highest level. Out of 17 participants, the average and median annual household income was in the range of $50,000 - $59,999 (*range* = $20,000 - $130,000+). The average BMI percentile (BMI percentile) was 72nd percentile (*SD* = 25.1, *range* = 15 - 98) out of the 22 participants. Three (14%) out of the 22 participants had both a tonsillectomy and adenoidectomy. For disease activity measures, the mean SLEDAI score was 5.27 (*SD* = 5.04, *range* = 0 - 21) out of 22 participants and the mean sedimentation rate was 28.7 (*SD* = 33.4, *range* = 1 - 106) out of 15 participants. Of the 22 participants, 13 (59%) had kidney disease and 10 (45%) had central nervous system (CNS) involvement.

Table 5 lists a summary of the standard scores for all the questionnaire and cognitive testing variables for the SLE sample as a whole. There were 22 families who completed the study questionnaires. Seventeen of these 22 participants completed the

cognitive testing measures. The means for the obstructive sleep apnea (OSA), Global Executive Composite, Category Switching Number Correct, Verbal Fluency Set-Loss Errors, Verbal Fluency Repetition Errors, Letter-Number Sequencing, Letter-Number Sequencing Errors, and Digit Span scores were 101.5 (*SD* = 12.8, *range* = 86 - 132), 98.5 (*SD* = 19.7, *range* = 79 - 146), 101.5 (*SD* = 12.3, *range* = 75 - 125), 110.0 (*SD* = 7.91, *range* = 90 - 115), 96.8 (*SD* = 14.8, *range* = 55 - 110), 98.8 (*SD* = 20.4, *range* = 55 - 130), 105.0 (*SD* = 7.07, *range* = 85 - 110), and 100 (*SD* = 15.7, *range* = 80 - 145), respectively. Table 5 lists the other subscale summary scores. Table 6 lists a summary of the scores in their original scoring format (i.e., t-scores, standard scores, scaled scores). Fourteen percent met the criteria for the possibility of sleep-disordered breathing on the OSA scale of the Sleep Disorders Inventory for Students. On executive function measures, the following percentages show the prevalence rates of those with possible mild cognitive difficulties defined by those with scores in the low average to below low average range: Global Executive Composite = 14%, Category Switching Number Correct = 6%, Verbal Fluency Set-Loss Errors = 0%, Verbal Fluency Repetition Errors = 24%, Letter-Number Sequencing = 30%, Letter-Number Sequencing Errors = 6%, Digit Span = 18%, and IQ = 0%. On the Depression scale, 19% had significant depressive symptoms.

Table 4 lists the demographic characteristics for the 24 participants selected as the control group. Not all data were available for all participants; therefore, averages were calculated for the available data. The average age of the 24 participants was 14.2 years (*SD* = 1.96 *range* = 9 - 17). Out of the 24 participants, 15 (63%) were female and 9 (37%) were male. Out of the 24 participants, 7 (29%) were African American, 0 (0%)

were Asian, 1 (4%) was Caucasian, 15 (63%) were Hispanic, and 1 (4%) was identified as other indicating a different ethnicity. Out of 17 of the participants, results from the Hollingshead Four Factor Index of Social Status indicated an average social class rating of 2 out of 5 (*range* = 1 - 4), which is the second lowest level. Out of 20 of the participants, the average annual household income was in the $20,000 - $29,999 range (*range* = $0,000 - $59,999) and the median annual household income was in the $30,000 - $39,999 range. The average BMI percentile (BMI percentile) was 70th percentile (*SD* = 28.7, *range* = 9 - 99) out of 23 of the participants. Six (25%) out of the 24 participants had tonsillectomies and 3 (13%) had adenoidectomies. Table 5 lists a summary of the standard scores for the SDIS variables for the control group as a whole. The mean obstructive sleep apnea (OSA) score was 98.0 (*SD* = 11.9, *range* = 85 - 129). Table 6 lists a summary of the scores in their original scoring format (i.e., t-scores). Seventeen percent met the criteria for the possibility of sleep-disordered breathing on the OSA scale of the Sleep Disorders Inventory for Students (SDIS).

The SLE group and selected control group were compared on age, socioeconomic status (income and Hollingshead), ethnicity, and gender to examine the equality of groups. Results of an independent samples t-test indicated the SLE group (*M* = 15.5, *SD* = 2.70, *N* = 22) did not significantly differ in age from the control group (*M* = 14.2, *SD* = 1.96, *N* = 24; *t* [37.9] = -1.78, *p* = .083). Results of an independent samples t-test indicated the SLE group (*M* = 6.82, *SD* = 3.28, *N* = 17) did significantly differ in income from the control group (*M* = 3.60, *SD* = 1.47, *N* = 20; *t* [21.4] = -3.74, *p* = .001. Results of another independent samples t-test indicated the SLE group (*M* = 47.2, *SD* = 12.6, *N* = 19) did significantly differ on the Hollingshead from the control group (*M* = 22.2,

SD = 10.5, *N* = 17; *t* [34] = -6.42, *p* = .000). Results of a Chi square analysis looking at gender indicated no association between SLE group/control group and gender (X^2 [1, *N* = 46] = 1.18, *p* = .277). Out of the 22 individuals in the SLE group, 77% (*n* = 17) were female, and out of 24 individuals in the control group, 63% (*n* = 15) were female. Results of a Chi square analysis looking at ethnicity indicated an association between SLE group/control group and ethnicity (X^2 [4, *N* = 46] = 13.9, *p* = .007). Out of 22 participants in the SLE group, 45% (*n* = 10) were African American and out of 24 individuals in the control group, 29% (*n* = 7) were African American. Results of an independent sample t-test indicated the SLE group (*M* = 72.3, *SD* = 25.1, *N* = 22) did not significantly differ in BMI percentile from the control group (*M* = 70.3, *SD* = 28.7, *N* = 23; *t* [43] = -.239, *p* = .812). Results of a Chi square analysis looking at tonsillectomies indicated no association between SLE/control group and tonsillectomies (X^2 [1, *N* = 46] =.942, *p* = .332). Out of 22 participants in the SLE group, 14% (*n* = 3) had tonsillectomies and out of 24 individuals in the control group 25% (*n* = 6) had tonsillectomies. Results of a Chi square analysis looking at adenoidectomies indicated no association between SLE/control group and adenoidectomies (X^2 [1, *N* = 46] =.013, *p* = .909). Out of 22 participants in the SLE group, 14% (*n* = 3) had tonsillectomies and out of 24 individuals in the control group 13% (*n* = 3) had tonsillectomies.

In the SLE group, those with and without central nervous system (CNS) involvement were compared on the study measures, by comparing the average standard scores. Results of an independent samples t-test indicated those with CNS involvement had better standard scores on the Letter-Number Sequencing test (*M* = 112.9, *SD* = 9.51, *N* = 7) than those without CNS involvement (*M* = 89.0, *SD* = 20.4, *N* = 10; *t* [13] = -3.23,

p = .006), which is in the opposite direction than would be expected. There were no differences between groups for the BRIEF Global Executive Composite, other paper/pencil cognitive test scores, Depression score, or OSA score. In those with CNS involvement, 30% met the criteria for the possibility of sleep-disordered breathing on the OSA scale of the Sleep Disorders Inventory for Students, compared to 0% of those without CNS involvement. On executive function measures, mild cognitive difficulties were defined by individuals with scores in the low average to below low average range. The following prevalence rates indicating possible mild cognitive difficulties were seen for CNS involvement versus no CNS involvement, respectively: Global Executive Composite = 10% versus 17%, Category Switching Number Correct = 0% versus 10%, Verbal Fluency Set-Loss Errors = 0% versus 0%, Verbal Fluency Repetition Errors = 43% versus 10%, Letter-Number Sequencing = 0% versus 50%, Letter-Number Sequencing Errors = 0% versus 10%, Digit Span = 29% versus 10%, and IQ = 0% versus 0%. In those with CNS involvement, 20% had significant depressive symptoms, compared to 18% of those without CNS involvement.

4.1.2 Sample representativeness

For those with SLE, those who were included in the study were compared to those who were not included in this study. Individuals were divided into 1) Group A (N = 22) made up of those who completed the questionnaires and/or testing and 2) Group B (N = 10) made up of those who were consented but did not complete any part of the study (n = 3), those who were not consented but agreed for us to contact them (n = 4), and those who declined to hear about the study (n = 3). Information on gender, age, and ethnicity

was available for group comparison on all 32 individuals. Results of an independent samples t-test indicated participants (M = 15.5, SD = 2.7, N = 22) did significantly differ in age from nonparticipants (M = 17.3, SD = 1.06, N = 10; t [29.7] = 2.77, p = .01). Results of a Chi square analysis looking at gender indicated no association between participants/nonparticipants and gender (X^2 [1, N = 32] = .73, p = .393). Out of 22 participants, 77% (n = 17) were female, and out of 10 nonparticipants, 90% (n = 9) were female. Results of a Chi square analysis looking at ethnicity indicated no association between participants/nonparticipants and ethnicity (X^2 [4, N = 32] = 1.5, p = .827). Out of 22 participants, 45% (n = 10) were African American, and out of 10 nonparticipants, 30% (n = 3) were African American.

For those with SLE included in the study, those who completed both the questionnaires and testing were compared to those who only completed the questionnaires. Individuals were divided into 1) Group A (N = 17) made up of those who completed both the questionnaires and testing and 2) Group B (N = 5) made up of those who only completed the questionnaires. Information on gender, age, ethnicity, socioeconomic status (income and Hollingshead), SLEDAI, CNS involvement, and kidney disease were available for group comparison. Results of an independent samples t-test indicated test and questionnaire completers (M = 15.5, SD = 2.79, N = 17) did not significantly differ in age from questionnaire only completers (M = 15.2, SD = 2.68, N = 5; t [20] = -.234, p = .817). Results of an independent samples t-test indicated test and questionnaire completers (M = 7.21, SD = 3.45, N = 14) did not significantly differ in income from questionnaire only completers (M = 5.00, SD = 1.73, N = 3; t [15] = -1.06, p = .304). Results of an independent samples t-test indicated test and questionnaire

completers (M = 48.3, SD = 11.8, N = 16) did not significantly differ on the Hollingshead from questionnaire only completers (M = 41.3, SD = 18.0, N = 3; t [17] = -.865, p = .399). Results of a Chi square analysis looking at gender indicated no association between test and questionnaire completers/questionnaire only completers and gender (X^2 [1, N = 22] = 1.90, p = .168). Out of 17 test and questionnaire completers, 71% (n = 12) were female, and out of 5 questionnaire only completers, 100% (n = 5) were female. Results of a Chi square analysis looking at ethnicity indicated no association between test and questionnaire completers/questionnaire only completers and ethnicity (X^2 [4, N = 22] = 8.19, p = .085). Out of 17 test and questionnaire completers, 53% (n = 9) were African American, and out of 5 questionnaire only completers, 20% (n = 1) were African American. Results of an independent samples t-test indicated test and questionnaire completers (M = 5.75, SD = 5.25, N = 17) did not significantly differ in SLEDAI score from questionnaire only completers (M = 3.60, SD = 4.34, N = 5; t [20] = -.837, p = .412). Results of a Chi square analysis looking at CNS involvement indicated no association between test and questionnaire completers/questionnaire only completers and ethnicity (X^2 [1, N = 22] = .552, p = .457). Out of 17 test and questionnaire completers, 41% (n = 7) had CNS involvement, and out of 5 questionnaire only completers, 60% (n = 3) had CNS involvement. Results of a Chi square analysis looking at kidney disease indicated an association between test and questionnaire completers/questionnaire only completers and kidney disease (X^2 [1, N = 22] = 4.09, p = .043). Out of 17 test and questionnaire completers, 71% (n = 12) had kidney disease, and out of questionnaire only completers, 20% (n = 1) had kidney disease.

For non-SLE individuals, those selected as controls were compared to those who were not selected as controls. Individuals were divided into 1) Group A ($N = 24$) made up of those who were selected to be in the control group and 2) Group B ($N = 48$) made up of those who completed the questionnaires but were not included in the control group. Information on gender, age, and ethnicity were available for group comparison. Groups were also compared on the OSA scale. Results of an independent samples t-test indicated controls ($M = 14.2$, $SD = 1.96$, $N = 24$) were significantly older in age than those not included as controls ($M = 10.8$, $SD = 1.76$, $N = 47$; $t\ [69] = -7.40$, $p = .000$). Results of an independent samples t-test indicated controls ($M = 3.60$, $SD = 1.47$, $N = 20$) had a significantly higher income than those not included as controls ($M = 2.59$, $SD = 1.71$, $N = 41$; $t\ [59] = -2.27$, $p = .027$). Results of an independent samples t-test indicated controls ($M = 22.2$, $SD = 10.5$, $N = 17$) did not significantly differ on the Hollingshead from those not included as controls ($M = 20.8$, $SD = 10.3$, $N = 40$; $t\ [55] = -.476$, $p = .636$). Results of a Chi square analysis looking at gender indicated no association between controls/those not included as controls and gender ($X^2\ [1, N = 72] = 3.37$, $p = .066$). Out of the 24 controls, 63% ($n = 15$) were female, and out of the 48 individuals not included as controls, 40% ($n = 19$) were female. Results of a Chi square analysis looking at ethnicity indicated no association between controls/those not included as controls and ethnicity ($X^2\ [4, N = 72] = 1.02$, $p = .906$). Out of the controls, 30% ($n = 7$) were African American, and out of those not included as controls, 31% ($n = 15$) were African American. Results of an independent samples t-test indicated controls ($M = 98.0$, $SD = 11.9$, $N = 24$) did not significantly differ on the OSA scale from those not included as controls ($M = 103.6$, $SD = 15.7$, $N = 48$; $t\ [70] = 1.53$, $p = .131$).

For non-SLE individuals, all those who completed the questionnaires were compared to those who did not complete the study questionnaires. Individuals were divided into 1) Group A ($N = 72$) made up of those who were recruited and completed the questionnaires (i.e., this included both those selected and not selected as controls), and 2) Group B ($N = 26$), nonparticipants, made up of individuals who were consented but did not return questionnaires ($n = 17$) and individuals who declined to hear about the study ($n = 9$ out of 14; i.e., this included only the individuals who we had demographic information on). Information on gender, age, and ethnicity was available for group comparison, although not on all individuals. Results of an independent samples t-test indicated questionnaire completers ($M = 11.9$, $SD = 2.43$, $N = 71$) did not significantly differ in age from nonparticipants ($M = 12.3$, $SD = 2.94$, $N = 25$; $t\,[94] = .61$, $p = .546$). Results of a Chi square analysis looking at gender indicated an association between questionnaire completers/nonparticipants and gender ($X^2\,[1, N = 98] = 6.81$, $p = .009$). Out of 72 questionnaire completers, 47% ($n = 34$) were female, and out of 26 nonparticipants, 77% ($n = 20$) were female. Results of a Chi square analysis looking at ethnicity indicated an association between questionnaire completers/nonparticipants and ethnicity ($X^2\,[4, N = 95] = 9.9$, $p = .041$). Out of 72 questionnaire completers, 30% ($n = 22$) were African American, and out of 24 nonparticipants, 67% ($n = 16$) were African American.

4.1.3 Description of data

The sampling distribution was examined for the SLE and control groups on the study variables. For the SLE group, the variables examined included the Obstructive Sleep Apnea, Global Executive Composite, Category Switching Number Correct, Verbal Fluency Set-Loss Errors, Verbal Fluency Repetition Errors, Letter-Number Sequencing, Letter-Number Sequencing Errors, and Digit Span scores. Statistical tests of normality including skewness and kurtosis, and investigation of histograms and quartiles, generally concluded the scales met the assumption of normality. When applying the rules of 2x the standard error of kurtosis/skewness to assess for skewness/kurtosis, very mild elevations were seen. For the control group, statistical tests of normality including skewness and kurtosis, and investigation of histograms and quartiles, revealed that the obstructive sleep apnea scale met the assumption of normality.

There were no missing data from paper/pencil measures used to assess cognition. The 17 participants completed all the cognitive testing measures. For the questionnaires, one family of the group with SLE did not complete the depression measure. For those who completed the questionnaires, there were a limited number of questions left blank, such that scores could be calculated without the missing question(s). For some individuals, recent blood levels were not available within a three month period; therefore data was not included for those individuals. Other information unavailable included weight, height, age, ethnicity, income, education, or employment information because the family member left out this information from the questionnaire. Some of the information including weight, height, age, and ethnicity was obtainable through medical chart review,

but some information was still unattainable. Therefore, individuals without this demographic information were left out of corresponding statistical analyses.

For the SLE group, 13 (76%) were tested at home and 4 (24%) were tested in the clinic. Results from independent samples t-tests indicated no difference on any of the primary study measures, whether children were tested at home or in the clinic. For the SLE group, 10 (59%) were administered order A of the cognitive tests and 7 (42%) were administered order B. There were no differences between those given administration order A or B on the main study measures. Fourteen (82%) cognitive assessments were completed by the primary test assessor, two (12%) were conducted by two other assessors but with the primary assessor in the room providing supervision, and one (6%) assessment was conducted by one of these two other assessors without the in-room presence of the primary assessor. There were no significant differences in cognitive testing results between those tested by the primary test assessor ($N = 14$) and those tested by the other assessors with or without the primary test assessor in the room ($N = 3$).

4.2 Preliminary Analyses

Since research indicates body mass index percentile (BMI percentile), age, and socioeconomic status are related to sleep-disordered breathing, preliminary correlation analyses looked at the association between the obstructive sleep apnea (OSA) score and these variables. These analyses were conducted to see if these variables should be covaried for using an ANCOVA in the examination of Hypothesis 1. Results from these analyses are listed in Table 7. Results indicated that the OSA scale did not correlate with BMI percentile for the SLE sample ($r = .20$, $p = .368$, $N = 22$) nor for the control sample

(r = -.09, p = .660, N = 23). The OSA scale did not correlate with age for the SLE sample (r = -.08, p = .731, N = 22) nor for the control sample (r = .04, p = .865, N = 24). There was no relationship between income and the OSA scale for the SLE sample (r = -.11, p = .669, N = 17) nor for the control sample (r = -.27, p = .259, N = 20). There also was no relationship between the Hollingshead Four Factor Index of Social Status scale and the OSA scale for the SLE sample (r = -.12, p = .627, N = 19) nor for the control sample (r = -.03, p = .910, N = 17). Therefore, none of these variables were included as covariates in the examination of Hypothesis 1.

Since some children have adenoidectomies and/or tonsillectomies to help resolve sleep-disordered breathing, these variables were also assessed for use as covariates. Results from these analyses are listed in Table 7. For the SLE group, there was a trend for a difference with those who did not have adenoidectomies having lower (i.e., better) OSA standard scores (M = 99.5, SD = 11.6, N = 19) than those who had adenoidectomies (M = 114, SD = 15.7, N = 3; t [20] = -1.94, p = .066). The same individuals who had adenoidectomies also had tonsillectomies; therefore, statistical results were the same for the tonsillectomy analysis. For the control group, there was no significant difference in OSA standard scores between those who did not have tonsillectomies (M = 96.2, SD = 10.8, N = 18) and those who had tonsillectomies (M = 103.7, SD = 14.6, N = 6); t [22] = -1.35, p = .190). For the control group, there was also no difference in OSA standard scores between those who did not have adenoidectomies (M = 97.1, SD = 10.6, N = 21) and those individuals who had adenoidectomies (M = 104.3, SD = 21.6, N = 3); t [21] = -.568, p = .624). Therefore, none of these variables were included as covariates in the examination of Hypothesis 1.

4.3 Examination of Hypotheses

4.3.1 Hypothesis 1: Sleep-disordered breathing in the SLE group compared to the control group

Hypothesis 1 stated that the SLE group would significantly differ in sleep-disordered breathing from the control group. The result for the main analysis for Hypothesis 1 is listed in Table 8 and can be seen in Figure 3. An independent samples t-test examined the difference in sleep-disordered breathing by using group (SLE and Control) as the independent variable and the obstructive sleep apnea (OSA) scale as the dependent variable. The analysis revealed that the mean score for the OSA scale for the SLE group (M = 101.5, SD = 12.8, N = 22) was not significantly different than the mean for the control group (M = 98.0, SD = 11.9, N = 24; t [44] = -.934, p = .356. Although preliminary analyses indicated body mass index percentile, age, income, socioeconomic status, tonsillectomies, and adenoidectomies were not correlated with the OSA scale, additional ANCOVA analyses were still conducted to covary for these variables. The ANCOVA analyses also concluded no difference between groups on the OSA scale. Hypothesis 1 was not supported.

4.3.2 Hypothesis 2: The relationship between sleep-disordered breathing and executive functioning in the SLE group

Hypothesis 2 stated that there would be a significant relationship between sleep-disordered breathing and executive dysfunction in the SLE group. Results for Hypothesis 2 are listed in Table 9. Sleep-disordered breathing was measured by the obstructive sleep apnea (OSA) scale. Executive functioning was measured by the Global Executive Composite, Category Switching Number Correct, Verbal Fluency Set-Loss Errors, Verbal

Fluency Repetition Errors, Letter-Number Switching, Letter-Number Sequencing Errors, and Digit Span scores. Results from correlation analyses between the OSA scale and the Global Executive Composite indicated a significant positive relationship ($r = .47$, $p = .026$, $N = 22$; see Figure 4). There was a trend for a relationship between the OSA scale and the Verbal Fluency Repetition Errors score ($r = -.49$, $p = .045$, $N = 17$). There were no significant relationships between the OSA scale and any of the other primary scales including the Category Switching Number Correct score ($r = -.34$, $p = .188$, $N = 17$), Verbal Fluency Set-Loss Errors score ($r = -.08$, $p = .764$, $N = 17$), Letter-Number Sequencing score ($r = .19$, $p = .459$, $N = 17$), Letter-Number Sequencing Errors score ($r = .29$, $p = .260$, $N = 17$), nor the Digit Span score ($r = -.13$, $p = .634$, $N = 17$). Hypothesis 2 was supported by the Global Executive Composite scale, but not by the other measures of executive functioning.

4.3.3 Hypothesis 3: An examination of risk factors in the relationship between sleep-disordered breathing and executive functioning in the SLE group

Hypothesis 3 stated that disease activity (i.e., Systemic Lupus Erythematosus Disease Activity Index, sedimentation rate) and disease severity (i.e., central nervous system involvement, kidney disease) would act as moderators, and depression would act as a mediator in the relationship between sleep-disordered breathing and executive dysfunction in SLE. Due to the small sample size, these analyses were unable to be conducted in this study.

4.4 Exploratory Follow-up Analyses

4.4.1 The relationship between the OSA scale and the other cognitive testing measures for the SLE group

Exploratory correlation analyses investigated any associations between the OSA scale and the other cognitive measures that were not used in the primary analyses. Table 9 contains a summary of the correlation analyses. When the Behavior Rating Inventory of Executive Function Global Executive Composite scale was divided into the Behavior Regulation Index and Metacognition Index, the Metacognition Index remained significantly correlated with the OSA scale ($r = .48$, $p = .024$, $N = 22$) and the Behavior Regulation Index displayed a trend for a significant relationship with the OSA scale ($r = .39$, $p = .066$, $N = 22$). Although there was a significant relationship between the Visual Scanning scale and the OSA scale ($r = .57$, $p = .017$, $N = 17$), this was in the opposite direction than would be expected. The Motor Speed scale demonstrated a trend for a relationship with the OSA scale ($r = .43$, $p = .089$, $N = 17$), but this was also in the opposite direction than would be expected. No other measures demonstrated significant relationships with the OSA scale (i.e., Letter Fluency, Category Fluency, Category Switching Accuracy, Number Sequencing, and Letter Sequencing).

4.4.2 A comparison of other sleep scales between the SLE and control groups

Exploratory independent samples t-tests examined the occurrence of any differences in the average standard score on any other sleep scale between the SLE and control groups. Results are listed in Table 8. There were no significant differences between the SLE and Control groups on the other sleep scales (i.e., Periodic Limb

Movement, Delayed Sleep Phase Syndrome, Excessive Daytime Sleepiness, Narcolepsy, and Sleep Disturbance Index; see Figure 5). According to the SDIS screening criteria, for the SLE sample, the possibility of excessive daytime sleepiness was 27%, periodic limb movement was 18%, delayed sleep phase syndrome was 32%, narcolepsy was 29%, and overall sleep disturbance was 22%. For the control sample, the possibility of excessive daytime sleepiness was 13%, periodic limb movement was 4%, delayed sleep phase was 21%, narcolepsy was 13%, and overall sleep disturbance was 13%.

4.4.3 The relationship between the other sleep scales and the cognitive variables for the SLE group

Exploratory analyses examined any other relationships between the other sleep scales and the cognitive measures. Results of the correlation analyses are listed in Table 9. For Periodic Limb Movement, there was a significant relationship with the Global Executive Composite ($r = .66$, $p = .001$, $N = 22$), and then subsequently the Behavior Regulation Index ($r = .70$, $p = .000$, $N = 22$) and Metacognition Index ($r = .59$, $p = .004$, $N = 22$). There was also a trend for a relationship between the Periodic Limb Movement scale and the Letter Sequencing score ($r = -.44$, $p = .076$, $N = 17$). For Delayed Sleep Phase Syndrome, there was a significant relationship with both the Number Sequencing score ($r = -.69$, $p = .002$, $N = 17$) and Letter Sequencing score ($r = -.63$, $p = .007$, $N = 17$). Trends for relationships were seen for Delayed Sleep Phase Syndrome with the Global Executive Composite ($r = .42$, $p = .053$, $N = 22$), Behavior Regulation Index ($r = .38$, $p = .081$, $N = 22$), and Metacognition Index ($r = .41$, $p = .059$, $N = 22$). Excessive Daytime Sleepiness demonstrated significant relationships with the Global Executive

Composite (r = .66, p = .001, N = 22), Behavior Regulation Index (r = .67, p = .001, N = 22), Metacognition Index (r = .59, p = .003, N = 22), Number Sequencing (r = -.61, p = .009, N = 17), and Letter Sequencing (r = -.59, p = .011, N = 17). The Narcolepsy scale showed a significant relationship with the Global Executive Composite (r = .56, p = .008, N = 21), Behavior Regulation Index (r = .58, p = .006, N = 21), Metacognition Index (r = .52, p = .017, N = 21), Number Sequencing (r = -.59, p = .015, N = 16), and Letter Sequencing (r = -.52, p = .038, N = 16) scores. The Sleep Disturbance Index demonstrated significant relationships with the Global Executive Composite (r = .62, p = .002, N = 22), Behavior Regulation Index (r = .61, p = .002, N = 22), Metacognition Index (r = .58, p = .005, N = 22), Number Sequencing (r = -.55, p = .022, N = 17), and Letter Sequencing (r = -.52, p = .032, N = 17) scores.

4.4.4 The relationship between the depression measure and the sleep and cognitive variables for the SLE group

Exploratory analyses examined any relationships between the Depression score and the sleep and cognitive measures. The Depression score demonstrated significant relationships with the Behavior Rating Inventory of Executive Function Global Executive Composite (r = .72, p = .000, N = 21), Behavior Regulation Index (r = .67, p = .001, N = 21), and Metacognition Index (r = .69, p = .001, N = 21) scores. No other cognitive measures (i.e., DKEFS Verbal Fluency test scores, DKEFS Trail Making test scores, or WISC-IV/WAIS-III Digit Span score) demonstrated a significant relationship with the depression score. The Depression score also demonstrated significant relationships with the Sleep Disorders Inventory for Students Obstructive Sleep Apnea scale (r = .49,

$p = .021$, $N = 21$), Periodic Limb Movement scale ($r = .51$, $p = .018$, $N = 21$), Excessive Daytime Sleepiness scale ($r = .56$, $p = .008$, $N = 21$), Narcolepsy scale ($r = .51$, $p = .022$, $N = 21$), and Sleep Disturbance Index scale ($r = .53$, $p = .014$, $N = 21$). There was no significant relationship with the Depression score and the Delayed Sleep Phase Syndrome score ($r = .25$, $p = .270$, $N = 21$).

CHAPTER 5: DISCUSSION

5.1 Overview of the Findings

The purpose of this study was to determine if sleep-disordered breathing differed between children and adolescents with SLE compared to those without SLE. This study also aimed to examine the relationship between sleep-disordered breathing and executive dysfunction in SLE, and examine risk factors that may contribute to this relationship. The goal was to provide information that would be helpful in identifying individuals with SLE who may be at risk for sleep-disordered breathing and, subsequently, cognitive problems.

In sum, results from the main analyses indicated that individuals with SLE did not differ in sleep-disordered breathing symptoms from the control group. Fourteen percent of the SLE group met criteria for the possibility of having sleep-disordered breathing on a parent-report questionnaire, compared to 17% of the control group. In the SLE sample, an increase in symptoms of sleep-disordered breathing was related to an increase in executive function difficulties as measured by the BRIEF. Risk factors that may have contributed to the relationship between sleep-disordered breathing and executive dysfunction were not examined because of the small sample size in this study. Exploratory follow-up analyses indicated no other subtypes of biologically based sleep problems (i.e., periodic limb movement, excessive daytime sleepiness, delayed sleep phase syndrome, narcolepsy, and overall sleep disturbance problems) compared to the control group. However, relationships were seen with these other sleep problems and some executive functioning measures. Exploratory analyses also indicated symptoms of

depression were related to some measures of cognitive and sleep functioning. A discussion of the results, consistency of the results with heuristic sleep-disordered breathing models, limitations for this study, clinical implications, and ideas for future research, are discussed in detail in the sections below.

5.2 Discussion of Hypotheses

5.2.1 Hypothesis 1

The first hypothesis in this study examined parent's report of sleep-disordered breathing in a sample of children and adolescents with SLE. Participants were included if they met the diagnosis of SLE according to diagnostic criteria. Based on the literature that indicates the involvement of immunoregulatory proteins in both SLE and in sleep-disordered breathing (Alberti et al., 2003; Gabay et al., 1997; Lacki et al., 1997; Tauman et al., 2004), it was hypothesized that children and adolescents with SLE would differ in amount of sleep-disordered breathing symptoms compared to a control group. Specifically, those with SLE were thought to be at increased risk for sleep-disordered breathing. The purpose of this examination was to add to the pediatric SLE literature on sleep functioning; an area scarcely studied in this population.

The results from this study indicated that the children and adolescents with SLE did not exhibit more symptoms of sleep-disordered breathing than those without SLE on a parent-report measure. These findings implied that sleep-disordered breathing was not a particular concern of these parents. In general, the findings suggest that sleep-disordered breathing is not a likely characteristic of SLE, as it may be in other pediatric

populations such as sickle cell disease, diabetes, ADHD, and spina bifida (Kirk et al., 1999; Kothare et al., 2005; Owens, Maxim, et al., 2000; Villa et al., 2000).

Although this statistical analysis had low power, was limited by a small SLE sample size, and had a low effect size, the means between the two groups were very close. For the SLE sample, 14% met criteria for the possibility of sleep-disordered breathing on the Sleep Disorders Inventory for Students, which was similar to the control group of 17% meeting criteria. When teasing out those with and without central nervous system (CNS) involvement no statistical difference was seen in the amount of sleep-disordered breathing symptoms. Interestingly, however, in those with CNS involvement, 30% met the criteria for the possibility of sleep-disordered breathing on the Sleep Disorders Inventory for Students questionnaire, compared to 0% of those without CNS involvement. These prevalence rates indicate the SLE sample as a whole is no different than non-SLE samples; however, CNS involvement may increase the risk of sleep-disordered breathing.

The findings from this analysis bring light to findings from other studies investigating sleep-disordered breathing in SLE. Findings from this study are similar to results from the Cruz and colleagues (2007) study that investigated adolescents with SLE. Five participants from the current study were recruited from the same pediatric rheumatology clinic as the Cruz and colleagues (2007) study. Both the Cruz and colleagues study and the current study were compared to separate control samples that were taken from the same pediatric ambulatory care clinic. The study by Cruz and colleagues investigated roughly the same number of participants as the current study. The Children's Sleep Habits Questionnaire, Sleep-Disordered Breathing scale, used in the

pilot study by Cruz and colleagues is reported to have unacceptable reliability (α = .51; Owens, Spirito, & McGuinn, 2000) and the subscale only includes three questions. However, when sleep problems were investigated with the more reliable Sleep Disorders Inventory for Students Obstructive Sleep Apnea scale (norming sample, α = .88 – 90; this study's SLE sample, α = 71) in this study, the SLE sample continued to show no difficulty in sleep-disordered breathing problems. However, because questionnaires were used in both the current study and the Cruz and Colleagues study, reporter bias may have affected the results.

Findings from the current study were contradictory to the findings by Valencia-Flores and colleagues (1999) that suggested sleep problems occurred in their sample of adults with SLE as indicated by a polysomnography study. The difference in sleep functioning may be related to age differences, in that disease severity and/or disease activity may not be as severe in younger individuals with SLE. Furthermore, the authors did not indicate whether participants in this study had central nervous system (CNS) involvement. Due to this study's limitations, polysomnography and actigraphy were unable to be performed. More formally based evaluations of sleep-disordered breathing and sleep latency might have identified mild sleep-disordered breathing in this young population.

Interestingly, parents whose child had an adenoidectomy or tonsillectomy reported more problems with sleep-disordered breathing. It is unclear whether the children in this sample had their adenoidectomies and tonsillectomies because of snoring and sleep problems, or because of other health or medical concerns. Either way, having an adenoidectomy and/or tonsillectomy in this sample signified more sleep-disordered

breathing symptoms. These parents may be more aware of their child's sleeping habits or their child may still have symptoms of sleep-disordered breathing despite their adenoidectomy and/or tonsillectomy.

5.2.2 Hypothesis 2

The second hypothesis in this study examined whether children and adolescents with SLE who exhibit increased sleep-disordered breathing symptoms have co-occurring executive functioning difficulties. Based on pediatric literature and heuristic models (Archbold et al., 2004; Beebe, 2005; Beebe & Gozal, 2002; Beebe et al., 2004), it was hypothesized that there would be an association between sleep-disordered breathing and executive dysfunction in this study's sample of children and adolescents with SLE.

Findings from this study indicated that the children and adolescents with SLE with more symptoms of sleep-disordered breathing on the Sleep Disorders Inventory for Students (SDIS) did have more executive functioning difficulties on the Behavior Rating Inventory of Executive Function (BRIEF). Despite this relationship, it should be noted that most of the SLE sample scored within the average range on the BRIEF Global Executive Composite (GEC) score. There was also more variability in the BRIEF GEC score at higher levels of the sleep-disordered breathing scale (i.e., OSA scale) of the SDIS. This means these findings are based on a small sample of children and adolescents with more sleep-disordered breathing problems. Analyses with other paper/pencil executive functioning measures did not indicate any significant associations. Overall, findings from these analyses suggest that those children and adolescents with more sleep-

disordered breathing symptoms may be more likely to have co-occurring executive functioning difficulties.

It was interesting that the parent-report of executive function was associated with parent-report of sleep-disordered breathing, but paper/pencil tasks of executive function were not. This may have occurred because parents may be better reporters of everyday functioning abilities. In addition, the BRIEF is more of an assessment of "neurobehavioral dysfunction," than the paper/pencil tasks. Neurobehavioral dysfunction is what many researchers describe as problems for children and adolescents with sleep-disordered breathing (Archbold et al., 2004; Beebe et al., 2004; Lewin et al., 2002). Some other studies have even found positive findings investigating sleep-disordered breathing and executive functioning by use of the BRIEF (Beebe et al., 2004). However, because parents completed both the BRIEF and SDIS, parent report bias may account for this association. Parents may be inaccurate reporters or may report more problems in hope to gain more services for their child. There also was a difference in the sample size for the analyses. For example, there were 22 participants included in the analysis looking at the relationship between the SDIS and the BRIEF. There were 17 participants included in the analyses investigating the relationship between the SDIS and the paper/pencil testing measures. Therefore, the sample size difference for the questionnaire versus paper/pencil testing analyses cannot be discounted as a reason for the difference in findings. Furthermore, the paper/pencil tests may have capitalized on individual functions that may not have been specific enough to detect relationships. In general, the BRIEF may be a better and quick measure to use to screen for executive functioning difficulties in SLE.

Previous research that has investigated cognitive functioning in children without SLE but with sleep-disordered breathing indicates these individuals have lower scores on executive functioning measures. For example, studies have concluded these individuals have lower scores on measures of impulsivity, emotional control, self-initiation of activities, working memory, planning, organization, self-monitoring, verbal fluency, sustained attention, vigilance, mental flexibility, and visual attention skills (Archbold et al., 2004; Beebe et al., 2004). The current study used correlation analyses to look at the relationship between sleep-disordered breathing and executive dysfunction. Findings from this study are consistent with pediatric sleep-disordered breathing research and proposed heuristic models that suggest an association between sleep-disordered breathing and executive dysfunction.

Interestingly, although previous research indicates children and adolescents with SLE have mild cognitive functioning difficulties (Papero et al., 1990; Wyckoff et al., 1995), the SLE group in this study scored overall in the average range on all testing measures. Prevalence rates for those with cognitive difficulties defined by scores in the low average to below low average range were fairly low. These findings may have occurred because the SLE sample was from a middle class population, perhaps suggesting average cognitive abilities. However, this study's sample had a similar socioeconomic status level, mean age, and number of participants to the Papero and colleagues (1990) study. The Papero and colleagues study included 21 children with SLE with a mean age of 15 years, with no overt central nervous system involvement. In the current study, 17 children were tested, 22 completed the questionnaire measures, and the mean age was also 15. This study did not separate out those with overt central nervous

system (CNS) involvement, who you might suspect to have more executive functioning problems. However, even with those individuals with CNS involvement included in this study's analyses, the overall sample scored in the average range on all study measures. When comparing those with and without CNS involvement, those with involvement did not demonstrate significantly poorer scores on the BRIEF or paper/pencil cognitive tests. Findings from the current study suggest that executive dysfunction is not an overall characteristic for children and adolescents with SLE as a group, but may be more of an individual concern.

Another interesting difference between the current study and previous research findings is in intelligence. A study by Wyckoff and colleagues (1995) indicated low average intellectual abilities. The demographics of the Wyckoff and colleagues study was unavailable, therefore, it is unclear if this sample had lower intelligence because of a lower socioeconomic status, small sample size (i.e., eight participants), or if the results were true findings. Interestingly, the overall score of intelligence from the current study sample was in the average range and is consistent with the findings from the Papero and colleagues (1990) study which had a sample of children from a similar socioeconomic status level as the current study. Although the current study used an abbreviated measure of intelligence, this study had a much larger sample size than the Wyckoff and colleagues study and a roughly similar sample size as the Papero and colleagues study. Findings suggest overall average intellectual abilities in children and adolescents with SLE as a group.

5.2.3 Hypothesis 3

The third hypothesis intended to examine potential risk factors that might be specific to SLE and that may contribute to the relationship between sleep-disordered breathing and executive dysfunction in this population. Based on a proposed heuristic sleep-disordered breathing model (Beebe, 2005), the current study hypothesized that disease activity (i.e., Systemic Lupus Erythematosus Disease Activity Index, sedimentation rate) and disease severity (i.e., central nervous system involvement, kidney disease) would moderate the relationship between sleep-disordered breathing and executive dysfunction in children and adolescents with SLE, and depression would mediate the relationship. However, due to a small sample size the statistical analyses could not be conducted and this hypothesis could not be examined.

5.3 Discussion of Exploratory Follow-up Analyses

The first set of follow-up exploratory analyses investigated any associations between sleep-disordered breathing and any of the other cognitive functioning measures. These analyses were conducted to further evaluate the use of the cognitive screening measures in this study. The findings indicated that individuals with SLE from this study displayed a significant relationship between scores on the sleep-disordered breathing scale and the Behavior Rating Inventory of Executive Function (BRIEF) Behavior Regulation Index and Metacognition Index. As previously noted, reporter bias may be a possible reason for the association between these measures. The small sample size also may affect the value of these results. No other paper/pencil testing measures were

significantly related to sleep-disordered breathing. Overall, the BRIEF continued to be a strong screening instrument for detecting executive functioning concerns.

The second set of follow-up exploratory analyses was conducted to further define sleep functioning in children and adolescents with SLE. In this sample, there were no significant problems specific to the SLE group compared to the control group on the other sleep scales. The findings indicated that compared to individuals without SLE, parents of children with SLE report that their children exhibit a relatively similar profile overall on scales measuring periodic limb movement, delayed sleep phase syndrome, excessive daytime sleepiness, narcolepsy, and overall sleep disturbance problems. In fact, in this study, both children with SLE and without SLE scored in the overall non-clinical range. According to the Sleep Disorders Inventory for Students (SDIS) screening criteria, for the SLE sample, the possibility of excessive daytime sleepiness was 27%, periodic limb movement was 18%, delayed sleep phase syndrome was 32%, narcolepsy was 29%, and overall sleep disturbance was 22%. Although a difference between groups was not evident, the control group showed a lower percentage of individuals with the possibility of these specific sleep problems. For the control sample, the possibility of excessive daytime sleepiness was 10%, periodic limb movement was 11%, delayed sleep phase syndrome was 24%, narcolepsy was 14%, and overall sleep disturbance was 13%. This follow-up analysis suggests that although these specific biologically based sleep problems are not an area of overall significant concern for parents of young individuals with SLE, these individuals do tend to exhibit somewhat more sleep problems than those without SLE. A larger sample size may have been able to better determine the small difference in these sleep functioning scores.

The third set of exploratory analyses was conducted to determine if any of the other screening areas of sleep functioning were related to the screening areas of cognitive functioning. Specifically, for periodic limb movement, there was a significant relationship with executive functioning measured by the BRIEF scales (i.e., Global Executive Composite, Behavior Regulation Index, and Metacognition Index). For Delayed Sleep Phase Syndrome, there was a significant relationship with the Trail Making Number Sequencing and Trail Making Letter Sequencing tests, which are tests of visual processing speed. For Excessive Daytime Sleepiness, there were significant relationships with the BRIEF scales (i.e., Global Executive Composite, Behavior Regulation Index, and Metacognition Index), as well as on visual processing speed measures including the Trail Making Number Sequencing and Trail Making Letter Sequencing. For Narcolepsy, there was a relationship with the BRIEF scales (i.e., Global Executive Composite, Behavior Regulation Index, and Metacognition Index), as well as on the Trail Making Number Sequencing and Trail Making Letter Sequencing tests. For the Sleep Disturbance Index, there was a significant relationship with the BRIEF scales (i.e., Global Executive Composite, Behavior Regulation Index, and Metacognition Index), as well as the Trail Making Number Sequencing and Trail Making Letter Sequencing tests. As previously indicated in other analyses, reporter bias may be a possible reason for the association between the questionnaire measures. These findings indicate that the BRIEF and paper/pencil tests of visual processing speed appeared to be the most successful screening measures, as indicated by their relationship with specific sleep problems.

The fourth set of exploratory analyses was conducted to explore any relationships between symptoms of depression and performance on sleep and cognitive functioning measures. The findings indicated that the Depression scale from the Depression and Anxiety in Youth Scale (DAYS) did demonstrate significant relationships with the BRIEF scales (i.e., Global Executive Composite, Behavior Regulation Index, and Metacognition Index). However, no other cognitive measures (i.e., DKEFS Verbal Fluency test scores, DKEFS Trail Making test scores, or WISC-IV/WAIS-III Digit Span score) demonstrated a significant relationship with the Depression scale. The DAYS Depression score also demonstrated significant relationships with the SDIS Obstructive Sleep Apnea scale, Periodic Limb Movement, Excessive Daytime Sleepiness, Narcolepsy, and Sleep Disturbance Index scores. There was no significant relationship between the Depression score and the Delayed Sleep Phase Syndrome score. Reporter bias also applies to these findings as a possible reason for the association between these measures. These findings suggest that children and adolescents with SLE with more symptoms of depression may be more likely to have executive functioning difficulties and sleep problems.

5.4 Limitations

There were several methodological limitations that may have limited the outcome and meaning of this study's findings. The small sample size of the SLE group reduced the power for this study's statistical analyses. The possible sample size was limited due to the age range. Since only 15% to 20% of SLE cases are children, there were a limited number of individuals who could be recruited (McGhee et al., 2004; Stichweh et al.,

2004). Similar to other medical populations, illness-related factors such as flare-ups make it difficult for individuals with SLE to adhere to study appointments. A larger sample size and more statistical power would have made it less likely of the probability of committing a type II error for Hypothesis 1. A larger sample size would also have allowed for a more meaningful interpretation of Hypothesis 2, making for less variability in the BRIEF GEC score at higher levels of the SDIS OSA score.

The equality of the control group to the SLE sample in this study may have affected this study's ability to accurately describe sleep functioning in the SLE sample. The control group differed in ethnicity from the SLE group, with more Hispanics (63%) than African Americans (29%). The SLE and control groups also differed in socioeconomic status, despite methodological procedures to develop an appropriate comparison group. The difference in socioeconomic status and ethnicity likely occurred because more of the SLE sample came from The Children's Hospital of Philadelphia which treats more of a middle class population, whereas the control group came from St. Christopher's Hospital for Children which treats individuals from more of a lower socioeconomic status population. Since lower socioeconomic status is associated with more sleep problems, the control group may have had more sleep symptoms than a socioeconomically matched control group. Having a control group that was comparable in ethnicity and socioeconomic status would have made for a more appropriate comparison to help describe sleep functioning in SLE.

The representativeness of the SLE sample may have limited this study's ability to generalize the results to the SLE population. For example, only 45% of the SLE sample was African American, which is not consistent with the literature that indicates SLE

occurs more in the African American population (Hopkinson et al., 1994). Relatively under control disease activity and mild disease severity in the SLE participants during their involvement in the study procedures, may also have made for a less representative sample. There was a low disease activity level in this sample probably because study appointments were unable to be completed during disease flare-ups. Additionally, disease activity measures were gathered through chart review, meaning disease activity levels may not have corresponded to the individual's disease activity level during measurement of cognitive and sleep functioning. There was also mild disease severity in this sample. Forty-five percent of the SLE sample had more severe disease as indicated by neuropsychiatric (i.e., CNS) involvement. This is lower than indicated in the literature, which indicates between 48% and 95% of children with SLE have neuropsychiatric problems (Sibbitt et al., 2002; Steinlin et al., 1995). Only 59% had kidney disease, compared to 67% to 82% reported in the literature (Cameron, 1994; Gibson, Ferris, Dooley, Huang, & Hogan, 2003; Klein-Gitelman et al., 2002). Lower disease activity and mild disease severity may explain why the group overall had normal sleep and average cognitive abilities than have been reported in other studies. A larger sample or different assessment procedures may have helped to incorporate more individuals with higher disease activity levels and more severe disease severity, and hence more possible functioning problems.

Parent report bias is always a question of concern in the pediatric literature and is especially a concern with adolescents. Parents may be unaware of their adolescents sleep and behavioral functioning. This may have led to an inaccurate documentation of sleep, behavioral, emotional, and cognitive abilities. The use of adolescent self report in

conjunction with parent report may have provided a more accurate description of these abilities.

The reliability of the Sleep Disorders Inventory for Students OSA scale may have affected this study's results. Although the OSA subscale for the adolescent version of the questionnaire had respectable reliability for the SLE group, the subscale had undesirable reliability for the control group. Since the reliability of the subscale with the adolescent control group was in the undesirable range, this may have affected the ability to accurately compare the sample groups. The construction of the ethnic representation of the Sleep Disorders Inventory for Students was similar to the 2000 U.S. Census report. Therefore, a majority of the normative sample was Caucasian, which may have affected the results of this study since only 32% were Caucasian in the SLE group and 4% were Caucasian in the control group. The socioeconomic status level reported for the normative data sample was in middle class range, which is similar to the SLE sample, but higher than the control group sample.

Different measures of cognitive functioning were used in other studies in the pediatric SLE literature than were used in the current study. Therefore the average cognitive abilities seen in this study may be evident because of test choice. Many of the tests in this study measured working memory, cognitive flexibility, and processing speed. The addition of tests measuring other areas of executive functioning and cognitive abilities, such as problem solving, attention, vigilance, and complex working memory, may have been able to better describe which cognitive abilities are related to sleep-disordered breathing in SLE.

5.5 Implications and Future Directions

5.5.1 Clinical directions and implications

Despite the many limitations that may have affected the results of this study, the main intent of this study was to provide further information regarding pediatric SLE for physicians, psychologists, patients, and caregivers. The children and adolescents with SLE in this sample, as a group, were under relatively good disease activity, had mild disease severity, demonstrated a normal profile for sleep-disordered breathing compared to individuals without SLE, and demonstrated average intelligence and executive functioning skills. Therefore, those with low disease activity and mild disease severity may be less susceptible to sleep and cognitive difficulties.

Despite these normal profiles, during testing and speaking with the families, some patients and their parents did indicate the patient was having sleep problems and was sleepy during the day. Sleep complaints consisted of difficulty falling asleep, difficulty staying asleep, and napping in the daytime. In this SLE sample, there appeared to be a specific subset of participants who had more sleep and cognitive difficulties. For example, 30% of individuals with central nervous system (CNS) involvement met the criteria for sleep-disordered breathing compared to 0% of those without CNS involvement according to the Sleep Disorders Inventory for Students (SDIS) questionnaire. This was also the case with the other sleep scales (i.e., excessive daytime sleepiness, periodic limb movement, delayed sleep phase syndrome, narcolepsy, and overall sleep disturbance), with individuals with CNS involvement demonstrating more sleep problems than those without CNS involvement according to the SDIS questionnaire. In addition, those with depressive symptoms tended to have more sleep

complaints (i.e., sleep-disordered breathing, periodic limb movement, excessive daytime sleepiness, and narcolepsy) and executive functioning difficulties as measured by the Behavior Rating Inventory of Executive Function (BRIEF). Therefore, children and adolescents with SLE with these risk factors may be at increased risk for sleep and cognitive problems.

One aim was to evaluate a potential screening battery for clinical use in determining any overall sleep or cognitive problems in this sample in order to provide these families with referrals for more comprehensive sleep or neuropsychological evaluations, if needed. Results from this study suggest that the Sleep Disorders Inventory for Students (SDIS) and the Behavior Rating Inventory of Executive Function (BRIEF) may be adequate screening measures to assess for sleep and executive functioning concerns. The Depression and Anxiety in Youth Scale (DAYS) depression subscale was also a reliable measure with this SLE sample. The BRIEF, SDIS, and DAYS screening measures are easy to administer, quick for parents to complete, and require little training to administer and score.

After children and adolescents are screened for any sleep, emotional, or cognitive problems, clinics should refer those individuals with problems for further evaluation. Those children who have more sleep problems would benefit from being referred on for a formal sleep evaluation including a polysomnography study. Those children exhibiting cognitive problems would benefit from a comprehensive neuropsychological evaluation. The neuropsychological evaluation can assist with determining any areas of significant concerns regarding cognitive functioning, as well as provide referral information for services for school or outside of school. Furthermore, psychotherapy,

psychopharmacological treatment, and monitoring of SLE inflammatory medications may be helpful in regulating depressive symptoms in this population.

5.5.2 Research directions

Although this sample of individuals with SLE did not demonstrate more symptoms of sleep-disordered breathing than a control sample, a relationship existed between sleep-disordered breathing and executive dysfunction. Due to the small sample size, these results are preliminary, and future studies should be conducted that incorporate larger samples. To increase participation, it will be important to employ multiple sites to obtain a larger set of eligible participants. Collaborative efforts should be made with physicians and nurses to help in the identification and recruitment of eligible participants. Future studies may benefit from including participants who are 19 and 20 years old to increase the sample size, as many of those with SLE are not diagnosed until their teenage years. To increase participation rates, studies may wish to incorporate a stipend to compensate for time spent participating in the study. In this study, 88% of those that were consented completed the study measures that were offered the stipend from one hospital, compared to 40% who were not offered a stipend in the other hospital. Home visits were also necessary and more successful for study completion. However, the use of a full time research assistant who is available during each participant's routine clinic visit and who can conduct home visits on a day to day basis may have an increased success rate with study completion.

Future studies should investigate risk factors specific to this population that may contribute to the relationship between sleep-disordered breathing and executive

dysfunction as proposed by the pediatric sleep-disordered breathing heuristic model by Beebe (2005). Although the current study could have considered conducting moderation and mediation analyses to examine risk and resilience factors, there was insufficient sample size for these analyses. Therefore, future studies that incorporate larger samples could investigate the contribution of illness related factors in the relationship between sleep-disordered breathing and executive dysfunction in SLE.

Future studies should devise ways to examine current disease activity levels during the time of the study procedures. For example, adding a form of physician global assessment of disease activity by use of a Likert rating scale would be helpful. The incorporation of a blood draw will allow for more accurate current disease activity information. Since previous studies involving children and adults indicate that specific immunoregulatory proteins are involved in sleep-disordered breathing and in individuals with SLE (Alberti et al., 2003; Gabay et al., 1997; Lacki et al., 1997; Tauman et al., 2004), inclusion of analyses involving immunoregulatory proteins in future studies will be important. Examination of medication usage which may affect disease activity may also be helpful. Including a review of MRI reports would help to confirm who to categorize as having more severe disease severity as indicated by CNS involvement.

A more thorough evaluation of executive functioning skills including tasks assessing problem solving (e.g., Wisconsin Card Sorting Test, Category Test) and attention/vigilance (e.g., Conner's Continuous Performance Test) would make for a more comprehensive and multimodal evaluation. Furthermore, the addition of memory measures (e.g., Wide Range Assessment of Memory and Learning, Children's Memory

Scale), could assess if sleeping problems are related to memory problems in this population. A full neuropsychological assessment would be helpful in this process.

Formal objective measures such as polysomnography and actigraphy might be useful in describing sleep functioning in SLE. A polysomnography study may help to determine mild sleep difficulties not observable by parent report and would not be subject to report bias. Specifically, researching a subset of children with central nervous system (CNS) involvement might be interesting, since findings from the current study indicted more of a prevalence of sleep-disordered breathing symptoms in those with CNS involvement. Since many of the children and adolescents in this study complained of feeling sleepy and many of the adolescents indicated they were having a difficult time sleeping at night, actigraphy studies could better describe sleep latency in SLE.

When using the Sleep Disorders Inventory for Students (Luginbuehl, 2006) questionnaire with the SLE population in research, it may be beneficial to look at the overall Sleep Disturbance Index score to obtain general sleep disturbance problems. Results from this study indicated the Sleep Disturbance Index score had excellent reliability. However, since findings from exploratory analyses concluded there were mild elevations on some of the SDIS subscales (i.e., excessive daytime sleepiness, periodic limb movement, delayed sleep phase syndrome, and narcolepsy) compared to the control group and there were associations between these subscales and areas of executive functioning, further investigation of different areas of sleep disturbance may be interesting.

This study used a control group for a more empirically based research design. However, the control group in this study only was administered the sleep functioning

questionnaire. Future prospective studies should also use a control group for a comparison group for the cognitive functioning measures as well. The control sample in this study differed in socioeconomic status from the SLE sample. Therefore use of a sibling and/or matched peer control group in future studies may be a better comparison group.

5.6 Conclusions

This study was one of the first to investigate sleep-disordered breathing and its association with executive functioning in children and adolescents with SLE. One might postulate that individuals with SLE would be at increased risk for sleep-disordered breathing, because many of the same immunoregulatory proteins involved in SLE are also involved in those with sleep-disordered breathing. In this study, children and adolescents with SLE did not show any more symptoms of sleep-disordered breathing than a sample without SLE. However, individuals with SLE with more symptoms of sleep-disordered breathing did have more executive functioning difficulties. Risk factors that may contribute to this relationship were unable to be examined because of the small sample size in this study. This study was consistent with sleep heuristic models that propose a relationship between sleep-disordered breathing and executive dysfunction.

This study advances our knowledge of SLE in children and adolescents. The discussion covered the importance of screening for sleep, emotional, and cognitive functioning problems in this population. The discussion highlighted the importance of providing referrals for a more comprehensive evaluation to those with sleep and cognitive problems. This study also suggested how the Behavior Rating Inventory of Executive

Function (BRIEF), the Sleep Disorders Inventory for Students (SDIS), and the Depression and Anxiety in Youth Scale (DAYS), would be a useful set of screening measurements for identifying individuals in need of further evaluations and services. Given many methodological limitations, the findings from this study are preliminary. Further research is required that incorporates larger samples, a sibling or matched control group, and recent disease activity measurements to examine the questions in this study. Future research in pediatric SLE may also benefit from using a polysomnography study to investigate sleep functioning and a more comprehensive cognitive evaluation to assess executive functioning skills.

LIST OF REFERENCES

Abu-Shakra, M., Urowitz, M., Gladman, D., & Gough, J. (1995). Mortality studies in systemic lupus erythematosus. Results from a single center. I. Causes of death. *Journal of Rheumatology, 22 (7),* 1259-1264.

American College of Rheumatology Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature. (1999). The American college of rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis & Rheumatism, 42 (4),* 599-608.

Alberti, A., Sarchielli, P., Gallinella, E., Floridi, A., Floridi, A., Mazzotta, G. et al. (2003). Plasma cytokine levels in patients with obstructive sleep apnea syndrome: a preliminary study. *Journal of Sleep Research, 12*, 305-311.

Ali, N., Pitson, D., & Stradling, J. (1996). Sleep-disordered breathing: Effects of adenotonsillectomy on behavior and psychological functioning. *European Journal of Pediatrics, 155 (1),* 52-62.

Anstead, M. (2000). Pediatric sleep disorders: new developments and evolving understanding. *Current Opinion in Pulmonary Medicine, 6*, 501-506.

Anstey, N.M., Bastian, I., Dunckley, H., & Currie, B.J. (1993). Systemic lupus erythematosus in Australian aborigines: high prevalence, morbidity and mortality. *Australian and New Zealand Journal of Medicine, 23 (6),* 646-651.

Antshel, K.M. & Waisbren, S.E. (2003). Timing is everything: Executive functions in children exposed to elevated levels of phenylalanine. *Neuropsychology, 17 (3),* 458-468.

Archbold, K., Girodani, B., Ruzicka, D., & Chervin, R. (2004). Cognitive executive dysfunction in children with mild sleep-disordered breathing. *Biological research for nursing, 5 (3)*, 168-176.

Arkachaisri, T. & Lehman, T. (1999). Systemic lupus erythematosus and related disorders of childhood. Pediatric and heritable disorders. *Current Opinion in Rheumatology, 11 (5),* 384.

Beebe, D. (2005). Neurobehavioral effects of obstructive sleep apnea: an overview and heuristic model. *Current Opinion in Pulmonary Medicine, 11*, 494-500.

Beebe, D. & Gozal, D. (2002). Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *Journal of Sleep Research, 11*, 1-16.

Beebe, D., Lewin, D., Zeller, M., McCabe, M., MacLeod, K., Daniels, S., et al. (2006). Sleep in overweight adolescents: Shorter sleep, poorer sleep quality, sleepiness, and sleep-disordered breathing. *Journal of Pediatric Psychology*, 1-11.

Beebe, D., Wells, C., Jeffries, J., Chini, B., Kalra, M., & Amin, R. (2004). Neuropsychological effects of pediatric obstructive sleep apnea. *Journal of International Neuropsychological Society, 10,* 962-975.

Blunden, S., Lushington, K., Kennedy, D., Martin, J., & Dawson, D. (2000). Behavior and neurocognitive performance in children aged 5-10 years who snore compared to controls. *Journal of Clinical and Experimental neuropsychology, 22 (5),* 554-568.

Bombardier, C., Gladman, D., Urowitz, M., Caron, D., & Chi Hsing, C. (1992). Derivation of the SLEDAI: a disease activity index for lupus patients. *Arthritis & Rheumatism, 35*, 630-640.

Cameron, J. (1994). Lupus nephritis in childhood and adolescence. *Pediatric Nephrology, 8,* 230-249.

Castele, R.J., Strohl, K.P., Chester, C.S., Brittenham, G.M., & Harris, J.W. (1988). Oxygen saturation with sleep in patients with sickle cell disease. *Archives of Internal Medicine, 146,* 722-725.

Chervin, R., Clarke, D., Huffman, J., Szymanski, E., Ruzicka, D., Miller, V., et al. (2003). School performance, race, and other correlates of sleep-disordered breathing in children. *Sleep Medicine, 4,* 21-27.

Chinn, R., Wilkinson, I., Hall-Craggs, M., Paley, M., Shortall, E., Carter, S., et al. (1997). Magnetic resonance imaging of the brain and cerebral proton spectroscopy in patients with systemic lupus erythematosus. *Arthritis & Rheumatology, 40 (1),* 36-46.

Ciftci, E., Yalcinkaya, F., Ince, E., Ekim, M., Illeri, M., Orgerin, Z., et al. (2004). Pulmonary involvement in childhood-onset systemic lupus erythematosus: a report of five cases. *Rheumatology, 43 (5),* 587-591.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences (2nd edition).* New York, NY: Lawrence Erlbaum Associates.

Cook, R., Gladman, D., Pericak, D., & Urowitz, M. (2000). Prediction of short term mortality in systemic lupus erythematosus with time dependent measures of disease activity. *Journal of Rheumatology, 27 (8),* 1892-1895.

Cronbach, L. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika, 16,* 297-334.

Cruz, M., Chawla, A., Adams, R., Martucci, C., Coleman, C., Grant, M., Fathalla, B., Goldsmith, D., & Kothare, S. (2007). Prevalence of sleep disorders in children with systemic lupus erythematosus. *Sleep, Abstract Supplement, 30*, A308.

Dahl, R. (1996). The impact of inadequate sleep on children's daytime cognitive function. *Seminars in Pediatric Neurology, 3*, 44-50.

Delis, D.C., Kaplan, E., & Kramer, J. (2001). *The Delis-Kaplan executive function system.* San Antonio: The Psychological Corporation.

Deonandan, R., Campbell, K., Ostbye, T., Tummon, I., & Robertson, J. (2000). A comparison of methods for measuring socioeconomic status by occupation or postal area. Chronic Diseases in Canada, 21 (3), 114-118.

DeVellis, R.F. (1991). Scale development: Theory and applications. Applied social science research methods series volume 26. London: Sage.

Dubois, E. (1953). The effect of the LE cell test on the clinical picture of systemic lupus erythematosus. *Annals of Internal Medicine, 38 (6),* 1265-1294.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*, 175-191.

Franco, M., Leong, M., Varlotta, L., Reber, D., Bauer, N., Dampier, C., et al. (1996). Sleep hypoxemia in children with sickle cell disease. *American Journal of Respiratory Critical Care Medicine, 153,* A494.

Gabay, C., Cakir, N., Moral, F., Roux-Lombard, P., Meyer, O., Dayer, J.M., et al. (1997). Circulating levels of tumor necrosis factor soluble receptors in systemic lupus erythematosus are significantly higher than in other rheumatic diseases and correlate with disease activity. *Journal of Rheumatology, 24 (2),* 303-308.

Gibson, D., Ferris, M., Dooley, M., Huang, K., & Hogan, S. (2003). Renal transplantation in children with lupus nephritis. *American Journal of Kidney Diseases, 41 (2),* 455-463.

Gioia, G., Isquith, P., Guy, S., & Kenworthy, L. (2000). *Behavior Rating Inventory of Executive Function Professional Manual.* Odessa, FL: Psychological Assessment Resources.

Greenberg, G., Watson, R., & Deptula, D. (1987). Neuropsychological dysfunction in sleep apnea. *Sleep, 10*, 254-262.

Hagelberg, S., Lee, Y., Bargman, J., Mah, G., Schneider, R., Laskin, C., et al. (2002). Long-term follow-up of childhood lupus nephritis. *Journal of Rheumatology, 29 (12),* 2635-2642.

Hawker, G., Gabriel, S., Bombardier, C., Goldsmith, C., Caron, D., & Gladman, D. (1993). A reliability study of SLEDAI: a disease activity index for systemic lupus erythematosus. *Journal of Rheumatology, 20 (6),* 1091.

Hill, W. (1889). On some cases of backwardness and stupidity in children. *British Medical Journal (Clinical Res Ed), 2,* 711-712.

Hochberg, M. (1997). Updating the American college of rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis & Rheumatism, 40,* 1725.

Hollingshead, A.B. (1975). The Four Factor Index of Social Status: A Working Paper. New Haven, CT: Yale University.

Hopkinson, N.D., Doherty, M., & Powell, R.J. (1994). Clinical features and race-specific incidence/prevalence rates of systemic lupus erythematosus in a geographically complete cohort of patients. *Annals of the Rheumatic Diseases, 53*, 675-680.

Johnson, E. & Roth, T. (2006). An epidemiologic study of sleep-disordered breathing symptoms among adolescents. *Sleep, 29 (9),* 1135-1142.

Jump, R., Robinson, M., Armstrong, A., Barnes, E., Kilbourn, K., & Richards, H. (2005). Fatigue in systemic lupus erythematosus: contributions of disease activity, pain, depression, and perceived social support. *The Journal of Rheumatology, 32 (9),* 1699-1705.

Kardestuncer, T. & Frumkin, H. (1997). Systemic lupus erythematosus in relation to environmental pollution: an investigation in an African American community in North Georgia. *Archives of Environmental Health, 52,* 85-90.

Kennedy, J., Blunden, S. Hirte, C., Parsons, D., Martin, A., Crowe, E., et al. (2004). Reduced neurocognition in children who snore. *Pediatric Pulmonology, 37 (4),* 330-337.

Kirk, V., Morielli, A., & Brouillette, R. (1999). Sleep-disordered breathing in patients with myelomeningocele: the missed diagnosis. *Developmental Medicine & Child Neurology, 41,* 40-43.

Klein-Gitelman, M., Reiff, A., & Silverman, E. (2002). Systemic lupus erythematosus in childhood. *Rheumatic Disease Clinics of North America, 28 (3),* 561-577.

Kothare, S., Grant, M., Coleman, C. & Dampier, C. (2005). The prevalence of sleep disorders in children with sickle cell disease. Poster presented at Associated Professional Sleep Societies, LLC, 19th Annual Meeting, Denver Colorado. Abstract published in *Sleep, Journal of Sleep and Sleep Disorders, Volume 28, Abstract Supplement.*

Kotzin, B. (1996). Systemic lupus erythematosus. *Cell, 85 (3),* 303-306.

Lacki, J., Samborsi, W., & Mackiewicz, S. (1997). Interleukin-10 and interleukin-6 in lupus erythematosus and rheumatoid arthritis, correlations with acute phase proteins. *Clinical Rheumatology, 16 (3),* 275-278.

Lash, A. (1998). Quality of life in systemic lupus erythematosus. *Applied Nursing Research, 11 (3)*, 130-137.

Lawrence, R.C., Helmick, C.G., Arnett, F.C., Deyo, R.A., Felson, D.T., Giannini, E.H., et al. (1998). Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis & Rheumatism, 41 (5),* 778-799.

Levanson, A., Tarasiuk, A., & Tal, A. (1999). Sleep characteristics in children with Down syndrome. *The Journal of Pediatrics, 134 (6)*, 755-760.

Lewin, D., Rosen, R., England, S., & Dahl, R. (2002). Preliminary evidence of behavioral and cognitive sequelae of obstructive sleep apnea in children. *Sleep Medicine, 3,* 5-13.

Luginbuehl, M. (2006). Summary of the SDIS development & psychometric qualities. Retrieved on August 14, 2006 from http://www.sleepdisorderhelp.com/documentation.php

Lupus Foundation of America, Inc., (LFA). (2006). Facts and overview. Retrieved August 14, 2006 from http://www.lupus.org/education/overview.html

Mallory, G., Fiser, D., & Jackson, R. (1989). Sleep-associated breathing disorders in morbidly obese children and adolescents. *Journal of Pediatrics, 115 (6),* 892-897.

Marcus, C. & Loughlin, G. (1996). Obstructive sleep apnea in children. *Seminars in Pediatric Neurology, 3,* 23-28.

McCarty, D., Manzi, S., Medsger, T., Ramsey-Goldman, R., LaPorte, R., & Kwoh, C. (1995). Incidence of systemic lupus erythematosus. Race and gender differences. *Arthritis & Rheumatism, 38,* 1260-1270.

McGhee, J., Kickingbird, L., & Jarvis, J. (2004). Clinical utility of antinuclear antibody tests in children. *BMC Pediatrics, 4*, 13.

Merrel, M. & Shulman, L. (1955). Determination of prognosis in chronic disease, illustrated by systemic lupus erythematosus. *Journal of Chronic Diseases, 1 (1),* 12-32.

Michet, C., McKenna, C., Elveback, L., Kaslow, R., & Kurland, L. (1985). Epidemiology of systemic lupus and other connective tissue diseases in Rochester, Minnesota, 1950 through 1979. *Mayo Clinic Proceedings, 60*, 105-113.

Miettunen, P., Ortiz-Alvarez, O., Petty, R., Cimaz, R., Malleson, P., Cabral, et al. (2004). Gender and ethnic origin have no effect on long-term outcome of childhood-onset systemic lupus erythematosus. *Journal of Rheumatology, 31,* 1650-1654.

National Institute of Arthritis and Musculoskeletal and Skin Diseases. (2001). Lupus: A patient care guide for nurses and other health professionals. Laboratory tests used to diagnose and evaluate SLE. Retrieved on August 14, 2006 from http://www.niams.nih.gov/hi/topics/lupus/lupusguide/chp3.htm

National Sleep Foundation (NSF). (2004, 2006). *Sleep in America Poll.* www.sleepfoundation.org,Washington, DC.

Newcomer, P., Barenbaum, E. & Bryant, B. (1994). Depression and Anxiety in Youth Scale (DAYS): Examiner's manual. Austin, TX: Pro-Ed.

Nived, O., Sturfelt, G., & Wollheim, F. (1985). Systemic lupus erythematosus in an adult population in southern Sweden: incidence, prevalence, and validity of ara revised classification criteria. *British Society of Rheumatology, 24 (2),* 147-154.

O'Brien, L.M., Mervis, C.B., Holbrook, C.R., Bruner, J.L., Smith, N.H., McNally, N., et al. (2004). Neurobehavioral correlates of sleep-disordered breathing in children. *Journal of Sleep Research, 13,* 165-172.

Owens, J., Maxim, R., Nobile, C., McGuinn, M., & Msall, M. (2000). Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. *Archives of Pediatric and Adolescent Medicine, 154,* 549-555.

Owens, J., Spirito, A., & McGuinn, M. (2000). The children's sleep habits questionnaire (CSHQ): Psychometric properties of a survey instrument for school-aged children. *Sleep, 23* (8), 1-9.

Palermo, T.M. & Kiska, R. (2005). Subjective sleep disturbances in adolescents with chronic pain: Relationship to daily functioning and quality of life. *The Journal of Pain, 6 (3),* 201-207.

Papero, P., Bluestein, H., White, P., & Lipnick, R. (1990). Neuropsychologic deficits and antineuronal antibodies in pediatric systemic lupus erythematosus. *Clinical and Experimental Rheumatology, 8 (4),* 417-24.

Paran, D., Fireman, E., & Elkayam, O. (2004). Pulmonary disease in systemic lupus erythematosus and the antiphospholipid syndrome. *Autoimmunity Reviews, 3 (1),* 70-75.

Parikh, S., Swaiman, K., & Kim, Y. ( ). Neurologic Characteristics of Childhood Lupus Erythematosus. *Pediatric Neurology, 13 (3)*, 198-201.

Prokunina, L., Castillejo-Lopez, C., Oberg, F., Gunnarsson, I., Berg, L., Magnusson, V. et al. (2002). A regulatory polymorphism in PDCD1 is associated with susceptibility to systemic lupus erythematosus. *Nature Genetics, 32*, 666-669.

Randazzo, A., Muehlbach, M., Schweitzer, P., & Walsh, J. (1998). Cognitive function following acute sleep restriction in children ages 10-14. *Sleep, 15,* 861-868.

Rogers, M., Waterhouse, E., Nagel, J., Roberts, N., Stern, S., Fraser, et al. (1992). I-123 iofetamine SPECT scan in systemic lupus erythematosus patients with cognitive and other minor neuropsychiatric symptoms: a pilot study. *Lupus, 1 (4),* 215-219.

Rood, M., ten Cate, R., van Suijekom-Smit, L., den Ouden, E., Ouwerkerk, F., Breedveld, F., et al. (1999). Childhood-onset systemic lupus erythematosus: clinical presentation and prognosis in 31 patients. Scandinavian *Journal of Rheumatology, 28 (4),* 222-226.

Sanchez-Armengol, A., Fuentes-Pradera, M.A., Capote-Gil, F., Garcia-Diaz, E., Cano-Gomez, S., Carmona-Bernal, C., et al. (2001). Sleep-related breathing disorders in adolescents aged 12 to 16 years: clinical and polygraphic findings. *Chest, 119 (5),* 1393-1400.

Shamsuzzaman, A., Winnicki, M., Lanfranchi, P., Wolk, R., Kara, T., Accurso, V, et al. (2002). Elevated c-reactive protein in patients with obstructive sleep apnea. *Circulation, 105*, 2462-2464.

Sibbitt, W., Brandt, J., Johnson, C., Maldonado, M., Patel, S., Ford, C., et al. (2002). The incidence and prevalence of neuropsychiatric syndromes in pediatric onset systemic lupus erythematosus. *The Journal of Rheumatology, 29 (7),* 1536-1542.

Siegel, M. & Lee, S.L. (1973). The epidemiology of systemic lupus erythematosus. *Seminars in Arthritis and Rheumatology, 3 (1),* 1-54.

Soper, D. (2007). Interaction [Computer software]. Retrieved February 16, 2007, from http://www.danielsoper.com/Interaction

Steinlin, M., Blaser, S., Gilday, D., Eddy, A., Logan, W., Laxer, R., et al. (1995). Neurologic manifestations of pediatric systemic lupus erythematosus. *Pediatric Neurology, 13 (3),* 191-197.

Stichweh, D., Arce, E., & Pascual, V. (2004). Update on pediatric systemic lupus erythematosus. *Current Opinion in Rheumatology, 16*, 577-587.

Sweet, J., Doninger, N., Zee, P., & Wagner, L. (2004). Factors influencing cognitive function, sleep, and quality of life in individuals with systemic lupus erythematosus: A review of the literature. *The Clinical Neuropsychologist, 18 (1),* 132-147.

Tan, E., Cohen, A., Fries, J., Masi, A., McShane, D., Rothfield, N., et al. (1982). The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis & Rheumatism, 25 (11),* 1271-1277.

Tauman, R., Ivanenko, A., O'Brien, L.M., & Gozal, D. (2004). Plasma c-reactive protein levels among children with sleep-disordered breathing. *Pediatrics, 113 (6)*, 564-569.

Ter Borg, E.J., Horst, G., Limburg, P.C., van Rijswijk, M.H., & Kallenberg, C.G. (1990). C-reactive protein levels during disease exacerbations and infections in systemic lupus erythematosus: a prospective longitudinal study. *Journal of Rheumatology, 17 (12),* 1642-1648.

Tsao, B., Cantor, R., Kalunian, K., Chen, C., Badsha, H., Singh, R., et al. (1997). Evidence for linkage of a candidate chromosome 1 region to human systemic lupus erythematosus. *Journal of Clinical Investigation, 99 (4),* 725-731.

Uramoto, K., Michet, C., Thumboo, J., Sunku, J., O'Fallon, W., & Gabriel, S. (1999). Trends in the incidence and mortality of systemic lupus erythematosus, 1950-1992. *Arthritis & Rheumatism, 42,* 46-50.

Urschitz, M., Guenther, A., Eitner, S., Urschitz-Duprat, P., Schlaud, M., Ipsiroglu, O., et al. (2004). Risk factors and natural history of habitual snoring. *CHEST, 126*, 790-800.

Valencia-Flores, M., Resendiz, M., Castano, V., Santiago, V., Campos, R., Sandino, S., et al. (1999). Objective and subjective sleep disturbances in patients with systemic lupus erythematosus. *Arthritis & Rheumatism, 42 (10)*, 2189-2193.

van der Linden, M., van der Slik, A., Zanelli, E., Giphart, M., Piterman, G., Schreuder, R. et al. (2001). Six microsatellite markers on the short arm of chromosome 6 in relation to HLA-DR3 and TNF-308A in systemic lupus erythematosus. *Genes and Immunity, 2,* 373-380.

Villa, M., Multari, G., Montesano, M., Pagani, J., Cervoni, M., Midulla, F., et al., (2000). Sleep apnoea in children with diabetes mellitus: effect of glycaemic control. *Diabetologia, 43,* 696-702.

Vyas, S., Hidalgo, G., Baqi, N., Von Gizyki, H., & Singh, A. (2002). Outcome in African American children of neuropsychiatric lupus and lupus nephritis. *Pediatric Nephrology, 17 (1),* 45-49.

Wallace, D. & Lyon, I. (1999). Pierre Cazenave and the first detailed modern description of lupus erythematosus. *Seminars in Arthritis and Rheumatism, 28, 305-312.*

Ward, S. & Marcus, C. (1996). Obstructive sleep apnea in infants and young children. *Journal of Clinical Neurophysiology, 13,* 198-207.

Wechsler, D. (1997). *Wechsler adult intelligence scale-3rd edition (WAIS-3).* San Antonio, TX: Harcourt Assessment.

Wechsler, D. (1999). *Wechsler abbreviated scale of intelligence (WASI).* San Antonio, TX: Harcourt Assessment.

Wechsler, D. (2003). *Wechsler intelligence scale for children-4th edition (WISC-IV).* San Antonio, TX: Harcourt Assessment.

Wyckoff, P., Miller, L., Tucker, L., & Schaller, J. (1995). Neuropsychological assessment of children and adolescents with systemic lupus erythematosus. *Lupus, 4,* 217-220.

Xing, Z., Gauldie, J., Cox, G., Baumann, H., Jordana, M., Lei, X., et al. (1998). IL-6 is an anti-inflammatory cytokine required for controlling local or systemic acute inflammatory responses. *Journal of Clinical Investigation, 101 (2),* 311-320.

Table 1. *Summary of All Measures*

Category	Variable	Analysis
Demographics	Age	D, P
	Ethnicity	D
	Body Mass Index Percentile	D, P
	Tonsilectomy	D, P
	Adenoidectomy	D, P
	Hollingshead Four Factor Index of Social Status	D, P
	Household Annual Income	D, P
Illness-Related Factors	Systemic Lupus Erythematosus Disease Activity Index	D, M
	Sedimentation Rate	D, M
	Kidney Disease	D, M
	Central Nervous System Involvement	D, M
Sleep Functioning	Sleep Disorders Inventory for Students	
	Obstructive Sleep Apnea Scale	D, P, M, E
	Excessive Daytime Sleepiness Scale	D, E
	Periodic Limb Movement	D, E
	Delayed Sleep Phase Syndromre	D, E
	Narcolepsy	D, E
	Sleep Disturbance Index	D, E
Cognitive Functioning	WASI: Abbreviated Full Scale IQ (Vocabulary and Matrix Reasoning)	D
	BRIEF: Global Executive Composite,	D, M, E
	Behavior Regulation Index, Metacognition Index	D, E
	WISC-IV & WAIS-III: Digit Span	D, M, E
	DKEFS Trail Making: Letter-Number Sequencing,	D, M, E
	Letter-Number Sequencing Errors,	D, M, E
	Visual Scanning, Number Sequencing, Letter Sequencing, Motor Speed	D, E
	DKEFS Verbal Fluency: Category Switching Number Correct,	D, M, E
	Verbal Fluency Set-Loss Errors, Verbal Fluency Repetition Errors,	D, M, E
	Letter Fluency, Category Fluency, Category Switching Accuracy	D, E
Psychiatric Functioning	Depression and Anxiety in Youth Scale: Depression Scale	D, M, E

WASI = Wechsler Abbreviated Scale of Intelligence
BRIEF = Behavior Rating Inventory of Executive Function
WISC-IV = Wechsler Intelligence Scale for Children, Fourth Edition
WAIS-III = Wechsler Adult Intelligence Scale, Third Edition
DKEFS = Delis Kaplan Executive Function System
D = Descriptive analyses; P = Preliminary analyses; M = Main primary analyses; E = Exploratory analyses

Table 2. *Reliability of Measures for SLE and Control Groups*

Variable	Cronbach Alpha	
	α	α
	SLE Adolescent Questionnaire	Control Adolescent Questionnaire
SDIS-OSA	.71	.65
SDIS-EDS	.93	.86
SDIS-PLM	.79	.42
SDIS-DSPS	.91	.67
SDIS-NAR	.90	.70
SDIS-SDI	.94	.87

Variable	Cronbach Alpha
	α
	SLE Group
BRIEF-GEC	.98
BRIEF-BRI	.93
BRIEF-MCI	.97
DAYS-Depression	.85

Reliability analyses were not conducted for the SDIS Children's form for the SLE and control groups because only one participant filled out these versions.
SDIS = Sleep Disorders Inventory for Students
OSA = Obstructive Sleep Apnea; EDS = Excessive Daytime Sleepiness;
PLM = Periodic Limb Movement; DSPS = Delayed Sleep Phase Syndrome;
NAR = Narcolepsy; SDI = Sleep Disturbance Index
BRIEF = Behavior Rating Inventory of Executive Function
GEC = Global Executive Composite; BRI = Behavior Regulation Index;
MCI = Metacognition Index
DAYS = Depression and Anxiety in Youth Scale

Table 3. *Order of Test Measures*

Order A
WASI: Vocabulary
WASI: Matrix Reasoning
WISC-IV/WASI-III: Digit Span
DKEFS: Trail Making Test
DKEFS: Verbal Fluency Test

Order B
WASI: Vocabulary
WASI: Matrix Reasoning
DKEFS: Verbal Fluency Test
DKEFS: Trail Making Test
WISC-IV/WASI-III: Digit Span

WASI = Wechsler Abbreviated Scale of Intelligence
DKEFS = Delis Kaplan Executive Function System
WISC-IV = Wechsler Intelligence Scale for Children, Fourth Edition
WAIS-III = Wechsler Adult Intelligence Scale, Third Edition

Table 4. *Descriptive Characteristics for the SLE and Control Groups*

	SLE Group			Control Group		
Variable	N[d]	%[e]	*M (SD)*	N[d]	%[e]	*M (SD)*
Gender (female)	17/22	77		15/24	63	
Age (in years)	22		15.5 (2.70)	24		14.2 (1.96)
Ethnicity						
African American	10/22	45		7/24	29	
Asian	1/22	4.5		0/24	0	
Caucasion	7/22	32		1/24	4	
Hispanic	3/22	14		15/24	63	
Other	1/22	4.5		1/24	4	
Socioeconomic Status						
Income	17		\$50,000-\$59,999[a]	20		\$30,000-\$39,999[a]
Hollingshead	19		4 out of 5[b]	17		2 out of 5[b]
Ilness-related factors						
Kidney Disease	13/22	59				
CNS[g] Involvement	10/22	45				
SLEDAI[c]	22		5.27 (5.04)			
Sedimentation Rate	15		28.7 (33.4)			
Tonsillectomy	3/22	14		6/24	25	
Adenoidectomy	3/22	14		3/24	13	
BMI[f] Percentile	22		72.3 (25.1)		23	70.3 (28.7)

[a] = median scores

[b] = Hollingshead score (1 is the lowest socioeconomic level, 5 is the highest level)

[c] = Systemic Lupus Erythematosus Disease Activity Index

[d] = Number out of total group number

[e] = Percentage out of group total

[f] = Body Mass Index

[g] = Central Nervous System

Table 5. *Summary Standard Scores for the SLE and Control Groups*

	SLE Group			Control Group		
Variable	N[b]	%[c]	*M (SD)*	N[b]	%[c]	*M (SD)*
Sleep Disorders Inventory for Students						
Obstructive Sleep Apnea	3/22	14	101.5 (12.8)	4/24	17	98.0 (11.9)
Excessive Daytime Sleepiness	6/22	27	102.2 (20.0)	3/24	13	95.3 (16.0)
Periodic Limb Movement	4/22	18	99.6 (14.4)	1/24	4	96.3 (10.4)
Delayed Sleep Phase	7/22	32	104.2 (23.3)	5/24	21	101.4 (15.7)
Narcolepsy	6/21	29	106.1 (14.9)	3/23	13	100.7 (9.51)
Sleep Disturbance Index	6/22	22	103.5 (16.9)	3/24	13	99.5 (12.8)
Behavior Rating Inventory of Executive Function						
Global Executive Composite	3/22	14	98.5 (19.7)			
Behavior Regulation Index	4/22	18	99.0 (20.8)			
Metacognition Index	5/22	23	98.7 (18.7)			
Wechsler Abbreviated Scale of Intelligence						
FSIQ	0/17	0	105.3 (11.3)			
Delis-Kaplan Executive Function System-Trail Making Test						
Visual Scanning	0/17	0	110.9 (7.75)			
Number Sequencing	2/17	12	105.6 (16.9)			
Letter Sequencing	1/17	6	106.8 (13.5)			
Letter-Number Sequencing	5/17	30	98.8 (20.4)			
Errors	1/17	6	105.0 (7.07)			
Motor Speed	0/17	0	107.4 (8.49)			
Delis-Kaplan Executive Function System-Verbal Fluency Test						
Letter Fluency	3/17	18	103.8 (17.4)			
Category Fluency	3/17	18	103.5 (16.5)			
Category Switching # Correct	1/17	6	101.5 (12.3)			
Category Switching Accuracy	1/17	6	102.9 (9.85)			
Set-Loss Errors	0/17	0	110.0 (7.91)			
Repetition Errors	4/17	24	96.8 (14.8)			
WISC-IV,WAIS-III[a]						
Digit Span	3/17	18	100 (15.7)			
Depression and Anxiety in Youth Scale						
Depression	4/21	19	98.8 (13.8)			

[a] = Wechsler Intelligence Scale for Children-IV; Wechsler Adult Intelligence Scale-III

[b] = Number out of total group number with difficulty in the specific area

[c] = Percentage out of group total with difficulty in the specific area

Table 6. *Summary Scores Listed as Original Test Measure Scores for the SLE and Control Groups*

	SLE Group			Control Group		
Variable	N[b]	%[c]	*M (SD)*	N[b]	%[c]	*M (SD)*
Sleep Disorders Inventory for Students (T Scores)						
Obstructive Sleep Apnea	3/22	14	50.8 (8.56)	4/24	17	48.5 (8.03)
Excessive Daytime Sleepiness	6/22	27	51.2 (13.5)	3/24	13	46.6 (10.8)
Periodic Limb Movement	4/22	18	49.5 (9.65)	1/24	4	47.3 (6.93)
Delayed Sleep Phase	7/22	32	52.6 (15.6)	5/24	21	50.7 (10.6)
Narcolepsy	6/21	29	53.7 (10.1)	3/23	13	50.3 (6.39)
Sleep Disturbance Index	6/22	22	52.2 (11.5)	3/24	13	49.3 (8.60)
Behavior Rating Inventory of Executive Function (T Scores)						
Global Executive Composite	3/22	14	48.7 (13.3)			
Behavior Regulation Index	4/22	18	49.1 (13.8)			
Metacognition Index	5/22	23	48.8 (12.6)			
Wechsler Abbreviated Scale of Intelligence (Standard Score)						
FSIQ	0/17	0	105.3 (11.3)			
Delis-Kaplan Executive Function System-Trail Making Test (Scaled Scores)						
Visual Scanning	0/17	0	12.2 (1.55)			
Number Sequencing	2/17	12	11.1 (3.37)			
Letter Sequencing	1/17	6	11.4 (2.69)			
Letter-Number Sequencing	5/17	30	9.8 (4.07)			
Errors	1/17	6	10.9 (1.41)			
Motor Speed	0/17	0	11.5 (1.69)			
Delis-Kaplan Executive Function System-Verbal Fluency Test (Scaled Scores)						
Letter Fluency	3/17	18	10.8 (3.47)			
Category Fluency	3/17	18	10.7 (3.29)			
Category Switching # Correct	1/17	6	10.3 (2.47)			
Category Switching Accuracy	1/17	6	10.6 (1.97)			
Set-Loss Errors	0/17	0	12.0 (1.58)			
Repetition Errors	4/17	24	9.47 (3.02)			
WISC-IV,WAIS-III[a] (Scaled Score)						
Digit Span	3/17	18	10.0 (3.14)			
Depression and Anxiety in Youth Scale (Standard Score)						
Depression	4/21	19	98.8 (13.8)			

[a] = Wechsler Intelligence Scale for Children-IV; Wechsler Adult Intelligence Scale-III

[b] = Number out of total group number with difficulty in the specific area

[c] = Percentage out of group total with difficulty in the specific area

Table 7. *Preliminary Analyses for the SLE and Control Groups: T-Tests and Correlations*

Correlations Between OSA and: 1) BMI percentile, 2) Age, 3) Income, & 4) Hollingshead			
Variable by Group	*N*	*r*	*p*
Body Mass Index Percentile (BMI percentile)			
SLE	22	.20	.368
Control	23	-.09	.660
Age			
SLE	22	-.08	.731
Control	24	.04	.865
Income			
SLE	17	-.11	.669
Control	20	-.27	.259
Hollingshead Four Factor Index of Social Status			
SLE	19	-.12	.627
Control	17	-.03	.910

OSA Compared by Group: 1) Tonsillectomy and 2) Adenoidectomy					
Group	Mean (*SD, N*)	Mean (*SD, N*)	*df*	*t*	*p*
	No Tonsillectomy	Tonsillectomy			
SLE	99.5 (11.6, 19)	114 (15.7, 3)	20	-1.94	.066*
Control	96.2 (10.8, 18)	103.7 (14.6, 6)	22	-1.35	.190
	No Adenoidectomy	Adenoidectomy			
SLE	99.5 (11.6, 19)	114 (15.7, 3)	20	-1.94	.066*
Control	97.1 (10.6, 21)	104.3 (21.6, 3)	21	-.568	.624

p-values are presented in parentheses; *p<.10

Table 8. The *SLE Group Compared to the Control Group on the SDIS Scales*

		SLE Group Standard Score		Control Group Standard Score			
Variable	*N*	Mean (*SD*)	*N*	Mean (*SD*)	*df*	*t*	*p*
OSA	22	101.5 (12.8)	24	98.0 (11.9)	44	-.934	.356
EDS	22	102.2 (20.0)	24	95.3 (16.0)	44	-1.30	.200
PLM	22	99.6 (14.4)	24	96.3 (10.4)	44	-.905	.370
DSPS	22	104.2 (23.3)	24	101.4 (15.7)	44	-.490	.626
NAR	21	106.1 (14.9)	23	100.7 (9.51)	33.4	-1.39	.173
SDI	22	103.5 (16.9)	24	99.5 (12.8)	44	-.916	.364

OSA = Obstructive Sleep Apnea

EDS = Excessive Daytime Sleepiness

PLM = Periodic Limb Movement

DSPS = Delayed Sleep Phase Syndrome

NAR = Narcolepsy

SDI = Sleep Disturbance Index

Table 9. *Correlations of SDIS Scales and Cognitive Measures*

Variable	OSA	EDS	PLM	DSPS	NAR	SDI
	(n = 22)	(n = 22)	(n = 22)	(n = 22)	(n = 21)	(n = 22)
GEC	.47 (.026)**	.66 (.001)***	.66 (.001)***	.42 (.053)*	.56 (.008)***	.62 (.002)***
BRI	.39 (.066)*	.67 (.001)***	.70 (.000)***	.38 (.081)*	.58 (.006)***	.61 (.002)***
MCI	.48 (.024)**	.59 (.003)***	.59 (.004)***	.41 (.059)*	.52 (.017)**	.58 (.005)***
	(n = 17)	(n = 17)	(n = 17)	(n = 17)	(n = 16)	(n = 17)
VS	.57 (.017)**	-.06 (.811)	.23 (.384)	-.07 (.796)	.04 (.895)	.11 (.671)
NS	.00 (.990)	-.61 (.009)***	-.30 (.235)	-.69 (.002)***	-.59 (.015)**	-.55 (.022)**
LS	.06 (.828)	-.59 (.011)**	-.44 (.076)*	-.63 (.007)***	-.52 (.038)**	-.52 (.032)**
LNS	.19 (.459)	-.29 (.250)	-.13 (.613)	-.27 (.297)	-.19 (.474)	-.17 (.511)
LNSE	.29 (.260)	.22 (.392)	.17 (.509)	.16 (.536)	.17 (.540)	.26 (.318)
MS	.43 (.089)*	-.37 (.141)	-.06 (.812)	-.23 (.369)	-.26 (.331)	-.14 (.592)
LF	-.03 (.923)	.03 (.899)	-.15 (.571)	-.00 (.990)	.03 (.911)	.001 (.997)
CF	.29 (.245)	.22 (.389)	.02 (.949)	.01 (.986)	.28 (.291)	.17 (.520)
CS#C	-.34 (.188)	-.30 (.242)	-.40 (.107)	.38 (.128)	-.26 (.323)	-.36 (.156)
CSA	-.39 (.123)	-.32 (.211)	-.41 (.100)	-.32 (.206)	-.31 (.242)	-.37 (.149)
VFSLE	-.08 (.764)	-.17 (.516)	-.12 (.653)	-.19 (.454)	-.15 (.571)	-.12 (.638)
VFRE	-.49 (.045)*	-.02 (.931)	-.11 (.683)	-.10 (.690)	-.13 (.633)	-.18 (.488)
DS	-.13 (.634)	-.23 (.379)	-.21 (.420)	-.19 (.461)	-.22 (.418)	-.23 (.370)

p-values are presented in parentheses; *p<.10; **p<.05; ***p<.01

GEC = Global Executive Composite; BRI = Behavior Regulation Index; MCI = Metacognition Index;
VS = Visual Scanning; NS = Number Sequencing; LNS = Letter-Number Sequencing;
LNSE = Letter-Number Sequencing Errors; MS = Motor Speed; LF = Letter Fluency;
CF = Category Fluency; CS#C = Category Switching Number Correct;
CSA = Category Switching Accuracy; VFSLE = Verbal Fluency Set-Loss Errors;
VFRE = Verbal Fluency Repetition Errors; DS = Digit Span;
OSA = Obstructive Sleep Apnea; EDS = Excessive Daytime Sleepiness;
PLM = Periodic Limb Movement; DSPS = Delayed Sleep Phase Syndrome;
NAR = Narcolepsy; SDI = Sleep Disturbance Index

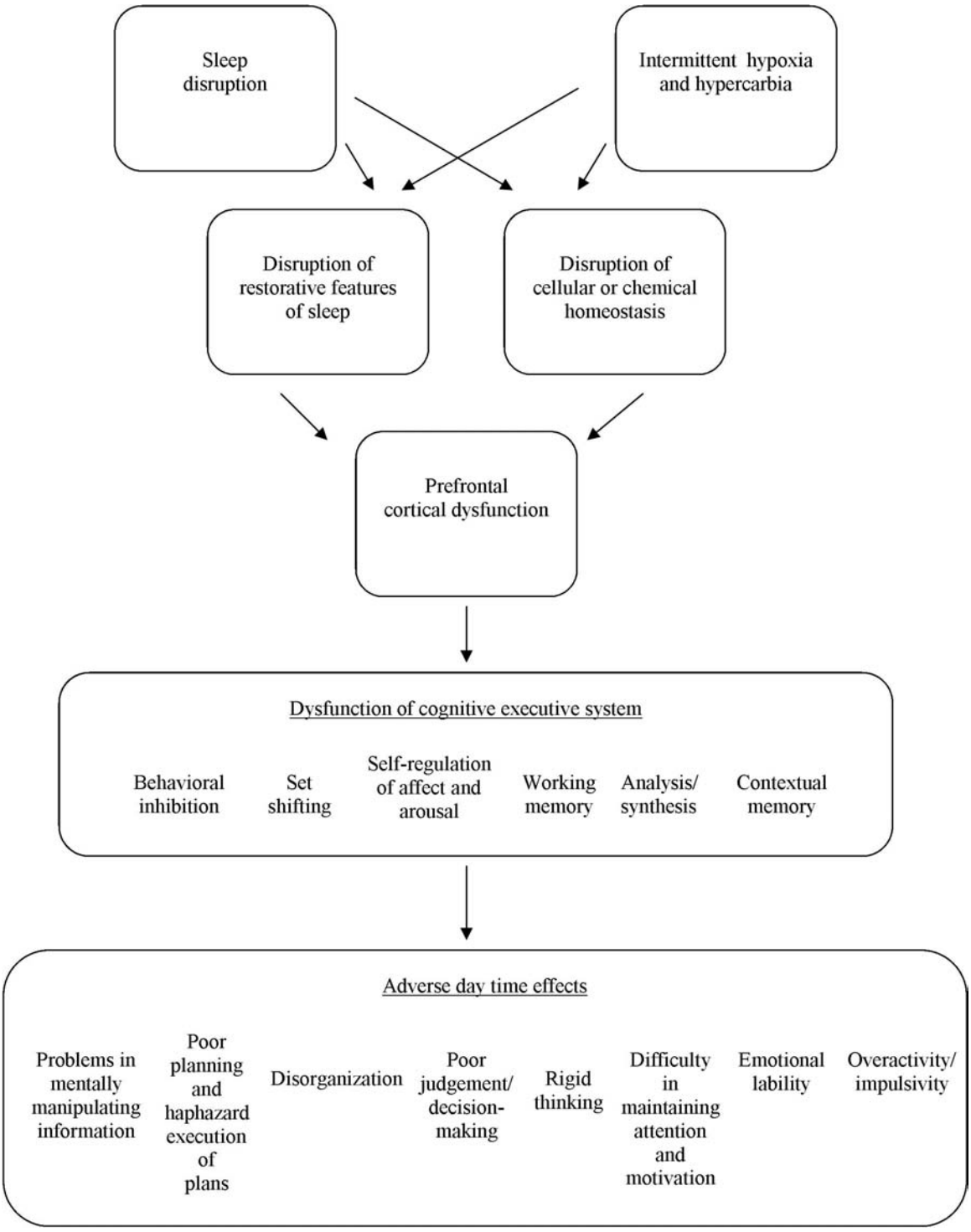

Figure 1: *The Prefrontal Model. (Beebe & Gozal, 2002)*

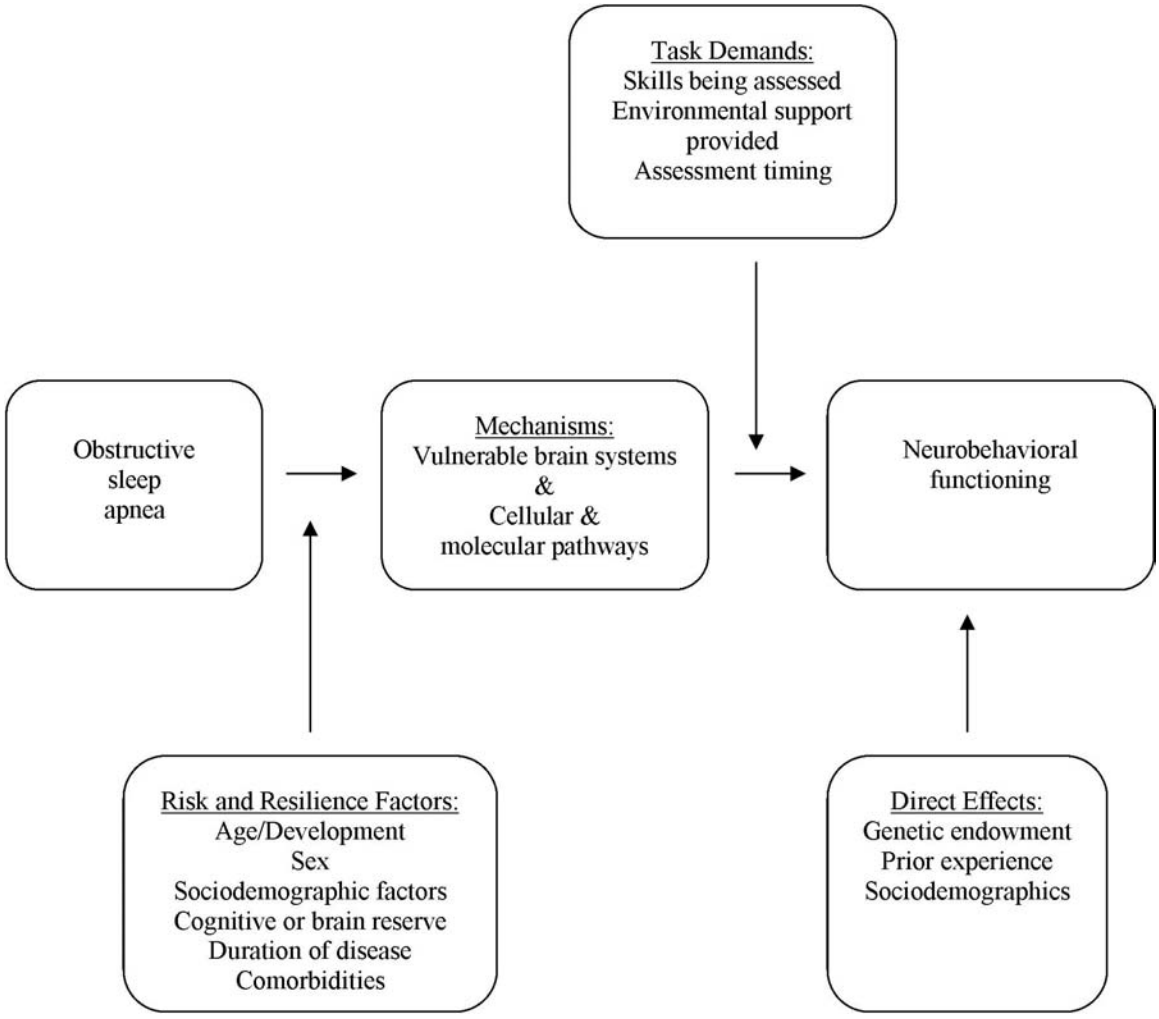

Figure 2: *Heuristic Model of the Neurobehavioral Effects of Obstructive Sleep Apnea (OSA). (Beebe, 2005).*

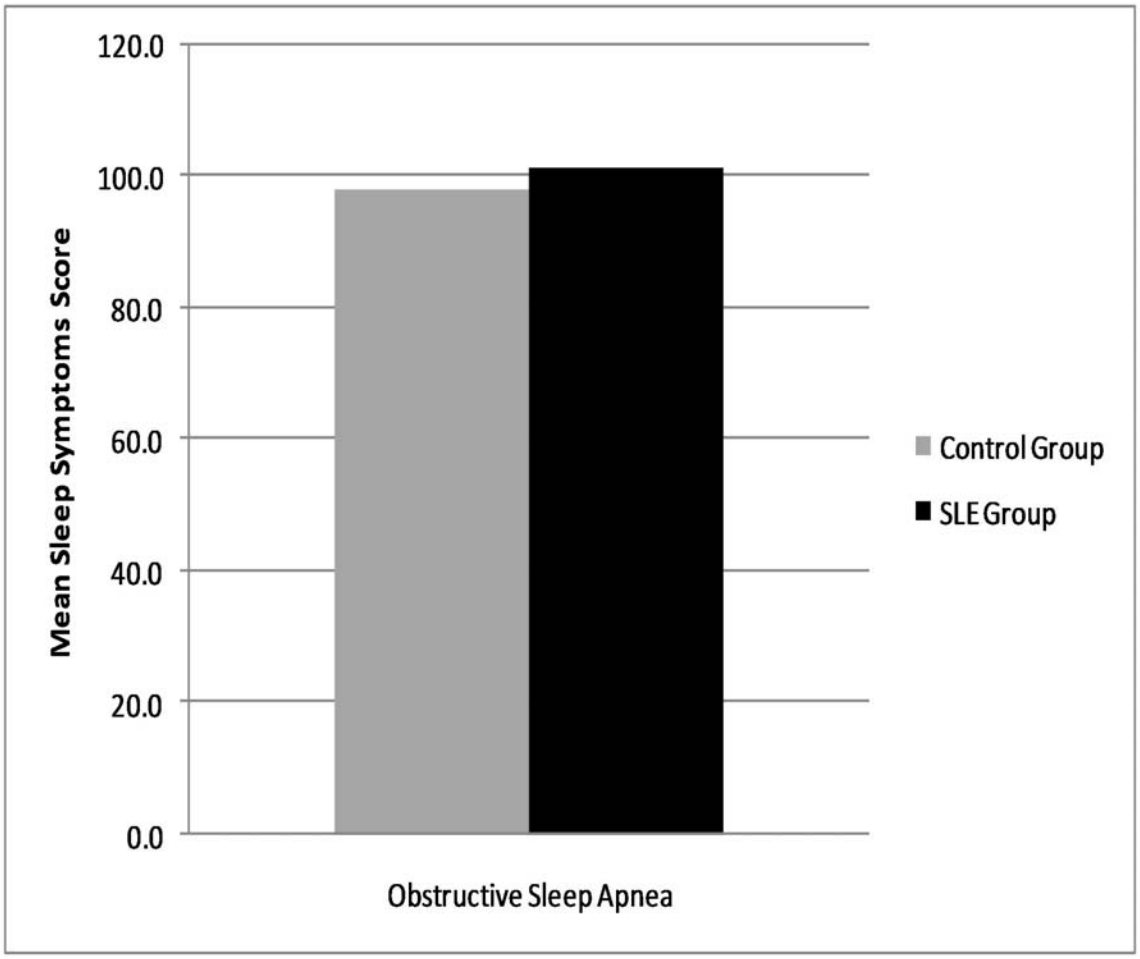

Figure 3: *Mean Standard Scores for the OSA Scale by Group.*

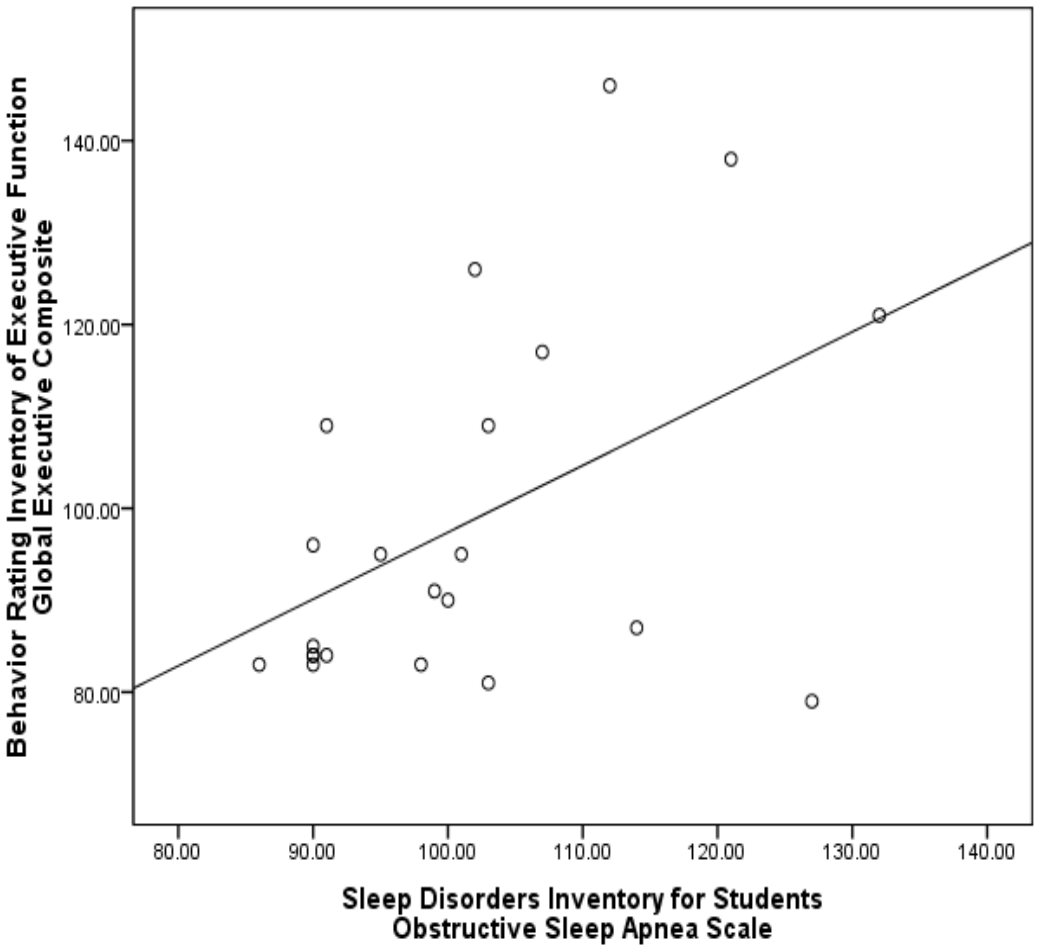

Figure 4: *The Association between the BRIEF GEC Standard Score and SDIS OSA Standard Score.*

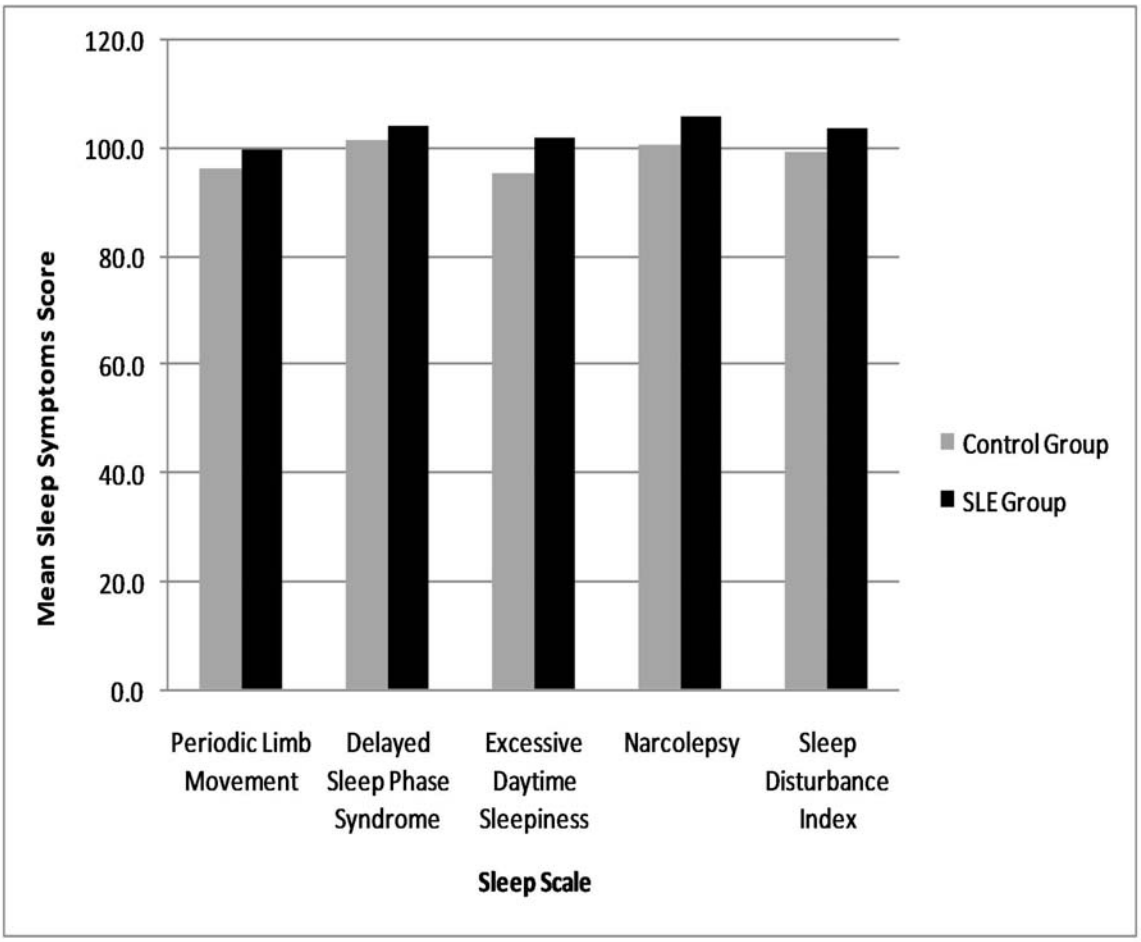

Figure 5: *Mean Standard Scores for the SDIS Exploratory Scales by Group.*

APPENDIX A1:
CHILD BACKGROUND QUESTIONNAIRE: SLE GROUP

CHILD BACKGROUND INFORMATION ID #:_____

Please fill in the following background information about your child.

1. Age of Child: _____

2. Child's gender:
   - Male ☐
   - Female ☐

3. Ethnicity of Child:
   - African American ☐
   - Asian ☐
   - Caucasion ☐
   - Hispanic ☐
   - Indian ☐
   - Native American ☐
   - Other ☐

   If other, please describe:

   _____

4. What is your child's weight? _____

5. What is your child's height? _____

6. Is your child on any medications?
   - Yes ☐
   - No ☐

   If yes, what type of medication:

   _____

   _____

   _____

7. Has your child had their adenoids or tonsils removed?
   - Yes ☐
   - No ☐

8. Does your child have frequent throat or ear infections?
   - Yes ☐
   - No ☐

9. For how many years/months has your child been diagnosed with SLE? _____

10. Please list any medical diagnoses or medical illnesses your child has. _____

APPENDIX A2:
CHILD BACKGROUND QUESTIONNAIRE: CONTROL GROUP

CHILD BACKGROUND INFORMATION ID #:_____

Please fill in the following background information about your child.

1. Age of Child: _____

2. Child's gender:
   - Male ☐
   - Female ☐

3. Ethnicity of Child:
   - African American ☐
   - Asian ☐
   - Caucasion ☐
   - Hispanic ☐
   - Indian ☐
   - Native American ☐
   - Other ☐

   If other, please describe:

   _____

4. What is your child's weight? _____

5. What is your child's height? _____

6. Is your child on any medications?
   - Yes ☐
   - No ☐

   If yes, what type of medication:

   _____

   _____

   _____

7. Has your child had their adenoids or tonsils removed?
   - Yes ☐
   - No ☐

8. Does your child have frequent throat or ear infections?
   - Yes ☐
   - No ☐

9. Is your child diagnosed with systemic lupus erythematosus?
   - Yes ☐
   - No ☐

10. Please list any medical diagnoses or medical illnesses your child has. _____

APPENDIX B:
PARENT BACKGROUND QUESTIONNAIRE

PARENT BACKGROUND INFORMATION ID #:_____

Please fill in the following background information about you and a second head of household, if any.

Please check which one best describes you and the other head of household, if any.

Head (s) of Household:

		Person 1	Person 2
1. Relationship to child:	Mother	☐	☐
	Father	☐	☐
	Other	☐	☐

If other, please describe relationship:

_____ _____

2. Check which person is filling out the questionnaires today: ☐ ☐

3. Education: *Please check the highest level of education for each person.*

	Person 1	Person 2
6th grade or less:	☐	☐
7th to 9th grade:	☐	☐
10th to 11th grade:	☐	☐
High School Graduate-12th grade/GED:	☐	☐
Some College/Specialized Training:	☐	☐
Undergraduate College/University Degree:	☐	☐
Graduate School/Professional Degree:	☐	☐

4. Occupation: *Please write in your occupation and the occupation of the other head of household, if any.*

_____ _____

5 Annual Household Income:

$0-9,999	☐	$70,000-79,999	☐
$10,000-19,999	☐	$80,000-89,999	☐
$20,000-29,999	☐	$90,000-99,999	☐
$30,000-39,999	☐	$100,000-109,999	☐
$40,000-49,999	☐	$110,000-119,999	☐
$50,000-59,999	☐	$120,000-129,999	☐
$60,000-69,999	☐	$130,000+	☐

6. Is your preferred language English?

Yes ☐
No ☐

If no, what language? _____

VITA

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Drexel University, Philadelphia, PA
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PUBLICATIONS AND POSTER PRESENTATIONS

Ayala Badgley, J., Chute, D.L., Barakat, L.P., Tiffany-Amaro, J., Melvin, J.J., Kothare, S.V., & Grant, M.L. (2007, November, and 2007, April). *Sleep Functioning in Children with Phenylketonuria and its Association with Phenylalanine Levels: A Pilot Study.* Poster presented at NAN in Scottsdale, AZ and Drexel University Research Day 2007, Philadelphia, PA (Honorable Mention).

Martin, N. & **Ayala, J**. (2004). Measurements of auditory-verbal STM span in aphasia: Effects of item, task, and lexical impairment. *Brain and Language, 89 (3),* 464-483.

Martin, N., Fink, R., Laine, M., & **Ayala, J.** (2004). Immediate and short-term effects of contextual priming on word retrieval in Aphasia. *Aphasiology, 18 (10),* 867-898.

Ayala, J., Jefferson, A., Cosentino, S., Kelley, R., Lippa, C., Koffler, S., Littlefield, L., Schatz, P., & Chute, D.L. (2003, October & 2003, September). *Validation of a computerized cognitive assessment tool: Assessing the locked-in patient.* Poster presented at NAN in Dallas, TX and at the Philadelphia Neuropsychological Society meeting in Philadelphia, PA (Francis Fields Memorial Award).

Ayala, J. & Martin, N. (2002, October). *Decompositional effects in the production of compound words in aphasia*. Poster presented at the annual meeting of Academy of Aphasia in NYC, NY.

Martin, N., **Ayala, J.**, & Saffran, E.M. (2002, October). *Lexical influences on serial position effects in verbal short term memory span in aphasia.* Poster presented at the annual meeting of Academy of Aphasia in NYC, NY.

Martin, N., **Ayala, J.**, & Saffran, E.M. (2002, July). *Semantic and phonological influences on serial position effects in immediate verbal recall: Evidence from aphasia.* Poster presented at the Conference on Short-Term/Working Memory, Quebec City, Canada.

Martin, N., Fink, R., Laine, M., & **Ayala, J.** (2001, October). *Differential effects of contextual priming on word retrieval impairments in aphasia.* Poster presented at the annual meeting of Academy of Aphasia, Boulder, CO.