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Using Video Games For Decreasing Pain Caused By Acute Painful Crisis In Adolescents With Sickle Cell Pain

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USING VIDEO GAMES FOR DECREASING PAIN CAUSED BY ACUTE PAINFUL CRISIS IN ADOLESCENTS WITH SICKLE CELL PAIN

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DEDICATION

This dissertation is dedicated to my parents and siblings, especially my brother Mostafa, for their love and support throughout my journey. My achievements have been their dream before they were mine and I'm thankful that the day has come that I am able to make these dreams come true. Thank you for all the dedication and sacrifices. I am who I am today because of all encouragement and unconditional love.

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CHAPTER 1

Introduction

Background of the Study

Sickle cell disease is a form of hemoglobin abnormality, in which the red blood cells are crescent shaped. This malformation of the red blood cells may cause multi-body system complications as they circulate throughout the body. The most common symptom of sickle cell disease is pain, which occurs as the cells clump compromising further blood flow to distal organs. Due to the multisystem nature of the disease, care and management of complications are of monumental complexity. Many children and adolescents' pain remains under treated despite the advancement in pain management, the availability of best practice guidelines, and the increased awareness for pain control (Uman, Chamber, McGrath, & Kisley, 2008). With the improvement of pharmacological and non-pharmacological therapies, greater resources are available for management of pain in adolescents. Pharmacological modalities when used alone to treat pain during a sickle cell crisis have been found to be inadequate (Beyer, 2000; Zempsky et al., 2008). The use of pharmacological modalities in conjunction with developmental appropriate non-pharmacological therapies can further alleviate pain symptoms. The purpose of this study is measure the effectiveness of a videogame as a developmentally appropriate non-pharmacological modality on pain in adolescents 12-21 years of age with sickle cell pain.

As a person with sickle cell disease ages they may experience secondary complications from the disease such as multi-system organ failure including the heart, lungs, and kidneys (McClish et al., 2005). Sickle cell disease has been identified as one of the most prevalent genetic blood disorders in the United States and worldwide (Stuart & Nagel, 2004). Recent statistics indicate that sickle cell disease occurs in 1/2,647 births, which exceeds the incidence of

other primary congenital diseases such as cystic fibrosis (1/3,900), and hypothyroidism (1/3,000) (Kliegman, Behrman, Jenson, & Stanton, 2007). Sickle cell disease is more prevalent among some ethnic groups as compared to others. For example, sickle cell disease has been found to be the most prevalent among African Americans occurring at a rate of 1/396 births compared to 1/36,000 births among Hispanics, and 1/16,000 births among Asian Indians (Kliegman et al., 2007).

The average hospital stay of an adolescent experiencing a vaso-occlusive crisis is 9 to 11 days (Ballas, 2007). Acute episodic sickle cell pain or vaso-occlusive crisis has been found to evolve throughout four distinct phases as described by Ballas (1995). The first phase is the pre-crisis or prodromal phase where changes occur at the cellular level including increase in number of dense red blood cells and reticulocyte count, and decrease in number of platelets and red blood cells. During this phase patients have the presence of clinical manifestations such as numbness, aches, and parasthesia. In the second phase or initial phase, affected parts of the body begin to become infarcted due to the sickling and clumping of red blood cells. This leads to increased pain intensity, while abnormal lab values start to normalize. Adolescents are usually hard to deal with by medical personnel during an emergency visit due to the increased level of fear and anxiety during the second phase (Brown, Connelly, Rittle, & Clouse, 2006). The third phase, also called established or post-infarctive, predominantly involves a persistent severe pain accompanied by an inflammatory process. Throughout the last 2 to 3 days or post-crisis phase, patients start to develop remission and pain levels decrease gradually. The use of these stages provides a trajectory of symptoms and enables providers to predict a course of treatment.

Within the United States, all health institutions are required to perform a newborn screening blood evaluation within the first few days of life ("Pediatric Genetics", 2013). The

newborn screening test was implemented into practice to detect specific medical conditions such as phenylketonuria, hypothyroidism, sickle cell anemia, and cystic fibrosis. Early identification of sickle cell disease can decrease morbidity and mortality and increase quality of life (Robitaille, Delvin, & Hume, 2006). For instance, treatments such as prophylactic penicillin and administration of routine vaccinations including haemophilus influenzae type B vaccine can reduce the risk of sepsis in infants diagnosed with sickle cell disease (Kliegman et al., 2007).

Sickle cell disease is a chronic unpredictable illness affecting a person's daily living, quality of life, and development. Daily management of the disease is variable based on the symptoms experienced. Vague symptoms such as headache or fever can be life threatening in persons with sickle cell disease as they may manifest stroke or sepsis. Fatigue, irritability, activity intolerance and pain may be regularly experienced from anemia (Kliegman et al., 2007). Children and adolescents can incorporate routine activities to avoid triggers of a crisis such as drinking fluids, avoiding cold, decreasing stress, and taking medication (Yale, Nagib, & Guthrie, 2000). The consistent need to implement these activities in addition to continuously seeking professional health care will add more to the burden caused by the disease (Gil et al., 2001). Furthermore, sickle cell disease will jeopardize the ability to partake in normal child or adolescent activities, household chores, sports, school, and hygiene practices (Beyer & Simmons, 2004). Children with sickle cell disease and their parents perceive there physical, emotional, and social health as well as school functioning of lower quality when compared to children without the disease (Conkin Dale, Cochran, & Jernigan, 2001).

Sickle cell crisis is an acute painful event in which the onset of pain is sudden, intense and unpredictable. The duration of symptoms of a crisis is variable. A sickle cell crisis occurs when the abnormally shaped red blood cells block blood vessels impairing blood flow

throughout the body. Pain can be experienced anywhere in the body including extremities and joints, depending on what vessels are affected. This process may be triggered by cold temperature, infection, high altitude, respiratory or metabolic acidosis, strenuous physical exercise and emotional stress (Brown, 2012). Persons experiencing a crisis may take over the counter pain medications or medications prescribed by there healthcare provider. They also may incorporated non-pharmacological techniques such as hypnosis, massage therapy, heat therapy, and distraction techniques into there pain management (Agargun, Öner, & Akbayram, 2001; Dampier, Ely, Brodecki, & O'Neil, 2002; Lemanek, Ranalli, & Luken, 2009). Persons experiencing severe pain that is unrelieved by home management may require hospitalization for more advance treatment.

Pain in Sickle Cell Disease

Pain is a subjective experience that can be measured and described by the person experiencing the sensation. People experiencing pain related to a sickle cell crisis express the characteristics of their pain by using a variety of terms including "throbbing", "sharp", "dull", "stabbing", and "shooting"(Ballas & Delengowski, 1993). Sickle cell disease strikes a large number of systems and organs in the body. As discussed earlier, the most pivotal complication of sickle cell disease is vaso-occlusive pain. These crises are caused when abnormally crescent-shaped red blood cells block the blood flow into different parts of the body which causes pain and organ damage (Brown, 2012). Episodes of severe pain in patients with sickle cell disease are both unpredictable and common (Platt et al., 1991). Sickle cell pain is characterized by an unremitting feeling of discomfort ranging from acute to chronic in duration and from mild to severe in intensity. Children and adolescents with sickle cell disease often describe pain as constant, dull, biting and throbbing. Pain caused by sickle cell disease is the most frequent

reason for hospitalization in children and adolescents (Shapiro, Cohen, & Howe, 1993). Additionally, pain from vaso-occlusive episodes has been cited by adolescents and their parents as the most distressing complication of sickle cell disease.

Whether patients cope with and treat pain adequately or not, it will have significant consequence as to how these patients' perceptions, development and experiences across their life spans will be affected. Moreover, painful episodes were also described by children and parents as "debilitating" (Amrolia, Almeida, Halsey, Roberts, & Davies, 2003) and a major problem that affects their lives interfering with activities of daily living (Graumlich et al., 2001). If not managed properly, painful episodes will have a variety of negative effects on children in terms of academic performance (Eaton, Haye, Armstrong, Pegelow, & Thomas, 1995), psychosocial adjustment (Barbarin, Whitten, & Bonds, 1994), coping (Gil et al., 1997), activities of daily living (Graumlich et al., 2001), and overall quality of life. By adolescence, many children develop ineffective coping strategies and demonstrate marked decline in academic and psychosocial functioning (Yoon, & Black, 2006). Also, children report greater anxiety in the presence of a major stressor such as pain (Yoon & Godwin, 2007).

Mechanism of Sickle Cell Disease Related Pain. Pain can occur throughout the body at any location that contains nociceptors. Nociceptors are primary sensory neurons that act as a first line of defense against potentially life-threatening or damaging stimuli (Wolf, 2002). Sickle cell pain can be localized, involve several areas or can be migratory. Sickle cell pain is most often reported in the chest, abdomen, and extremities (Taylor, Stotts, Humphreys, Treadwell, & Miaskowski, 2010). However, other locations in the body have been found to be affected by sickle cell pain such as lumbar spine, femoral shaft, head, shoulders, penis, hip, knees and heels.

Sickle cell pain is unpredictable occurring as chronic or acute in nature, or as a combination of the two. Chronic pain is a result of ongoing organ damage and necrosis of tissue but not as a continuation of acute episodes. Examples of underlying complications that can cause chronic sickle cell pain include leg ulcers, avascular necrosis of humoral or femoral heads, and bone infarcts (Ballas, 2007). Two types of chronic pain have been identified in the literature, chronic pain with obvious etiology and intractable chronic pain with no obvious etiology. Chronic pain with obvious etiology can be related to one of the underlying complications mentioned above such as leg ulcers and avascular necrosis. In contrast, intractable chronic pain with no obvious etiology only includes subjective persistent pain as described by the patient. Intractable chronic pain is believed to be a transition from acute episodic sickle cell pain that is not managed properly throughout the course of the disease (Ballas, 2007). In this case, the pathophysiology of transition from acute to chronic pain is unknown (Ballas, 2007).

The phenomenon of central sensitization is one of the possibilities that can explain this transition. Central sensitization occurs when excessive signals are transmitted from the peripheral to the nervous system causing the sensation of pain to be amplified (Ballas, Gupta, & Adams-Graves, 2012). Clinical manifestations of central sensitization can include significant decrease in pain threshold, where minimal sensations might cause severe pain sensation or allodynia. Additionally, patients are able to feel pain beyond the location of original injury; this is also known as expanded receptive fields. Prolonged pain sensation even after the resolution of the original injury is also a clinical manifestation of central sensitization (Ballas et al., 2012).

Significance

Patients with sickle cell disease require a lifetime of medical management to oversee their disease and related complications. U.S. sickle cell disease–related pediatric costs were

"conservatively" estimated at $335 million (Dobson & Byrne, 2014). Medical costs for disease related insurance claims over an effected person's lifetime are estimated to be just over $460,000 dollars per person (Kauf, Coates, Huazhi, Mody-Patel, & Hartzema, 2009). Healthcare dollars related to sickle cell disease are most commonly spent on emergency room visits and hospitalizations due to vaso-occlusive crisis, office visits, and prescription medications (Kauf et al., 2009; Mvundura, Amendah, Kavanagh, Sprinz, & Grosse, 2009).

Kauf et al. (2009) compared the average health care costs spent between different age groups among 4,294 patients. Within this sample, an average of 51.8% of medical claims was related to sickle cell disease. The greatest proportion of medical claims related to sickle cell disease compared to non-sickle cell disease claims were made by 0-9 year olds (49.2%) and 10-19 year olds (55.4%). Typically, a person with sickle cell disease spends $1946 disease related healthcare dollars per month, not including hospitalizations, with increasing expenses as a person ages. The average distribution of healthcare dollars were found to be spent on (a) 80.5% on hospitalization; (b) 3.6% on prescriptions; (c) 3.2% on emergency room visits; (d) 0.9% on physician visits; (e) 11.7% on other expenses. Early diagnosis of correlating complications, health maintenance, and preventative treatment may help reduce a person's healthcare costs related to sickle cell disease.

The transfusion of red blood cells in patients with sickle cell disease is a common treatment for complications such as aplastic crisis, stroke, and anemia (Kliegman et al., 2007). Patients who receive frequent blood transfusions can acquire high serum iron levels that require specific treatment to prevent toxicity and organ damage. This necessary treatment of intravenous chelation therapy has been shown to increase a child's annual healthcare expense from $10,195 to $39,861 (Mvundura et al., 2009). Chelation therapy may be costly; however it is a necessary

treatment for certain symptoms and benefits the patient long term. As health care costs increase every day, hospitalizations can be a great burden on the families and their children. This can be an additional burden in conjunction with the physiological and psychosocial complications that affect essential elements of the adolescent's life on a daily basis.

In addition to the financial burden as a result of sickle cell pain management, the psychosocial and developmental functioning of adolescents is greatly affected. Evidence from the literature indicates that adolescents with sickle cell disease are at higher risk for psychological, social and developmental problems due to interruptions in daily life from the effects of sickle cell disease (Brandow, Brousseau, Pajewski, & Panepinto, 2010). Examples of adjustments that impact psychological, social and development of an adolescent's life include school, peers, family, and sexual orientation. When adolescents suffer from frequent vaso-occlusive crises, the adjustment process in any of the abovementioned aspects is interrupted. Moreover, the frequent need for hospitalization and complicated pain management will also affect the development of the family's relationship with the adolescent as well as their mental health, and working life (Brandow et al., 2010).

Most of the barriers to pain control referenced in the literature for children and adolescents are related to analgesic use. More attention should be directed towards other holistic and non-pharmacological approaches in conjunction with analgesics to help with pain management in children and adolescents. Unfortunately, many practitioners in primary and acute care settings lack the appropriate knowledge about the importance of using non-pharmacological modalities to control pain. MacLaren, Cohen, Larkin, & Shelton (2008) stated 21% of nurses failed a survey that assessed knowledge of non-pharmacological interventions and only 50% of nurses in the study reportedly used cognitive behavioral techniques in their pain

control practice. In most institutions, guidelines or protocols for the use of non-pharmacological interventions during painful episodes in sickle cell patients are not being utilized.

The importance of using non-pharmacological modalities in conjunction with analgesics to treat pain in children and adolescents has been stressed in the literature (Lassetter, 2006). Studies have shown that children with sickle cell disease can have more effective pain management at home when they learn the appropriate use of non-pharmacological approaches and incorporate them into their lives (Dumaplin & Sagraves, 2006; Sabinga et al., 2006; Yoon & Black, 2006). Hence, allowing children and adolescents to manage their own pain at home or in the hospital setting gives them a sense of control and a more active role in a functional life with their pain. In fact, using non-pharmacological modalities as part of a multimodal program to treat pain has the potential to help decrease the costs of medical care for families and the health care system because fewer hospitalizations and treatments are needed (Bernatzky, Presch, Andreson & Panksepp, 2011). In a report done by the National Institutes of Health (NIH) in 2008, it was evident that parents were more likely to opt for their child to use non-pharmacological modalities when they were unable to afford conventional therapies than when the cost of conventional therapies was affordable (Barnes, Bloom & Nahin, 2008). In addition, non-pharmacological approaches can be more accessible to children and adolescents than pharmacological modalities.

More recently, and with the emerging technological advances, researchers' attention has been drawn to modalities with multi-sensory nature such as virtual reality and videogames. The reason for this interest stems from the immersive and distractive nature of these modalities which can be utilized to divert a patient's thoughts from the sensation of pain. Currently, most videogames provide the player with many options including difficulty levels, character selection

and customization, and mission selection. Videogames can be either played using personal computers, gaming consoles, or through the use of virtual reality goggles or display helmets. Przybylski, Rigby, & Ryan (2010) also added that in regard to the relatedness need, videogames and virtual worlds could serve as a social media by allowing players to interact and communicate through voice or text. Videogames can be utilized and incorporated in a variety of settings for the management of pain.

Statement of the problem

The National Institutes for Health (NIH) has published guidelines for the treatment of sickle cell disease related pain. The most recent publication in 2002 advises health care providers to guide therapy on an individual basis. Providers should always utilize patient preference and pain history as a source for management. Individuals seeking treatment from an institution should be considered a medical emergency, and initial management includes intravenous morphine or hydromorphone. Self report of pain should be reassessed frequently and medications titrated until the pain level is tolerable. A pharmacological combination may be used by the addition of medications such as NSAIDS, acetaminophen, or anti-histamines. The NIH recommends once pain is tolerable and under control the patient should be prescribed a medication regimen that provides sufficient pain control for maintenance.

Over the past decade pain management has advanced and changed, therefore the NIH has established an expert panel for the management of sickle cell disease pain that released an updated recommendations report for providers in 2014. The expert panel report included recommendations for the management of sickle cell chronic pain as well as pain from vaso-occlusive crisis. In addition to the use of pharmacological interventions such as opioid to manage pain during a vaso-occlusive crisis, the panel also recommends the use of non-pharmacological

approaches such as distraction to enhance pain management (National Institute of Health, 2014). Furthermore, the 2014 NIH report recommends using non-pharmacological approaches for all types of chronic sickle cell pain. Non-pharmacological approaches for the management of chronic sickle cell pain listed in the 2014 NIH expert panel report include deep tissue/deep pressure massage therapy, muscle relaxation therapy, and self-hypnosis (NIH, 2014).

The management of sickle cell disease in children requires a multidisciplinary approach. Physicians, child life specialists, social workers, parents, psychologists, and other disciplines all play an integral part in providing care for effected persons (Brandow, Weisman, & Panepinto, 2011; Hall, Chiarucci, & Berman, 1992). Pain is the most prevalent symptom experienced by children with sickle cell disease; therefore, pain management is of utmost importance. Pain can be medically managed at home or in the hospital as medications can be administered in a variety of ways depending on the patient and the response to treatment. Research indicates that the majority of healthcare providers do not routinely instruct and educate patients and families on non-pharmacological modalities to further alleviate or prevent pain (Pegelow, 1992; Post-White, Fitzgerald, Hageness, & Spencer, 2009; Sibinga, Shindell, Casella, Duggan, & Wilson, 2006). However, parents and children learn and implement available modalities such as massage, distraction, music, and hypnosis into their pain management.

The use of pharmacological interventions for the treatment of sickle cell pain related pain is imperative due to the severity of a pain episode. There are several different classifications of analgesics utilized in the treatment of pain including opioid, non-opioid, non-steroidal anti-inflammatory, and combination drugs. Different medications have been found to decrease pain symptoms; however they do not completely resolve them. The inadequacy of proper pain management can be related to a variety of factors including but not limited to fear of becoming

addicted, adverse effects, disliking medication because of its smell, taste, or shape, and cultural or religious reasons (Ameringer & Pickler, 2009). The use of non-pharmacological therapies in conjunction with medications can further alleviate pain symptoms in children and adolescent with sickle cell disease. The use of videogames and virtual reality in pain management have yielded positive outcomes for different types of pain, therefore guided the purpose of this current study.

Study Purpose

The purpose of this study is to evaluate the effectiveness of using videogames to decrease pain in a sample of adolescents 12-21 years of age during sickle cell pain. Additionally, the level of engagement induced when playing the videogame and relationship to pain will be measured. A descriptive profile will be provided on the use of non-pharmacological interventions to control pain in the selected population.

Research Question/Hypotheses

Research question 1: What is the level of engagement among the adolescents with sickle cell disease?

Research hypothesis 1: Upon using videogames for the reduction of pain intensity, adolescents with sickle cell pain will report less pain.

Research hypothesis 2: Engagement level will be negatively correlated with self-reported pain level.

CHAPTER 2

Literature Review

Chapter two includes a literature review on key topics related to the proposal. The pathophysiology and critical components of sickle cell disease are discussed. Literature pertaining to non-pharmacological techniques utilized to relieve non sickle cell related pain such as hypnosis, guided imagery, music, virtual reality, and videogames are critiqued. Non pharmacological as well as pharmacological modalities utilized in persons with sickle cell disease related pain are described. A review of virtual reality and videogames and the pertinent key concepts pertaining to their effectiveness are examined.

Pathophysiology of Sickle Cell Disease

Sickle cell disease is an autosomal recessive disorder, meaning that two copies of the gene or allele must be present for the trait of the disease to be phenotypically apparent (Kliegman et al., 2007). Normally, two hemoglobin alleles (HBA) are inherited from both parents; to form the genotype HBA/A (Brown, 2012). Due to structural or quantitative malformations, the sickle hemoglobin (HBβS) can be formed instead of HBA. The presence of one sickle gene is sufficient to say that an individual is a sickle cell disease carrier. However, in order for the clinical characteristics to be present, two genes HBS/S must be inherited from both parents (Stuart & Nagel, 2004).

Several classifications have been identified as types of sickle cell disease with sickle cell anemia being the most common. In sickle cell anemia, the abnormality is caused by the homozygosity of the β_s allele and therefore it is sometimes referred to as HBS/S or hemoglobin S due to the presence of two sickle genes (Stuart & Nagel, 2004). Other forms of sickle cell disease include HBS/C which is linked to the heterozygosity of the β_s and βc alleles, HBS/β^+

Thalassemia and HBS/β^0 Thalassemia (Ashley-Koch, Yang, & Olney, 2000). The latter two sub-types of sickle cell disease are caused by the coinheritance of the β-thalassemia and βs alleles (Rees, Williams, & Gladwin, 2010). Other more rare genotypes of hemoglobin include HBSD, HBSE, and HBSO Arab (Wethers, 2000). The variety of clinical characteristics between the types of sickle cell disease has been linked to the difference in genotype.

When inherited from both parents, the deoxygenated form of HBS leads to polymerization in the nucleus of red blood cells, causing overgrowth inside the cell. The abnormal growth of the nucleus inside the cell leads to dehydration and disruption of the shape and flexibility of the cell (Kliegman et al., 2007). This process of polymerization inside the cell causes the irregular sickle shape of red blood cells. The tendency of red blood cells to obstruct small blood vessels (vaso-occlusion) due to their abnormal shape affecting blood perfusion is the major causative factor of clinical symptoms in sickle cell anemia (Stuart & Nagel, 2004). Vaso-occlusion is caused by the entrapment of abnormally shaped red blood cells in the microcirculation, preventing the distribution of normal oxygenated cells and nutrients throughout the body. This deprivation of blood supply and oxygen may lead to damage in vital organs, ischemia, and typically excruciating pain (Ballas et al., 2012). In addition, other factors can contribute to the occurrence of vaso-occlusive crisis such as the enhanced ability of abnormal red blood cells to adhere to the endothelium of blood vessels and abnormal vasomotor tone causing vasoconstriction.

Sickle cell disease affects multiple systems in the body. Repetitive acute progressive episodes of the disease cause damage to essential organs which may affect their function (Rees et al., 2010). As described previously splenic sequestration, bone marrow infarction, fat embolization, and acute chest crisis are all examples of complications related to sickle cell

disease affecting different organs and body systems. Additionally, all patients with sickle cell disease, regardless of their age, are at an increased risk for infection as a result of malfunction of the spleen. However, severity of clinical symptoms varies greatly between individuals due to the presence of secondary effector genes. The variation in symptom severity has been linked to the dissimilarity in secondary effector genes among individuals (Stuart & Nagel, 2004). The presence of secondary effector genes, also called pleiotropic genes, can either ameliorate or exacerbate multiple symptoms depending on the mutation of those genes. Studying pleiotropic genes offers a promise in identifying risk factors in patients with sickle cell disease and planning interventions before the onset of organ damage.

Symptoms and Complications

Sickle cell disease is associated with a number of symptoms and life threatening complications. A person who has inherited the disease may experience a range of mild to severe symptoms after the first five months of life. Prior to five months of age, clinical presentation of sickle cell anemia is very rare due to the presence of fetal hemoglobin which prevents the polymerization of red blood cells (Stuart & Nagel, 2004). The most prominent symptoms and complications of sickle cell disease are discussed below.

Vaso-Occlusive Crisis. Vaso-occlusive crisis is the most common manifestation of sickle cell anemia in adolescents (Jakubik & Thompson, 2000). The clinical presentation of vaso-occlusive crisis frequently manifests as pain in the chest, abdomen, or extremities. These crises occur when abnormally crescent-shaped red blood cells block the blood flow into different parts of the body which causes pain (Brown, 2012). Although vaso-occlusive crisis is a self-limiting complication that is not linked to organ damage, it is the most important and most bothersome

complication of sickle cell anemia from the patient's perspective (Rees et al., 2010). The painful episodes occur amongst individuals in varying frequency and quality.

Acute Chest Syndrome. Acute chest syndrome is considered the second most common cause of hospitalization in adolescents with sickle cell anemia (Castro et al., 1994). Acute chest syndrome is responsible for about half of the deaths in children and adolescents with sickle cell disease who are less than 20 years of age (Vichinsky et al., 1997). Moreover, 13% of patients with acute chest syndrome require admission to the intensive care unit and the use of mechanical ventilation (Vichinsky et al., 2000). On radiological examination, acute chest syndrome can be identified as a new pulmonary infiltrate involving at least one complete lung segment. The major cause of the syndrome is hypoxia of the lung, in contrast with other vascular beds in the body; this causes vasoconstriction of vascular beds akin to vaso-occlusive crisis. Hypoxia and vasoconstriction in lung tissue is known to further exacerbate polymerization and sickling of red blood cells (Stuart & Nagel, 2004). Multiple factors contribute to the severity of acute chest syndrome including vaso-occlusion of pulmonary microcirculation, fat embolism, and infection. Multi-modality interventions are used for the treatment of acute chest syndrome. Additionally, broad-spectrum antibiotics, oxygen, bronchodilators and avoidance of over-hydration are used for the management of symptoms (Vichinsky et al., 2000).

Aplastic Crisis. In persons experiencing aplastic crisis, there is a profound decrease in bone marrow function that is usually limited to red blood cell precursors. Thus patients have increased anemia due to the cessation in the production of red blood cells during this crisis. Patients experiences symptoms related to low hemoglobin such as fatigue, shortness of breath, and pallor. Aplastic crisis is usually associated with an acute infection of human parvovirus B19 (Wen, Zhon, Li, Feng, & Wang, 2012). Supportive treatment including infusion of packed red

blood cells is indicated as aplastic crisis is self-limiting within a few days (Stuart & Nagel, 2004).

Neurologic complications. Stroke most commonly occurs in children with sickle cell disease. Eleven to twenty percent of children with sickle cell anemia will have overt or silent strokes before they turn 18 years old (Adams et al., 1998). Overt stroke is referred to as a focal neurological deficit with or without cerebral infarction that can be seen on magnetic resonance imaging (MRI) and lasts greater than 24 hours. In comparison, silent strokes demonstrate the presence of a lesion on MRI indicating cerebral infarction. Other neurological complications include headaches, seizures, and cerebral venous thrombosis (CVT). Treatment of neurologic complications includes the administration of oxygen, and blood transfusions (Rees et al., 2010).

Renal Complications. The renal medulla in persons with sickle cell disease tend to have low partial pressure, low pH, and high osmolality increasing the occurrence of erythrocyte polymerization (Rees et al., 2010). As a result, red blood cells assume a crescent shape, causing the renal vasculature to be occluded which will consequently lead to renal complications. Some of the renal complications can include hematuria, proteinuria, renal infarction, papillary necrosis and renal insufficiency. In patients with proteinuria, angiotensin converting enzyme inhibitors have proven effective (Stuart & Nagel, 2004).

Review Strategy

Relevant papers reflecting non-pharmacological interventions used among children and adolescents to manage pain were identified from MEDLINE, PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and PsycINFO databases. The search strategy employed was to identify articles with “non-pharmacologic interventions”, “complementary therapies”, “alternative therapies”, “multimodal intervention”, “hypnosis”, music therapy”,

"virtual reality", "guided imagery", "videogames", "pain", "vaso-occlusive crisis", "sickle cell disease", "virtual reality" and "immersion" as main subject headings (exploded) or text words in titles and abstracts. Papers published in English language between 1995 and 2013 were considered. Findings from relevant reviews were also considered. Furthermore, the ancestry search approach was used to identify additional relevant literature.

Published articles on non-pharmacological modalities that address pain management in children and adolescents either in the hospital or home settings were considered. Samples from selected studies included children and adolescents between 2-17 years of age. To cover a broad variety of studies and to assess the efficacy of non-pharmacological modalities on different types of pain, articles addressing children and adolescents with either chronic or acute pain were included. For the purpose of reviewing the most recent evidence, research articles published prior to 1995 and non-research articles were excluded.

Pharmacological Interventions in Sickle Cell Disease Pain

The majority of literature pertaining to pain management in children and adolescents with sickle cell disease discusses the effectiveness of a variety of pharmacological approaches. The characteristics of pain caused by sickle cell vaso-occlusive episodes vary between patients which is evident by patient documentation in pain diaries (Dampier et al., 2002; Gil et al., 2001). Treatment regimens are based on healthcare provider preference, patient past experience, and medication availability. Medications can be administered orally, intravenous, continuous, as needed, or by patient controlled just to list a few. Moreover there are several different types of medications approved for the use in the pediatric population to treat pain.

In present day, there are no universal protocols for vaso-occlusive pain management in children and adolescent with sickle cell disease. However many institutions and researchers

have analyzed a variety of standard of practice protocols that have been initiated in a variety of settings. Morrissey et al. (2009) discussed the effectiveness of practice guidelines in the emergency department that were developed by a multidisciplinary team at Children's Hospital of Boston. Compared to patient outcomes prior to the implementation of the protocols there were improvements in the use of pain scales, appropriate medication dosing, improved utilization of patient controlled analgesics (PCA) and a decrease from 80 to 65 minutes in which the first dose of medication was given. Brandow et al. (2011) discussed protocols and roles of each multidisciplinary team member in the standards of practice implemented in a pain clinic for children with sickle cell disease. With the use of pharmacological and non-pharmacological pain management approaches the number of hospitalization in the participating children decreased by 50% (Brandow et al., 2011). Frei-Jones, Field, and DeBaun (2009) discussed the change in practice which included standardized orders, monthly physician in-services, and parent/patient education with the goal to decrease the 30-day readmission rate for children with sickle cell pain. After the implementation of these guidelines the 30-day readmission rate decreased from 28% to 11%. Although these studies had different goals relating to children with sickle cell related pain, they collectively demonstrated that with appropriate practice guidelines improved pain management can be achieved.

In 2000, Beyer analyzed the effectiveness of analgesics in 21 children and adolescents experiencing pain caused by vaso-occlusive episodes. The participants received either nalbuphine, fentanyl, or hydromorphone by continuous or PCA dosing. In addition to the intravenous medications they also received scheduled oral medications. Among the 21 children, only five children reported adequate pain control. The other 16 children reported moderate to high levels of pain while still on their ordered pain management regimen. Similar results were

found by Zempsky et al. (2008) who, in a retrospective review, evaluated the treatment of vaso-occlusive pain in children with sickle cell disease. All 59 participants received analgesics, most of which continued to have moderate to severe pain. In a study by Frei-Jones, Baxter, Rogers, & Buchanan (2008) 12 out of 106 children and adolescents returned to the emergency department within 96 hours after discharge for persistent or continued vaso-occlusive pain. Jacob & Mueller (2008) reviewed patient charts of children who had prolonged hospitalization for sickle cell pain. The data among the 29 admissions reported the use of over 10 different medications prescribed for pain management during the hospitalizations as well as high, uncontrolled pain scores throughout the children's admissions. Medication dosing, route of administration, previous medications utilized, response to treatment and many other factors must be taken into consideration when appropriately treating an individual's pain. These studies demonstrated the need for non-pharmacological therapies in conjunction with medications for more adequate pain control.

PCA devices are utilized among older children and adolescent who are capable of understanding how to use the device. This route of medication administration allows patient to receive both continuous and or on demand bolus doses of a prescribed medication within its controlled limitations.

In a retrospective chart review by O'Connor, Trentadue, Kachoyeanos, & Lea (1998) the difference in medication dosing using a PCA device was compared in children with sickle cell pain related to vaso-occlusive episodes. The study included 26 children who utilized a morphine PCA device during 60 different occasions. The patients were divided evenly into two groups; group 1 received high PCA bolus dose with low dose basal infusion and group 2 received low PCA bolus dose with high dose basal infusion. It was found that children in group 1 used less

morphine, were weaned off the PCA sooner, and had less hospitalized days compared to group 2. The patients in group 1 experienced improved pain control. These patients received lower continuous infusion, and were able to administer higher doses of morphine on demand, as needed. This study demonstrated how the same medication can have diverse effects on sickle cell pain when administered in different doses.

In many of the studies describing the use and effectiveness of non-pharmacological techniques, the authors also discussed details of pharmacological interventions as well. The majority of participants were asked to continue their prescribed pain medications and consume them based on symptoms severity. In the pain diaries analyzed by Oshikoya, Senbanjo, Kjokanma, & Soipe (2008) morphine was taken 26.4% of days and meperidine 13.9% of days patients experienced sickle cell related pain. In Beyer and Simmons (2004) parents stated administering medications such as codeine, vicodin, and hydrocodone as the most common ways to "catch their pain." In Dinges et al. (1997) the participants were advised to continue their prescribed analgesic medications while participating in the study, which resulted in no significant difference in the number of sickle cell pain days medication was consumed. In Yoon & Black (2006) parents reported 57.4% of the children were taking between 1-3 analgesics with the most common ibuprofen, acetaminophen, and oxycodone. In a survey conducted by healthcare providers, Pegelow (1992) reported that 20 out of 21 healthcare providers treated sickle cell pain with opioid analgesics.

Non-Pharmacological Interventions for Pain

Traditional treatment for vaso-occlusive crisis includes warmth, hydration, transfusion therapy, and analgesic medication (Gil et al., 2001). Additionally, the use of non-pharmacological modalities to reduce pain such as virtual reality, music, and videogames have

been reported (Ahmadi, 2001; Hoffman, Doctor, Patterson, Carrougher, & Furness, 2000). Although non-pharmacological modalities used as adjunctive tools with conventional therapy has been shown to successfully decrease pain, anxiety, and discomfort in children (Ahmadi, 2001), there is little empirical evidence to support one specific strategy over another. Only a few studies have evaluated the use of non-pharmacological modalities to control pain in children and adolescents with sickle cell disease. However, no studies have been found to support the effectiveness of using videogames as a non-pharmacological modality to control pain in adolescents with sickle cell disease during vaso-occlusive episodes.

Non-pharmacological therapies, also known as complementary and alternative therapies (CATs), are treatments that fall outside of, but go in conjunction with, the mainstream of conventional medicine (Kelly, 2004). Non-pharmacological modalities reported in the literature to control pain in children and adolescents include hypnosis, guided imagery, music therapy, massage, videogames, cognitive behavioral therapy and virtual reality.

Hypnosis. Hypnosis is a technique that constitutes attention and suggestibility which in turn leads to relaxation. The person under hypnosis is guided by a trained therapist to respond to suggestions that may alter perceptions, ideas, behaviors, or emotions related to subjective experiences (Landier & Tse, 2010). Hypnotic suggestibility can be direct, such as suggestions for numbness (e.g. allow your back to go to sleep), glove anesthesia (e.g., anesthesia transfers from hand to affected body part), local anesthesia, and switchbox (e.g., allowing the person to switch off responsible part of the brain) (Gardner & Olness, 1981) or it can be indirect, which can be as simple as imagining a relaxing setting sun. Studies using hypnosis as a non-pharmacological modality have shown that patients experienced less pain and anxiety, fewer procedural complications, and economized time because their procedures take less time to

complete (Butler, Symons, Henderson, Shortliffe, & Spiegel, 2007). Moreover, the use of hypnosis saved an average of $338 in medical claims per patient undergoing a voiding cystourethrography due to fewer complications and reduction in medication use (Butler et al., 2007). These findings indicated that using hypnosis can be cost-effective to both families and institutions.

Studies to evaluate the effectiveness of using hypnosis for the purpose of pain management in children and adolescents were first conducted in the 1980s. Since then, most of the studies have focused on pain related to medical procedures, such as bone marrow aspirations and lumbar punctures. The majority of studies reported that hypnosis is more effective than distraction in reducing pain especially when used with younger patients. (Kuttner, Bowman, & Teasdale, 1988; Milling, 2008; Zeltser & LeBaron, 1982). However, the effectiveness of videogames to decrease pain has not been tested in adolescents with sickle cell crisis.

In the late 1990s, researchers attempted to compare the effectiveness of different types of hypnotic suggestions. In 1998, Hawkins, Liossi, Ewart, Hatira, & Kosmidis conducted a study to compare the effectiveness of using direct and indirect hypnotic suggestions to alleviate pain in children and adolescents with Hodgkin's lymphoma and leukemia undergoing lumbar punctures. There were 30 participants in this study, with ages ranging from 6 to 16 years. The study involved a random assignment into two groups: direct hypnotic suggestions or indirect hypnotic suggestions. Results from this study showed that both groups experienced significantly lower pre and post pain scores with no difference between the intervention groups. In this study, the difficulty in interpreting the findings can be related to the absence of a control group and the relatively small sample size.

In order to address the limitations in the Hawkins et al. (1998) study, Liossi and Hatira conducted a follow-up study in 2003. The study involved a larger sample size of 80 participants with the same population characteristics as in Hawkins et al. (1998). In the Loissi and Hatira (2003) study, children and adolescents were randomly assigned to the same hypnotic suggestion groups as in Hawkins et al. (1998), but there was an addition of two control groups. The control groups were attention control or standard medical procedures. Reports from this study showed that both hypnotic suggestion groups had more significant results compared to the control groups. However, there was no difference in effectiveness between the direct and indirect hypnotic suggestion intervention groups.

Results from studies from the year 2006 and 2009 by Liossi, White and Hatira are consistent with similar studies from Liossi and Hatira (1999, 2003) and Hawkins et al. (1998). These studies used hypnotic suggestions for pain control during medical procedures, such as venipunctures, lumbar punctures and bone marrow aspirations. The intervention groups reported significantly lower pain and distress scores than the control groups that consisted of receiving medical standard of care or attention control alone. When compared to other CATs such as music and massage, hypnosis was a superior modality in reducing pain scores in children and adolescents (Liossi & Hatira, 1999). Findings from these studies raise the possibility that hypnosis can be effective in alleviating pain associated with certain medical procedures.

The majority of hypnosis literature emphasized the use of hypnosis in acute pain in pediatrics rather than its usefulness in chronic pain. However, adult literature supports the use of hypnosis for chronic pain caused by medical conditions such as cancer (Elkins, Cheung, Marcus, Palamara, & Stearns, 2004), arthritis (Gay, Phillipport, & Luminet, 2002), sickle cell disease (Dinges et al., 1997), and disability-related pain (Jensen et al., 2005). Additionally, hypnotic

effects vary from one person to another, but it is evident that hypnosis is more efficient when used with children and adolescents than when it is used with adults (Evans, Tsao, & Zeltzer, 2008). The difference in efficacy can be related to the tendency of children and adolescents to be engaged in more fantasy and make-believe activities. Accordingly, it is possible to postulate that the use of hypnosis in children and adolescents' with chronic pain can be effective.

As illustrated in hypnosis studies reviewed above, researchers were interested in evaluating the effectiveness of using hypnotic suggestibility to manage pain in children and adolescents. Moreover, these studies revealed that hypnosis is an effective and promising modality to manage pain within children and adolescents. Due to a group of well-controlled studies, it has been proven that hypnosis is a "well-established" modality for pain control (Montgomery, DuHamel, & Redd, 2000). However, most of these studies fail to address the relationships and differences among hypnotic suggestions and treatment outcome. Additionally, the reviewed studies did not take into consideration participant's characteristics such as beliefs, attitudes and preferences. Other methodological considerations noted in the review include the relatively small samples sizes used in some of the studies which can limit the representation and generalizability of the sample. Finally, it is also important to note that to use hypnosis effectively; one must have substantial training, experience (Anbar, 2001), and time to use it.

Hypnosis is a non-pharmacological technique that has been utilized by many to assist in the management of different types of pain. Dinges et al. (1997) assessed the effectiveness of self-hypnosis on pain related to sickle cell disease in children, adolescents, and adults. The study included 37 participants of which were 11 children (5-11 years old), 17 adolescents (12-19 years old), and 9 adults (20-51 years old). The participants were asked to continue their normal daily routines and pain management regimens as they documented twice a day in a pain diary that

included characteristics of pain, medications taken, school and work disturbance and practice of self-hypnosis techniques. After four months, the participants attended age appropriate behavioral treatment sessions during which they learned self-hypnosis techniques, participated in group discussions, and practiced their skills. The sessions took place over 18 months, in which the frequency of sessions decreased overtime. Twenty one thousand two hundred and thirty seven pain diaries were collected over the two year study. In analyzing the diaries it was found that children reported fewer sickle cell related pain days and lower intensity of pain compared to adults. Moreover patients with homozygous sickle genotype experienced pain episodes of longer duration compared to those with heterozygous hemoglobin genotype. After initiation of self-hypnosis participants reported a decrease in the frequency of pain episodes. The reports of pain free days increased from 41-80% to 90% after self-hypnosis intervention. Patients also reported better sleep on days without pain, however no significant effect on sleep while they were experiencing pain. Furthermore, there was no effect on school or work absenteeism, medication use, or intensity of pain episodes.

In a case study reported by Agargun et al. (2001), a nine year old female with sickle cell disease underwent hypnotic suggestion. She experienced frequent episodes of pain in multiple body sites that were only relieved by the opioid analgesic meperidine (Demerol). The child underwent hypnotic sessions to assist in coping after being transferred to a psychiatry department. The sessions included relaxation, imagery, and analgesic suggestions. The hypnotic analgesic suggestions provided detailed guidance to request feelings numbness and administration of local anesthesia to painful areas. She was trained to provide self- hypnosis during painful episodes at home. In a six month follow-up she was found to be hospitalized again for severe pain and meperidine dependency. The intervention was found not to be

effective for this particular patient. For hypnosis to be effective the mind must be able to concentrate and give into the hypnotic suggestions. The results may be due to her psychological history of depression and anxiety as well as her dependency to meperidine.

Guided Imagery. Guided imagery is a form of self-regulation therapy. In self-regulation therapy a patient experiences a state of deep muscle relaxation, which in turn allows the patient to be guided to actively create images that help with the resolution of problems (Weydert et al., 2006). Guided imagery is different from hypnosis in that the patient can independently create his or her own images with minimal involvement (i.e., without the need of a therapist). When imagery is used, participants visualize and imagine pleasant and comfortable images or scenes to help them cope with their pain and distress (Uman et al., 2008).

In 2014, Dobson and Byrne conducted a quasi-experimental study to measure the effectiveness of using guided imagery in young children with sickle cell disease pain. 20 participants, 6-11 years of age, were purposefully enrolled from one sickle cell clinic, 12 girls and 8 boys. Participants in this study were trained on the use of guided imagery and were allowed to use it over a month period afterward. A diary was completed by each participant in which they recorded different variables such as pain scores, the use of guided imagery, and the use of medications. Results from this study showed significant decrease in pain levels. Additionally, the amount of medications used was also decreased overtime.

Guided imagery has been evaluated for its efficacy with a variety of conditions and medical procedures. For example, studies that evaluate the effectiveness of guided imagery on recurrent abdominal pain in children and adolescents were prevalent in literature searches. In 2009, Tilburg and colleagues developed an eight week guided imagery treatment compact disc for at home use with thirty-four participants who were 6-15 years of age. Participants in this

study were diagnosed with recurrent abdominal pain and were randomly assigned to receive two months of standard medical care with or without guided imagery. Participants and their parents completed assessment questionnaires at the beginning and completion of the eight-week treatment period. The treatment period consisted of three bi-weekly sessions that included suggestions to induce relaxation. These sessions sequentially included imagining floating comfortably on a big puffy cloud, sitting in a gently rocking boat, and sitting on a flying blanket and enjoying a flight to a mountaintop. The authors found that guided imagery intervention in conjunction with standard medical care was more efficacious than standard medical care alone for the treatment of recurrent abdominal pain. These results were congruent with the findings of an earlier study done by Weydert et al. (2006) to test the effectiveness of guided imagery on recurrent abdominal pain.

Imagery has also been utilized in acute care settings, such as pediatric critical care units. In a 2010 study done by Kline et al., guided imagery was examined for its effectiveness in forty-four children and adolescents, between 6-18 years of age, with pain caused life-threatening injuries or illnesses and/or medical procedures. Participants in this study were conscious, extubated and verbal. In this study, children and adolescents were assigned to one of two intervention groups, mental imagery or detailed inquiry. In the mental imagery group, the assigned participants were instructed to employ the pleasant imagery of light shining through their body to help relieve their pain. The detailed inquiry group involved activities such as expression of thoughts and feelings about participants' current pain-related experiences, active listening, and providing information and comfort. Findings from this study indicate that mental imagery significantly reduced self-reported pain scores after the intervention. Pain scores were also found to be lower in boys compared to girls. Moreover, these results led the hospital in

which the study was conducted, to implement a training protocol for new nurses and staff to use and teach mental imagery for patients with pain.

Two studies found in the literature tested the effectiveness of guided imagery on post-operative pain in children and adolescents (Huth, Broome, & Good, 2004; Pölkki, Pietil, Vehvilinen-Julkunen, Laukkala, & Kiviluoma, 2008). Participants' ages in these studies ranged from 7-12 years of age who underwent ambulatory surgeries, such as tonsillectomy, appendectomy, or upper/lower limb surgery. Both studies were randomized controlled trials with an average sample size of 66.5 participants. There was no difference found in the amount of analgesics used after the interventions. However, there were consistent findings compared to studies by Tilburg et al. (2009) and Kline et al. (2010) showing that guided imagery was associated with lower pain scores in the intervention groups.

On the contrary, guided imagery was not a promising intervention when used to reduce pain in children and adolescents during cardiac catheterization. In 1995, Pederson evaluated the effectiveness of imagery on pain caused by cardiac catheterization in children and adolescents 9-17 years of age. This study involved the following three groups, a control group, a presence group, and an imagery group. Participants in the control group underwent the procedure in a routine manner. Participants in the presence group were accompanied by a research team member who provided eye contact and conversations throughout the procedure. In the imagery group, participants were accompanied by a research team member who provided imagery suggestions, such as participants describing going to their favorite places and doing their favorite activities throughout the procedure. Inconsistent with results from previously reviewed studies, implementation of the imagery intervention showed lack of significant difference between

groups on self-reported pain scores and distress. The results can be related to the small sample size of 24 participants divided amongst three groups.

Music. The applications of music in health have been utilized for thousands of years. The uses and benefits of music in health are cited in multiple religious books and historical scripts (Avers, Mathur, & Kamat, 2007). The American Music Therapy Association defines music therapy as "the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program ("What is Music Therapy,"1998-2013)." Due to its effectiveness and acceptance in clinical practice, music became a modality that requires a certified music therapist to implement it. Certifications can be earned through professional credentialing bodies such as the Certification Board for Music Therapists. A variety of settings can benefit from music therapists including medical facilities, rehabilitations centers and nursing homes.

Multiple factors can affect the type of music that someone might benefit from. Age, gender, and religious background, can all factors into which type of music can be used. Hence, music is individualized, which means that one patient can benefit from classical music to deal with pain, whereas another patient might benefit from hard rock for the same purpose (Avers et al., 2007).

Currently, researchers and clinicians have been more interested in the application of music in the area of pain management for both pediatrics and adults. A considerable amount of literature was found on the use and effectiveness of music therapy for pain control under different circumstances. For instance, Kristjansdottir and Kristjansdottir (2011) looked at the effectiveness of music with and without headphones for pain caused by immunizations in adolescents. The study included 118 participants who were between 13-15 years old undergoing

a routine polio vaccination. The participants were randomized into three groups; standard care, music with headphones, and music without headphones. Adolescents in both interventions groups received an explanation on the purpose of the music, were asked to concentrate on or 'disappear into' the music for 2-3 minutes before and after the injection. The study revealed that adolescents in the intervention groups reported significantly less pain during the immunization after having listened to their music of preference than did the standard of care group. Furthermore, the intervention was more effective amongst the adolescents who listened to music without the use of headphones.

Literature shows that music has also been used for pain management in various medical procedures because the treatments of many disease processes involve repetitive painful procedures. Most studies pertaining to the use of music therapy in pediatrics study the effectiveness of music during painful procedures. In a systematic review of over four hundred randomized controlled trials including infants, children and adolescents, Klassen, Liang, Tjosvold, Klassen, & Hartling (2008) investigated the effectiveness of using music therapy on pain caused by medical procedures. The researchers concluded that music is an effective intervention in the reduction of pain and anxiety in children and adolescents going through painful medical procedures in a variety of settings. Further, the authors emphasized the importance of music therapy in reducing the need for pharmacological interventions during and after painful medical procedures. However, the authors described some of the reviewed studies as having a poor methodology such as the lack of randomization and small sample size, which can affect the validity of the results.

The effectiveness of using music to help reduce postoperative pain and the use of analgesics needed postoperatively has also been evaluated. Nilsson, Kokinsky, Nilsson,

Sidenvall, & Enska (2009) conducted a randomized-controlled study of eighty participants, ages 7-16 years. Participants were randomly assigned to either receive standard care only or to listen to music from time of admission to 45 minutes postoperatively in addition to standard care. In this study, although music did not significantly decrease pain scores, it is important to note that it did show a significant decrease in the consumption of morphine postoperatively. Moreover, in answering postoperative qualitative questions, participants from the intervention group indicated that they found the music calming and relaxing.

In a similar pursuit, Nguyen, Nilsson, Hellström, & Bengtson (2010) conducted a double-blinded randomized control trial using both quantitative and qualitative data to determine whether music therapy reduces pain in children with leukemia undergoing routine lumbar punctures (LPs). Forty participants, ages 7-12 years were randomized into two groups; music or control groups. The control group received standard care and wore headphones without music. In addition to standard of care, the music group selected preferential music to listen to via headphones before and throughout the procedure. Children reported significantly lower pain scores in the music group during and after the LPs. Further, ten children were asked three open-ended questions about their feelings of pain, fear, and whether they liked the music. Analysis of the qualitative data revealed that participants in the music group experienced less pain, decreased anxiety, were relaxed, and expressed wanting music therapy during subsequent LPs.

In another study, Whitehead-Pleaux and colleagues (2006) sought explanations on how effective music therapy is on children and adolescents with burns during site donor dressing change. The study consisted of two groups, an intervention music group, and a control verbal interaction only group. Fourteen participants between the ages of 6 and 16 years were enrolled in the study; six participants were in the control group and eight were in the intervention group.

Participants in the intervention group were given the opportunity to choose from a list of age-appropriate songs, while those from the control group were simply asked about their interests. Surprisingly, the intervention group experienced higher levels of pain and anxiety than the control group throughout the procedure. However, the authors suggested that the intervention was calming enough to bring pain and anxiety scores down to the level of the control group after the procedure. Results from this study showed that the effectiveness of music on children and adolescents with burns throughout a site donor dressing change is unclear and inconclusive. This may be due to the small sample size.

There has only been modest work to explore the effectiveness of using music for pain in children and adolescents. In contrast, research to explore the effectiveness of using music for pain in adults has been more extensive in a variety of settings. For instance, Good, Anderson, Ahn, Cong, and Stanton-Hicks (2005) tested the effectiveness of music and relaxation on pain following intestinal surgery. The study included 167 participants who were randomly assigned to one of four groups; relaxation group, music group, relaxation and music group, and a control group. The relaxation group was instructed to use the jaw relaxation technique while the music group was given the opportunity to choose from five types of soothing music. The control group was only provided with ten minutes of discussions. Postoperatively, participants from the music group were provided with earphones to listen to a sixty minute music tape. If they were from the combined group, participants were instructed to repeat the relaxation technique at one-minute intervals while listening to the tape. Data from this study indicated that participants in all three interventions groups had significantly less pain than the control group. However, no significant difference was found during post-ambulation on postoperative day one and two or at post-recovery on day two. The authors concluded that the interventions were clinically significant.

This data was also consistent with findings from studies investigating the effectiveness music on pain in other conditions such as chronic non-malignant pain (Siedliecki & Good, 2006), and cancer pain (Huang, Good & Zauszniewski, 2010).

The studies reviewed on the effectiveness of music for pain management in children and adolescents revealed some methodological considerations. For instance, some of the reviewed studies did not give participants the opportunity to choose which music they prefer to listen to (Nilsson et al., 2009). Music chosen by patients can be more effective than music chosen by another person (Bernatzky et al., 2011). Additionally, most of the reviewed studies lacked the blinding component of the outcome assessor which affects the validity of the overall methodology and results. An important point to note is that some studies failed to provide similar conditions for the control and intervention groups (Kristjansdottir & Kristjansdottir, 2010) while others avoided this methodological weakness (Nguyen et al., 2010), for example headphones versus to no headphones. Some of the studies did not include a representative sample size. A larger sample size would allow for a more accurate generalization as well as reflection of the variance in scores.

Despite the inconsistency of results, and methodological considerations among the reviewed articles, it was evident that using music as a non-pharmacological modality to reduce acute pain in children and adolescents can be effective. This can be related to its appeal, relaxing and distracting qualities, and accessibility. More research is needed on the effectiveness of music with chronic pain in children and adolescents.

Massage therapy. Children and adolescents can experience pain caused by vaso-occlusive crisis in a variety of locations within their body. The use of massage for pain relief by caregivers at home has been reported by Beyer & Simmons (2004), Oshikoya et al. (2008), Post-White et al.

(2009), and Yoon & Black, (2006). Lemanek et al. (2009) conducted a randomized control trial to assess the effectiveness of massage therapy at home in children with sickle cell disease. Among the 34 participants, depression, anxiety and pain scores were assessed between the massage therapy group and attention control group. In the massage therapy group caregivers were instructed on specific massage techniques which were to be performed daily for 30 days. During the one month time, massage therapists conducted weekly home visits for reinforcement and variable measurements. The participants in the attention control group did not receive any intervention, however during the one month period they completed weekly forms. The results indicated that children in the massage therapy group had lower levels of depression, anxiety and pain compared to the attention control group. It was also found that parents in the massage therapy group rated higher levels of self-depression and anxiety, which may relate to the increased responsibility of caregivers participation in their child's daily home pain management.

Cognitive behavioral therapies. Gil et al. (1997) conducted a randomized control trial to assess the effectiveness of cognitive coping skills training, using laboratory induced pain in children with sickle cell disease. The study included 49 African American children with a mean age of 11.9 years. The children were divided into two groups; the cognitive coping skills condition and the shared care control condition. In the cognitive coping skills condition the children attended a 45 minute training session on deep breathing/counting relaxation, pleasant imagery and calming self-statements. They also attended a one week follow-up review session and obtained training audio tapes and homework for daily practice. The children in the shared care control condition received routine medical care during the painful stimuli. The painful stimulus was induced by the Forgione-barber focal pressure stimulator which applied pressure to the finger based on the amount of weight added. Children rated their pain scores on the verbal 1-10 pain scale.

Children also completed a coping strategies questionnaire regarding the cognitive, behavioral, and physiological approaches they use for pain management. The comparison of the pre and post-tests between the two conditions revealed that the cognitive coping skills condition group had lower negative thinking scores as well as reports of pain less frequently during low levels of pain. Furthermore there was found to be no difference between the two groups during mid and high levels of pain. The correlation of this data can be compared to children's pain during vaso-occlusive pain episodes. Based on the study results the non-pharmacological techniques learned in the cognitive coping skills condition can be utilized during a pain crisis. Moreover, they may also be helpful in relieving and coping with low levels of pain.

To further analyze the long-term effectiveness of the interventions adapted by Gil et al. (1997), Gil et al. (2001) expanded the research study. Gil et al. (2001) conducted a randomized control trial to assess the efficacy of daily coping practice for one month in children with sickle cell disease. The study included 46 African American participants who were ages 8-17 years old. Forty five of these children participated in the study by Gil et al. (1997). The participants were randomly divided into the coping intervention group or the standard care control group. The 26 children in the coping intervention group were trained in deep breathing relaxation, pleasant imagery, and calming self-talk strategies. The children were given an audiotape with the techniques and asked to keep daily diaries. The participants had minimal phone contact with therapists during the one month interval. The standard care control group did not receive any interventions but were asked to complete daily diaries. Post training and one month follow-up pain analysis was conducted using induced pain by the Forgione-barber focal pressure stimulator as in the previous study by Gil et al. (1997). Children in the initial post training assessment reported less negative thinking and pain during low levels of stimulation compared to their one

month follow-up. After analysis of the diaries, children in the coping intervention group who utilized their coping strategies during a pain episode were less likely to seek medical care and more likely continue their normal daily activities. The initial post training results are similar to those of Gil et al. (1997) in which shortly after training on non-pharmacological techniques, children reported less pain and negative thinking. However, long term effectiveness of these interventions was not demonstrated after minimal contact with therapists and the utilization of home training materials.

Many healthcare institutions and providers have developed routine and standard care for pain management in children with sickle cell disease. Hall et al. (1992) developed and implemented an interdisciplinary program for children with sickle cell disease experiencing pain from vaso-occlusive episodes. The program consisted of a medical team, nursing, psychology and social work. The goal of the program was to avoid excessive use of opioids in patients and to teach them techniques such as relaxation and imagery to assist in relieving pain. Children participated in this program when it was found that coping factors influenced their pain management. The assessment of each participant included a self-reported pain level, 90 item symptom check list, and psychophysiological profile including peripheral finger temperature, heart rate, and galvanic skin response. The tools utilized to measure the psychophysiological profile demonstrate fluctuation in these indicators based on the level of patient distress. Each child had a treatment regimen designed specifically for them including pharmacological and non-pharmacological interventions.

To demonstrate the intervention's effectiveness, a case report about a nine year old female with sickle cell disease who had multiple episodes of pain, school absenteeism, and frequent hospitalizations was discussed. This patient attended sessions in which she learned the

self-regulation therapies, relaxation and imagery, for continued home practice. This patient was seen frequently at one time a month for six months, then only three times the following year. After only the second session her finger temperature increased from her baseline of 78.7 to 93 degrees indicating a decrease in distress. During her first year she was able to regularly attend school due her decrease in pain. The patient had a relapse one year later in which she began to experience frequent pain requiring absence from school and more pain medications. She began to attend sessions again and practiced her self-regulation therapies at home. In just two follow up sessions she had increased her finger temperature to 91 from 86 and decreased her skin conductance level by 10 units. In a one week follow-up, she had no pain symptoms and was attending school. This case report demonstrated the effectiveness in the programs approach to the use of individualized relaxation and imagery to assist in pain alleviation. Furthermore the management of pain symptoms allows the child to attend school and resume normal daily activities.

The effectiveness of cognitive behavioral group therapy was examined by Thomas, Dixon, & Milligan (1999). The study included 97 adolescent and adult participants with sickle cell disease whose ages were between 15-35 years old. The participants were randomly assigned into the cognitive-behaviour therapy group, attention placebo group, or the control group. The cognitive-behaviour therapy group attended a one hour weekly group session over a two month period. They were also given homework to practice the skills learned from there sessions including; progressive muscle relaxation, distraction, and identifying and challenging negative pain-related thoughts. The attention placebo group attended a one hour weekly patient led open discussion about sickle cell disease over a 2 month time period. The control group received standard medical care. All participants completed questionnaires pertaining to pain control,

severity of pain, there perception of how they function in daily life, coping strategies, and anxiety and depression. The results indicated that the participants in the cognitive-behaviour therapy group perceived their pain to be less distressing, had increased positive coping strategies, and had increased confidence in their ability to control and live with their sickle cell pain compared to the two other groups.

The use of non-pharmacological therapies at home

Parents and caregivers of children and adolescents with sickle cell disease are most often the people that manage their pain symptoms at home. They are familiar with their child's response to pharmacological and non-pharmacological interventions and can recognize the need for further care. Parents and caregivers are also the people administering, supplying, and supporting interventions for pain management. Sibinga et al. (2006) assessed parental use of complimentary and alternative medicine (CAM) for their children with sickle cell disease. Fifty-seven parents participated in this study whose children were an average age of 8.2 years old. Qualitative and quantitative data was obtained from phone surveys. The surveys discussed parental demographics, severity of sickle cell disease, 19 specific CAM utilized, and their perception of healthcare provider interest and communication with CAM. Fifty-four percent of reported the use of CAM for their child. The most commonly utilized therapies included prayer, relaxation, spiritual healing, and exercise. The use of CAM was found to be provided more often to children who were older and had more severe sickle cell disease. Sixty percent of parents stated they were willing to try different types of CAM for their child.

In another study assessing pain management by caregivers, Yoon & Black (2006), investigated therapies utilized, prevalence, and future interest of CAM by caregivers. Sixty-three caregivers were surveyed whose children with sickle cell disease had a mean age of nine years

old. The questionnaire completed, solicited pharmacological and CAM therapies utilized by their children as well as interest in future CAM use. The questionnaire provided of list of 16 CAM in which the most commonly used by caregivers were prayer, spiritual healing, massage, and relaxation. The use of CAM was found to be significantly higher in children who were taking two or more analgesics for their pain and children greater than 13 years old. It was reported that 70% of caregivers had provided at least one CAM in the past six months. Among these caregivers an average of 3.67 CAM were used for the management of their child's sickle cell pain. In reviewing the caregivers response to future use of CAM for their child's sickle cell pain 62 of 63 participants stated they would utilize a type of CAM. Caregivers were most interested in future use of prayer, massage, relaxation, spiritual healing, and music. This study supported caregiver willingness to try different and alternative pain management techniques for their child with a chronic condition. It also correlated the use of alternative treatments provided by caregivers when analgesics are not sufficient in relieving pain caused by sickle cell disease. This study had similar findings to Sibinga et al. (2006) in which parents provided alternative therapies to help children with more severe disease and who are older in age.

Oshikoya et al. (2008) studied the use of CAM in children with chronic health conditions including epilepsy, sickle cell disease, and asthma. Qualitative data was obtained by questionnaires completed during an interview process of 318 parents of children with a chronic health condition. The study assessed past and present treatments, types of CAMs utilized, parental resources, and perceived cost, benefits, and adverse effects of CAM. Of the 318 participants 99 parents utilized CAM as part of their child's disease treatment. Among those who have used a type of CAM, 36% had sickle cell disease, 38% had epilepsy, and 25% had asthma. The most frequently used CAM in participants with sickle cell disease was biological products

including ginger, herbs, and jobelyn products. Prayer/spiritual healing was also used by many. These results for the utilization of CAM in children with sickle cell disease are comparable to those participants with asthma and epilepsy.

Post-White et al. (2009) conducted a survey among 281 parental participants to determine the frequency, reason, and factors that influenced the use of CAM in their child's care. The survey consisted of 31 questions which included a list of 26 different CAM. Of the participants, 19 were parents of children with sickle cell disease. Other diagnoses included in this study were epilepsy, pulmonary, oncology, and general pediatrics. It was found that 47.4% of the sickle cell participants used at least one type of CAM for their child. The most commonly used CAM within this population included prayer, massage, and music. Parents indicated they utilized CAM for their child because they found it helpful and they themselves have use the technique. It was also found that 33% of parents of children with sickle cell disease did not tell their healthcare providers about the use of CAM for reasons including; they were never asked about it, they were unsure it helped, and their provider was not knowledgeable about CAM. Similarly, none of the parental participants discussed the use of CAM in Oshikoya et al. (2008) due to not being asked and apprehension of lack of healthcare provider treatment. The evidence supports positive parental views on the use of CAM for sickle cell pain management and coping. CAM should be part of the patients history and management regimen, therefore should be openly discussed with healthcare providers.

The previous literature found that parents are willing to utilize CAM to assist in pain management and coping for their children with sickle cell disease. Beyer & Simmons (2004) assessed individual multiple factors and interventions used by parents related to vaso-occlusive pain in children including how to avoid them, keeping a normal routine, catching the pain,

getting the pain off their mind, and helping their child get through a pain episode. Interviews were conducted with 21 caregivers whose hospitalized children were between 5-19 years of age. The questionnaire included eight open-ended questions and enabled parents to list their own non-pharmacological interventions used. To avoid painful episodes, the majority of parents provided good nutrition and fluid intake, allowed rest, and followed-up routinely with physicians. In order for parents to make their child feel normal they allowed them to participate in household chores and school. Parents tried to decrease pain before it became intense by administering medications, heat, and touch. The most widely used non-pharmacological interventions used were massage, heat therapy, fluids, and prayer. To divert children from their pain symptoms, parents choose distraction techniques such as rocking, diversion, drawing, videogames, movies, and television. With the wide variety of non-pharmacological interventions utilized during different stages of painful episodes, parents found the interventions to be effective 40-80% of the time. At different stages of a pain crisis, parents utilized a variety of non-pharmacological interventions that were individualized to each situation. This study supports the need for individualized non-pharmacological techniques depending on the patient's symptoms, past experience, and availability of resources.

The use of diaries by children and adolescents with sickle cell disease has been found to be an effective tool in analyzing their painful experiences (Gil et al., 2001). Dampier et al. (2002) utilized daily diary reports from 39 participants to assess their characteristics of sickle cell related pain and non sickle cell related pain episodes. In addition, children and adolescents recorded their pain management strategies and limitation of activities. The participants whose ages ranged between 5-19 years old were instructed to write twice a day in their structured pain diary. Over a three year time frame 28-417 diaries were collected per participant. The

information provided from the diaries showed children and adolescents had 8.4% of days with sickle cell pain and 2.7% of days with non-sickle cell related pain. The participants choose to take an analgesic 85% of days they experienced sickle cell pain. The children and adolescents also choose non-pharmacological techniques to manage there pain either in conjunction with an analgesic or alone. The most common non-pharmacological techniques reportedly used were watching TV or reading, talking to someone, sleeping, and heat therapy. The diaries collected over a 3-year period demonstrated the child or adolescents' personal pain experience. This type of research data allows further investigation into the patterns of qualitative and quantitative data obtained.

A variety of non-pharmacological interventions have been shown to be effective in reducing pain as well as positively influencing related measurable variables in children and adolescents with sickle cell disease pain. As discussed earlier, hypnosis, guided imagery, music therapy, massage, videogames, cognitive behavioral therapy and virtual reality have been utilized in the research. Many researchers have collected data related to children and adolescents with sickle cell pain from caregivers and detailed documented diaries on pain experience. Caregivers and children attempt to initiate non-pharmacological interventions during low levels of pain and utilize them more frequently during severe pain episodes (Beyer & Simmons, 2004; Sibinga et al., 2006; Yoon & Black, 2006). The research demonstrates the effectiveness and preference of the variety of non-pharmacological modalities available for the treatment of sickle cell disease pain alone, and in conjunction with medications.

Videogames and Virtual Reality

Virtual reality is a technologically advanced system in which the user is placed in a simulated virtual world (Li, Montano, Chen, & Gold, 2011). The user may have the ability to

control or move within the virtual world using specialized tools. For instance, videogames are a form of virtual reality that a user may control when connected to the appropriate tools or controllers. When using videogames and virtual reality, users are engaged by the utilization of a combination of tools, including goggles (Maani et al. 2008), a head-mounted display (Dahlquist et al. 2009), headphones (Mahrer & Gold, 2009) and joysticks or controllers (Parry et al. 2012). Combining two or more of these technological tools will provide a multi-sensory engagement providing the user with a strong illusive feeling and distraction from reality. Utilizing a multi-sensory intervention involves higher engagement of conscious attention and cognitive resources, leaving fewer cognitive resources for painful stimuli resulting in lower pain sensations (Chan, Chung, Wong, Lien & Yang, 2006; Hoffman, Patterson, Carrougher & Sharar, 2001). The use of technological tools has become a widely accepted form of managing pain in people and has shown significantly positive results in different settings, such as burn care (Schmitt et al. 2011), cancer pain (Schneider & Workman, 2000), and painful medical procedures (Gold et al. 2005).

Adolescence is a transitional stage between childhood and adulthood involving an array of biological, psychological, and social changes (Buitelaar, 2012). According to earlier cognitive developmental theories, adolescents develop a more complex understanding of pain (Hurley & Whelan, 1988). As they expand their cognitive abilities, adolescents will reason and think more abstractly, which gives them the ability to communicate their pain and feelings in more abstract terms (Gaffney & Dunne, 1986). Neurophysiological studies showed that different regions of the adolescent brain are activated in response to different painful and emotional stimuli and in a greater frequency than in adults (Monk et al., 2003). Moreover, tasks of different purposes that require a significant amount of attention in adolescents, in the context of painful and emotional stimuli, do not result in adult-like activation of specific brain regions (Monk et al., 2003). Based

on this data, it can be inferred that different age groups require developmentally appropriate interventions to cope with and manage pain. Adolescents tend to be more technology friendly than adults are, therefore, playing interactive sophisticated graphics videogames may be an effective technique for distracting and diverting their thoughts from the unpleasant feelings of pain.

The subjective experience of playing videogames or using virtual reality systems can be described by concepts of engagement such as immersion, presence, and flow. Immersion represents the depth of engagement in a virtual environment while retaining awareness of one's surroundings (Banos et al., 2004). Additionally, immersion has been defined in terms of engagement, which leads to the feeling of being attached to the virtual environment (Wirth et al. 2007). Presence constitutes the experience of being part of, and integrated in a mediated virtual world while maintaining a state of consciousness (Ryan, Rigby & Przybylski, 2006). The difference between presence and immersion stems from the level of engagement where the latter involves a higher level of engagement and control. Presence can be achieved by simply placing the user in a virtual world, whereas to be immersed the user needs to achieve a level of engagement and control over the environment in which they are placed (Tamborini & Skalski, 2006). Flow, another important concept of engagement has been described as one's feeling of being rewarded and motivated to achieve a specific goal while being continuously engaged and in control of a virtual world (Chen, 2007). Jennette and colleagues (2008) explained that being immersed is a result of an enjoyable gaming experience where almost all attention is focused on playing the videogame but not to the point that the user experiences motivation to continue playing the game or flow. Therefore, immersion is thought to be a precursor to flow where presence is a continuous process along all levels of engagement. In the literature, a variety of

media has been used to incite engagement ranging from conventional media such as books to new media such as videogames (Brockmyer et al. 2009).

Current Trends in Virtual Reality and Videogames for Pain Management. Virtual reality is a technology used to immerse the user into a computer-simulated virtual world through multimodal stimuli (Li et al., 2011). The images used in gaming systems can either be of real or imaginary environments. Users are engaged in a fully-immersive multimodal simulation through the use of a head mounted display with head tracking, headphones, joysticks to control the virtual world or a combination of these technologies. Virtual immersion can be passive such as simply watching a movie (Sullivan, Schneider, Musselman, Dummett, & Gardiner, 2000), or it can be interactive such as using a videogame (Dahlquist et al., 2009).

In health, virtual reality and videogames have been used in a wide variety of applications such as pain management, physical rehabilitation (Bryanton et al., 2006) and treatment of psychiatric disorders (Rizzo, Difede, & Rothbaum, 2009). Data from recent evidence shows that virtual reality can effectively be used for the reduction of acute pain in children and adolescents in different settings (Hoffman et al., 2011; Malloy & Milling, 2010; Morris, Louw, & Grimmer-Somers, 2009), such as hospital, clinics or home settings. The effectiveness of virtual reality in pain management can be related to employing immersive multimodal stimuli including tactile, visual and auditory stimuli for distraction.

The use and effectiveness of virtual reality for pain management in children and adolescents during burn care has been investigated. For instance, Schmitt and colleagues (2011) investigated the effectiveness of using the virtual reality software SnowWorld to alleviate pain in children and adolescents with burns during physical therapy. The system was coupled with the use of a head-mounted display. Participants in this study explored the virtual reality

environment and had the chance to interact by "throwing" virtual snow balls at penguins, mammoths and snowmen using a controller. Using a crossover study design, fifty-four burn participants spent equivalent time in both virtual reality and control conditions while receiving constant pharmacologic analgesia and range of motion exercises. Each physical therapy session lasted six to twenty minutes of which three to ten minutes included virtual reality. Participants were asked to rate their pain at the end of each condition. Results from this study showed that pain ratings from the use of virtual reality in conjunction with pharmacologic therapy condition were significantly lower than pharmacologic therapy alone. These results are also consistent with findings from other randomized-controlled trials that use virtual reality to alleviate pain in children and adolescents with burns (Das, Grimmer, Sparnon, McRae, & Thomas, 2005; Hoffman et al., 2000; Hoffman et al., 2001; Hoffman et al., 2011; Mott et al., 2008).

The efficacy of using virtual reality has also been examined during routine medical procedures. A study done by Gold et al. (2005), investigated the effectiveness of using virtual reality during a routine outpatient blood draw. One hundred children 8-12 years of age were randomly assigned to one of four conditions; no distraction, cartoon distraction, virtual reality via computer, or virtual reality via head-mounted helmet. Visual occlusion was controlled to prevent children from seeing the blood draw. Evidence from this study indicated that children assigned to the virtual reality helmet group experienced less frequent moderate to severe pain intensity compared to the other groups. In a similar study by Gold, Kim, Kant, Joseph, and Rizzo (2006), the authors also examined the effectiveness of virtual reality on pain related to IV placement prior to CT/MRI procedures in twenty children who were between 8-12 years old. Participants were randomly assigned to receive virtual reality via helmet with topical anesthesia or topical anesthesia alone. Results from this study were not consistent with the previous study

by Gold et al. (2005). There was no difference in pain intensity among groups. However, participants, parents and nurses performing the procedure expressed higher satisfaction about using the virtual reality intervention as a distraction during the IV placement.

Although the reviewed literature shows promising results that virtual reality can effectively be used to help control pain in medical and experimental procedures, some limitations and weaknesses need to be addressed. For example, the sample size in the majority of the reviewed studies was relatively small. Additionally, outcome measures, technologies, and virtual environments varied among the reviewed studies. These factors can reduce the generalizability of results unless similar methodology is used. Additional considerations include the use of standardized pain self-report measures. In order for data to better evaluate health outcomes, such as pain, subjective pain self-report measures should be combined with behavioral and observational measures. Due to the fact that children and adolescents in some studies were visually occluded by devices such as helmets, their ability to watch the painful stimulus, such as a needle poke, was limited. Some researchers have hypothesized that when children are not able to view a particular medical procedure such as a needle poke, their anxiety level can increase due to the fear of the unknown (Greshon, Zimand, Lemos, Rothbaum, & Hodges, 2003). Finally, the implementation of virtual reality to control pain in children and adolescents can be costly depending on the complexity of the system as wel as the accessories used compared to other non-pharmacological modalities. Thus, more research is needed to address these limitations and provide a more generalizable and valid data.

Videogames for pain. Recently, researchers examined the effectiveness of virtual reality on experimentally induced pain in healthy participants. The rationale for conducting this type of study is to monitor the direct effect on pain tolerance and perception with the exclusion of other

confounding variables such as disease pathology and the use of analgesics (Dahlquist et al., 2007; Dahlquist et al., 2009; Dahlquist et al., 2010; Weiss, Dahlquist, & Wohlheiter, 2011). Hence, in 2007, Dahlquist and colleagues assessed the effectiveness of virtual reality on pain threshold and pain tolerance in children and adolescents, ages 5-13 years old, experiencing cold pressor pain. The 40 participants were randomly assigned to one of three goups; interactive virtual reality, passive virtual reality, or the control group. The interactive group played a videogame while wearing a head-mounted display helmet whereas the passive group watched footage from a pre-taped replay of the same videogame while wearing the display helmet. Compared to the control group, children in both the interactive and passive groups had significantly higher pain threshold and tolerance. In addition, the interactive group had significantly lower pain scores when compared to the passive group. In 2009, Dahlquist et al. further investigated the significance of the use of the head-mounted virtual reality display helmet with interactive gaming among 49 children ages 6-14 years undergoing the same cold pressor conditions. The results were similar to those of Dahlquist et al. (2007); however, it was found that the use of the head-mounted virtual reality display helmet was more effective in older children between the ages of 11-14 years when compared to the younger age group.

In 2010, Dahlquist et al. studied the effectiveness of videogaming virtual reality using the head mounted display helmet within a younger age group. 50 children ages 6-10 years underwent the same cold pressor conditions from previously discussed studies utilizing the head-mounted virtual reality display helmet. Participants in this study were randomized to two groups playing an interactive videogame with or without the display helmet. The results on the effectiveness of pain threshold and tolerance were similar to those of Dahlquist et al. 2007 & 2009. However, there was no difference between playing the videogame with or without the

display helmet. Using the same research design as Dahlquist et al. (2007), Weiss et al. (2011) assessed the use of interactive versus passive virtual reality distraction in 61 participants who were between 3-5 years of age. Children in the interactive group played a videogame displayed on a television screen, while the passive group only watched the videogame on the screen during cold pressor stimuli. Results were similar to previous studies in the reduction of pain threshold and tolerance; however, no difference was noted between the interactive and passive videogame groups in pain scores.

Raudenbush, Koon, Cesssna, and McCombs (1999) conducted two coinciding studies that assessed videogame effectiveness on reducing pain caused by cold pressors. Thirty participants with a mean age of 18.5 years were randomly assigned into one of three groups; action-oriented game, non-action-oriented game, and no game. The action-oriented group played Death Crimson OX, a videogame that involves dark cities and shooting villains. The non-action-oriented group played Mahjong which is a strategic computer gaming involving matching and removing tiles. The painful stimulus was induced by submerging the participants' non-dominant hand into a reservoir tank of 3 degree Celsius water. The results revealed that the action-oriented videogame group had significantly lower pain scores and was able to tolerate the cold pressor for a longer period of time. These results prompted further research into assessing the use of different types of videogames and their effectiveness in reducing pain.

In a different study, Raudenbush et al. (1999) also assessed the difference in pain scores and duration in participants undergoing the same cold pressor experimental design between six different types of videogame genres and a control group without videogames. The videogames compared in this study included action, fighting, boxing, puzzles, sports, and arcade. Results showed a significant increase in time in which participants tolerated the painful stimuli in the

fighting, sports, and boxing groups, compared to the control. Moreover, the boxing group had the lowest pain scores compared to all other groups. A NASA task load index which measures mental demand, physical demand, temporal demand, effort, frustration, and performance on the use of the variety of videogames was conducted. Boxing was found to be the most frustrating and physically demanding videogame whereas all action videogames were mentally demanding. Furthermore, all videogames required more effort compared to the control group. Consequently, action videogames including fighting, sports, and boxing appeared to have the greatest effect on participants' pain response. This may be related to the increased immersion and distraction created while playing the videogames due to the high levels of control, engagement and attention needed.

In 2011, Law et al. conducted a study to assess cognitive processing and compare the effectiveness of passive versus interactive distraction in children undergoing cold pressor tasks. There were 79 participants in this study, with ages ranging from 6 to 15 years. Each participant underwent a cold pressor task with passive distraction, interactive distraction, and without distraction. During the passive distraction trial the child wore a virtual reality head mounted display helmet while watching recorded footage of a videogame. During the interactive trial, the children wore the same helmet except they were able to manipulate and interact with the videogame by using their voice. Results from this study demonstrated children had significantly higher pain tolerance during interactive distraction compared to the other study groups. Moreover, older children had a greater change in pain tolerance when compared to younger children in the interactive distraction trial. Additionally, the authors concluded the amount of attention and engagement induced by manipulating the videogame during the interactive trials required higher cognitive processing resulting in greater distraction from the painful stimuli.

In 2013, Wohlheiter & Dahlquist conducted a study to compare the effectiveness of using interactive and passive distraction on young children undergoing cold pressor trials. The authors also took into consideration and compared the results by patient age. There were 65 participants, with ages ranging from 3 to 6 years old. Each participant underwent a cold pressor task while playing a videogame, watching a videogame, and without distraction. Results from this study demonstrated that during an interactive distraction or while playing a videogame, children had an increase in pain tolerance compare to the other study groups. Furthermore, in comparison of younger children (3-4 years old) to older children (5-6 years old), older children had an overall improved pain tolerance during cold pressor tasks in both distraction groups.

In 2013, Nilsson, Enskar, Hallqvist, & Kokinsky conducted a study to compare the effectiveness of different distraction techniques on pain, distress, and anxiety in children undergoing wound care. There were 60 participants in this study undergoing different types of wound care, with ages ranging from 5 to 12 years. The study involved a random assignment into three groups: serious gaming, the use of lollipops, and a control group. The serious gaming group played an interactive videogame using a laptop and Wiimote while undergoing wound care. The lollipop group licked a lollipop for 3-5 minutes prior to and throughout wound care. Results from this study showed that serious gaming significantly decreased observed pain behavior and self-reported distress compared to the lollipop and control groups. Self-reported pain was not found to be significantly different between the study groups. This may be related to the children's cognitive ability in self-reporting pain and the relatively small sample size.

The use of videogames as a non-pharmacological modality to treat pain within this population lacks research. It has been shown to be effective in children and adolescents with pain caused by other disease processes and during laboratory-induced painful procedures

(Dahlquist et al., 2007; Nilsson, Finnstrom, Kokinsky, & Enskar, 2009; Windich-Biermeier et al., 2007). Videogames require different levels of imagination, immersion, presence and other related variables to be successful in reducing pain (Witmer & Singer, 1998). Videogames incorporate a multi-sensory mechanism that helps individuals focus their attention away from painful stimuli. Children and adolescents possess the qualities necessary for making videogames age and developmentally appropriate interventions for relieving pain. Therefore, further research should be conducted to demonstrate the effectiveness of videogames in reducing pain related to sickle cell disease in children and adolescents.

Measurement of Engagement

Recently, researchers have been interested in quantifying the amount of immersion and engagement experienced while playing a videogame. There is also interest in quantifying the amount of immersion and engagement placed in a virtual reality environment. For example, Mayes and Cotton's (2001) research attempted to examine the quality of a videogame through measuring the construct of engagement. To do this, the authors introduced the engagement questionnaire (EQ) to investigate five aspects that are believed to directly influence the level of engagement. The five aspects thought to directly influence the level of engagement are interest, authenticity, curiosity, involvement and fidelity. Mayes and Cotton (2001) believed that the level of engagement directly influences enjoyment. The questionnaire developed by Mayes and Cotton (2001) was further expanded by Brockmyer and colleagues in 2009.

The game engagement questionnaire was proposed by Brockmyer and colleagues in 2009, focused on measuring the subjective experience of engagement in violent videogames, which is a sum of immersion, presence and flow. The term 'engagement' was used as a generic indicator of involvement in a videogame. The participants in the study were 107 college students

ranging from 18-26 years old, all males. In this study, lower scores on the questionnaire indicated less engagement while higher scores indicated deeper levels of engagement. Age was controlled to explore whether a player's previous experience in terms of years playing videogames would influence whether his level of engagement increased or decreased. Controlling for age was accomplished using the dissociative experiences scale (DES) which will be discussed later in this paper. The participants completed the 19-item Game Engagement Questionnaire after playing a videogame for 30 minutes. The Game Engagement Questionnaire items completed by the participants included questions pertaining to the engagement experience level. Reponses ranged from "I really get into the game" as the lowest response on the scale to "I feel scared" for the highest response on the scale, indicating a highest level of engagement or psychological absorption, considering the fact that the violent videogame was utilized. After reliability testing was done, Cronbach's alpha for the 19-item version of the Game Engagement Questionnaire was 0.85. The Rasch estimate of person reliability (the Rasch analog to Cronbach's alpha) for the 19-item version was .83 and the item reliability was .96. At the conclusion of the study, data analysis showed that the Game Engagement Questionnaire is a reliable measure to assess the depth of engagement while playing a videogame. A weakness in this study that should be noted is all participants were males which may bias the results. Differences in responses based on gender need to be considered in future evaluations. Additionally, the questionnaire needs to be evaluated with different age groups and types of games other than violent videogames.

Despite the importance of the concepts of presence and immersion, only a few tools have been developed in an attempt to measure them. In a survey done by Barfield and Weghorst (1993), the factors and conditions that influence presence were examined by surveying

participants after they experienced two different virtual environments. Participants answered specific questions about "being there", "inclusion" in the virtual environment, and "presence". Responses to the questions correlated positively with factors such as presentation quality, comfort, ease of interaction and enjoyment. Witmer and Singer (1998) proposed two questionnaires to study the concepts of presence and immersion; the presence questionnaire (PQ) and the immersive tendencies questionnaire (ITQ). The presence questionnaire is a 19-item tool developed to measure the degree of presence that individuals experience while using a virtual environment as well as assessing the factors that influence the degree of presence. In their study, Witmer and Singer (1998) categorized the factors that affect the degree of presence into control, sensory, distraction and realism factors. The 18-item immersive tendencies questionnaire was developed to measure the tendency and level of immersion and involvement in a virtual environment. In addition to items specific to virtual environments, some items in the ITQ questionnaire were designated to measure the level of immersion achieved by playing videogames. Internal consistency measures of reliability (Cronbach's Alpha) for ITQ and PQ yielded reliabilities of 0.81 and 0.88 for the ITQ and PQ, respectively. Additionally, content and construct validity were discussed for both questionnaires.

Elements of engagement have also been assessed using other measures in the literature. For example, scores from a 28-item DES (Bernstein & Putnam, 1986) were used in the literature to assess how often certain psychological absorption experiences occur. Responses on the DES are made on a 0-100% scale with 10% intervals about common non-pathological dissociation experiences. Additionally, more tools have been found to measure dissociative experiences and depth of engagement in different age groups. For example, Putnam, Helmers, & Trickett's (1993) child dissociative observer-based checklist (CDC) for children ages 5-12 included 20

items rated on the scale from 0 (not true) to 20 (very true). A score of 12 or higher on the CDC is an indication of a pathological dissociation. Moreover, the adolescents dissociative experiences scale (A-DES) is a 30-item self-report scale for adolescents 11-18 years old. On the A-DES, a score of 4 or more indicates pathological dissociation (Armstrong, Putnam, Carlson, Libero, & Smith, 1997).

The level of the participants' state of presence can be measured by the presence self-assessment manikin scale (SAM). This self-assessment tool allows participants to rate their sense of presence or how much they felt involved in the videogame. The 9 point pictorial SAM was developed by Schneider, Lang, Shin, and Bradley (2004) to assess gamer's presence during first person shooter videogames with and without a storyline. This scale includes five pictures of a manikin with a television at different distances away from the manikin. The participant marks a picture or between pictures to represent how much they felt in the videogame. In the initial study by Schneider et al. (2004) both the verbal and SAM scales were utilized to assess presence in which it was found that participants reported high level of presence during the games with storylines. The results reported by the verbal and SAM scales were compared and found to be moderately correlated. The presence SAM was further utilized in 2013 by Seranno, Botella, Banos, and Alcaniz to assess the level of presence while manipulating a housing virtual reality environment in customers. Results reported from the presence SAM indicated a higher level of presence during the virtual reality environment.

CHAPTER 3

Methods

Chapter three breaks down and describes methodological sections of the proposal. Key concepts explained include design, setting, sample, data collection procedures, instruments, and data analysis plan for this study.

The purpose of this study is to evaluate the effectiveness of using videogames on a sample of adolescents 12-21 years of age with sickle cell disease related pain. Additionally, the level of engagement induced when playing the videogame and relationship to pain will be measured. A descriptive profile will be provided on the use of non-pharmacological interventions to control pain in the selected population.

Design

A one-group repeated measure quasi-experimental design will be used to evaluate the effectiveness of using videogames on pain in a sample of adolescents 12-21 years of age. Using a repeated measures design permits intensive scrutiny of within-patient variability. Quasi-experimental study designs have been developed to provide alternative means of examining causality in situations not conducive to experimental controls. The aim is to control as many threats to validity as possible in a situation in which two of the three components of true experimental design (randomization, comparison groups, and manipulation of the treatment) is lacking.

Setting

Recruitment of participants was undertaken at University of Illinois Children's Hospital and Advocate Children's Hospital. The sampling methodology was a convenience sample of adolescents who meet the inclusion criteria. Potential research participants were identified by

each floor's charge nurse who identified adolescents with sickle cell disease who are experiencing acute episodes based on the inclusion criteria.

Sample

A sample of 30 hospitalized adolescents (12-21 years of age) diagnosed with sickle cell disease and experiencing pain were asked to participate in this study. This sample size was based on a 80% power, a critical effect size of 0.25, a correlation coefficient of at least 0.5 between repeated measures at 4 time periods, and significance level of 0.05 in addressing Research Hypotheses 1 and 2. For addressing hypothesis1 and 2, the sample size of 30 adolescents was deemed sufficient to provide a critical effect size of 0.45 and 80% power at a significance level of 0.05. G*Power computer software (Version 3) was used to calculate the required sample size (Faul, Erdfelder, Lang, & Buchner, 2007).

Inclusion Criteria. The sampling criteria was a convenience sample of hospitalized adolescents experiencing pain related to sickle cell disease with a pain score of 4 and above on a 0-10 Likert scale, at University of Illinois Children's Hospital and Advocate Children's Hospital. Adolescents was included in the study if they report having an acute painful episode, and reporting a pain rating of 4 or more on the Likert pain scale from 0 to 10. Participants were 12-21 years of age, male or female, with normal age appropriate development. The rationale for selecting this age range is that adolescents at this point should have sufficient cognitive and neuro-musculoskeletal development, which makes it easier to learn the skills necessary to play and interact with the videogame (Burns, Dunn, Brady, Starr, & Blosser, 2009). At this stage, adolescents should have a longer attention span, where they become more thorough and better adapted to the demands of tasks (Burns et al., 2009). They start to establish strategies where they can become more effective when it comes to using their knowledge and capable of learning a

process in a more efficient and timely manner. All the factors just mentioned, when they develop normally, help adolescents to become highly efficient when doing tasks such as playing a videogame or trying to complete a mission in the videogame level in which they are playing (Hoffman et al., 2000). According to Piaget, adolescents enter the cognitive developmental stage of formal operational. Adolescents in this stage develop the ability to think abstractly, problem solve, and have creative minds (Berk, 2001). These cognitive qualities are important to possess when playing videogames because they allow the player to understand the game concepts, anticipate actions, and become more engaged in the environment. Participants must be able to read and communicate in the English language fluently.

Exclusion Criteria. The exclusion criteria include:

1. Adolescents with vision disability.
2. Adolescents who are paralyzed or have disorders that can limit their movement and interaction with the videogame such as cerebral palsy.
3. Adolescents with cognitive impairment.
4. Adolescents who are unable to participate because of the severity of their illness.
5. Inadequate finger dexterity.

Intervention

The game used was developed by Multimedia Molecule and published by Sony entertainment and released in 2011. Approval to use this videogame in the study was obtained from Sony Computer Entertainment®. The Entertainment Software Rating Board (ESRB) rating of the game is (E) which means for everyone 6 years of age and older. LittleBigPlanet 2 (www.littlebigplanet.com) is a Playstation 3™ game in which players control characters referred to as Sackboy for males and Sackgirl for females. The characters in the game can be customized

and modeled in different colors and clothing according to the player's preference or liking. The game is fully 3-dimensional in 2-dimensional environments which include a variety of themes and backgrounds such as a city, garden, or a playground. To control their Sackboy/Sackgirl characters, the playstation analogue stick can be used to move the characters, while buttons are used to jump with varying degrees of height depending on the pressure applied to the button. Additionally, analogue sticks and buttons in the controller are used to interact with objects in the game environment and objects by either moving or swinging on them.

The game includes the story mode which includes an already developed storyline and the "my moon" mode which is can be customized for the purpose of the study. The investigator of this study used the "my moon" mode to design a game level dedicated for this study. The videogame includes obstacles and adventures in addition to activities such as running and jumping and manipulating objects by hanging onto them or by dragging or pushing them. While playing the game, and in order to successfully pass through some obstacles or gates, participants were asked to complete puzzles and incomplete words in the game related to their health such as, "RELAX", and "NO PAIN", "DEEP BREATH", "CALM" by selecting the letters from a collection of stickers within the game. Although the puzzles used are simple and easy to solve, the degree of attention needed to find and complete the answers was proposed to further distract the player from the sensation of pain.

Procedure

Once approval was obtained from Investigational Review Board (IRB) at Wayne State University, University of Illinois and Advocate Children's Hospital, data collection took place at University of Illinois Children's Hospital and Advocate Children's Hospital. Also, approval was obtained from each unit manager. The charge nurse and assigned registered nurse was

approached by the principal investigator (PI) or research assistant to determine which patients are appropriate and get approval for study enrollment. Study purpose and procedure were explained to the charge nurse and assigned registered nurse at the time of data collection. A summary sheet was provided to the staff which states the purpose and procedure of the study (***see Appendix F***). The teen and parent/guardian were approached by the assigned registered nurse and were offered an opportunity to participate in the study before they are approached by the study personnel. If they were interested in the study, the teen and parent/guardian were approached by the PI or research assistant and given a copy of the information sheet (***see Appendix C***). Research personnel were available if participants or parents have any questions or concerns. Consents and assents were used with participants from University of Illinois Children's Hospital while approach consents used for all participants from Advocate Children's Hospital. Those adolescents interested were invited to participate in the study. The survey instruments and data collection sheets were coded and colored for data collection purposes. No patient identifiers were used; documents contained a study code ID number that corresponded with participants in the study. The PI did look at the patients' medical records but was able to obtain information regarding patient's reason for hospitalization and chief complaints from the charge nurse or assigned registered nurse.

The adolescents, parents/guardians and nurses were informed about the purpose of the study. If they agree to participate in the study, participants were given a brief demographic questionnaire (***see Appendix B***). Additionally, a tutorial was provided by the PI or research assistant to help participants with the basic commands to play the game. Any questions that the teen, parent and nurse have were answered by the PI or research assistant. Participants were prompted to rate their pain using the integrated faces scale in the game and the Wong-Baker

FACES scale before playing the videogame, at 15 minutes, 30 minutes and after they are done playing the videogame. Participants played the game until they finish the pre-built level that was designed for the proposed study, it took approximately 45 minutes to finish. The PI or research assistant left the room as the study participant starts playing the game and entered the room at 15 minutes, 30 minutes and at the end of the videogame to answer any questions or concerns.

At the conclusion of the game, participants were asked to fill out an engagement questionnaire to assess the level of engagement induced while playing the game. Study procedures were concluded by completing the 19-item immersion/engagement questionnaire and the presence self-assessment manikin scale. The immersion/engagement questionnaire and the presence self-assessment scales were adapted from the original publications and some of the words were changed to be more understandable to the study population. A Target gift card (for the amount of $10) was given to each participant as compensation for their time upon completion of the study.

Instruments

A variety of pain scales have been developed to assist adolescents in pain self-report their pain and communicate it with families and health care providers. However, none of these pain assessment tools have been identified as the most effective in all circumstances (Cohen, 2008). Examples of these scales include the numeric pain scale, Wong-Baker Faces Scale, and the FLACC pain scale. These scales are also used by clinician to assess pain in children and adolescents.

The Wong-Baker (1988) FACES pain rating scale (WBS), used in children to rate pain severity, has been validated in different settings with a test-retest reliability score of 0.74 (Wong, Hackenberry-Eaton, Wilson, Winkelstein & Schwartz, 2001). When using the faces scales,

adolescents are not required to translate their pain experience into a numerical value; but rather, adolescents have to rate their pain level based on levels depicted in pictures of faces with different expressions. For the purpose of this study, a built-in faces scale from the game was used to rate pain. The built-in faces scale was available for the study participant to choose from while playing the game. Seven faces were used in the study and were scored accordingly from 0-6 where 0 indicates no pain and 6 indicates worst pain possible (***see Appendix D***). The built-in faces scale was used in a previous unpublished pilot study and was proven to be effective as a pain measurement tool. Additionally, participants from the same pilot study said "yes" to the built-in faces scale than the Wong-Baker FACES scale in a questionnaire conducted during the study.

The level of engagement was measured using the Game Engagement Questionnaire adopted from Brockmyer et al (2009). The participants completed the 19-item Game Engagement Questionnaire after playing the videogame for up to 45 minutes. The Game Engagement Questionnaire items included questions pertaining to the engagement experience level. Reponses ranged from "I really get into the game" as the lowest response on the scale to "I feel happy" for the highest response on the scale, indicating a highest level of engagement. Participants answered each item with 0 indicating no engagement (marked as No), 1 indicating that they were not sure but think positively of the videogame (marked as Maybe) or 2 indicating that they were engaged (marked as Yes) (S***ee Appendix G***). If level of engagement is to be calculated by an instrument, the total score cannot range from 0 to 5.

In addition to the Game Engagement Questionnaire, the presence self-assessment manikin adopted from Schneider, Lang, Shin, and Bradley (2004) was used to measure participants' presence after playing the videogame (***see Appendix H***).

Infection control

To prevent spread of infection from participant to another with study equipment, a hospital-approved disinfectant was used before and after every participant to cleanse equipment such as the monitor, controllers, and gaming console.

Data Management and Analysis Plan

The latest versions of SPSS computer programs was used for data management and analysis. All data files were password protected and stored as "read only" files. The first phase of the analysis consisted of using descriptive statistics on demographic variables in computing the summary measures (mean, median, quartiles, standard deviation, and range) for the variables measured on interval or ratio scales and frequency distributions (absolute frequency and percent) for the variables measured on nominal or ordinal scales. Significance level was set at a p-value equal to or less than 0.05. Item analysis was done to address Research Question 1. For addressing Hypothesis 1, multivariate repeated-measures analysis of variance and covariance was used to determine the change in pain intensity and immersion level within patients. Hypothesis 2 was addressed using Pearson correlation analysis to determine the significance of the relationship between pain and engagement level.

CHAPTER 4

Results

The purpose of this research study was to measure the effectiveness of a videogame as a developmentally appropriate non-pharmacological modality to decrease pain in adolescents 12-21 years of age with sickle cell pain. The purpose of this chapter is to describe the research participants and the results of data analysis, organized according by the research questions.

Description of the Sample

The sample of this study was adolescents (12-21 years of age) diagnosed with sickle cell disease and experiencing sickle cell related pain admitted for pain management or experiencing pain during a clinic visit. Based on the results of power calculations, 30 participants were enrolled and completed the study procedure. The ages of participants ranged from 12 to 21 years and pain scores before administering the intervention ranged from 4 to 6 on the built-in faces scale which ranges from 0 to 6. All participants enrolled in this study were African Americans.

Demographic Data

The demographic data analysis was obtained from 30 subjects. Participants included 15 females (50%, n=15) and 15 males (50%, n=15). Participants visited or were admitted to the hospital for a variety of reasons, shown in Table 1.12 (40%) of the participants came to the hospital because of pain were whereas the rest (60%, n=18) had pain concurrent with other symptoms such as anemia, checkup visits and other unidentified reasons.

Table 1

Reason for seeking care

Approach	Frequency	Percent
Anemia	1	3.3
Aphersis	1	3.3
Checkup	1	3.3
Follow-up visit	1	3.3
Headache	1	3.3
Hematuria	1	3.3
Pain	14	46.6
Sickle cell crisis	2	6.7
Sickle cell disease	6	20.0
Swelling	1	3.3
Transfusion	1	3.3
Total	30	100.0

When answering the question of whether they play videogames at home or not, 29 participants (96.7%) answered with yes, while only one participant (3.3%) answered with no, as shown in Table 3. The types of videogame consoles used at home included Playstation 2, Playstation 3, Xbox360, Wii and others with a frequency of how many times they play videogames at home ranging from none a day (6.7%, n=2) to more than 3 times a day (23.3%, n=7) shown in Tables 2 and 3.

Table 2

Type of Videogame System

Type of system	Frequency	Percent
PS2	1	3.3
PS3	8	26.7
Xbox360	8	26.7
Wii	2	6.7
Other	1	3.3
More than one	9	30.0

Table 3

Using Videogames at Home and Frequency per day

Variables		Frequency	Percent
Videogames at home	No	1	3.3
	Yes	29	96.7
How many times a day	None	2	6.7
	1 Once	10	33.3
	2 Twice	8	26.7
	3 Three times	3	10.0
	4 More than 3 Times	7	23.3

In addition to using videogames to distract them from pain, participants used a variety of other modalities to treat their pain. Table 4 shows the measures used at home when participants

were experiencing pain according to their answers on the demographics questionnaire. Examples of most common modalities used at home included the use of medications (76.7%, n=23), sleep (26.7%, n=8), watching TV (23.3%, n=7) and playing videogames (20%, n=6). Surprisingly, as shown in Table 4, not all participants exclusively used medications to treat their pain. Some of the participants used some sort of distraction technique to try to manage their pain at home.

Table 4

Approaches Used at Home to Manage Pain

Variable		Frequency	Percent
Medication	No	7	23.3
	Yes	23	76.7
Rest	No	24	80
	Yes	6	20
Heating pad	No	23	76.7
	Yes	7	23.3
Icy hot	No	29	96.7
	Yes	1	3.3
Sleep	No	22	73.3
	Yes	8	26.7
Watching TV	No	23	76.7
	Yes	7	23.3
Walking	No	29	96.7
	Yes	1	3.3

Table 4

Continued

Variable		Frequency	Percent
Talk to people	No	29	96.7
	Yes	1	3.3
Playing with dog	No	29	96.7
	Yes	1	3.3
Eating	No	28	93.3
	Yes	2	6.7
Hydration	No	27	90
	Yes	3	10
Reading	No	29	96.7
	Yes	1	3.3
Music	No	25	83.3
	Yes	5	16.7
Yoga	No	29	96.7
	Yes	1	3.3
Using computer	No	29	96.7
	Yes	1	3.3
Videogames	No	24	80
	Yes	6	20

Regarding the site of their pain, participants used the provided full body diagram to point out the location of their pain. The most common pain locations included back (63.3%, n=19), abdomen (33.3%, n=10), chest (26.7%, n=8). Other less common pain locations included thighs (23.3%, n=7), hip and head (13.3%, n=4), as shown in Table 5.

Table 5

Pain Location

Variable		Frequency	Percent
Head	No	26	86.7
	Yes	4	13.3
Neck	No	27	90
	Yes	3	10
Shoulders	No	27	90
	Yes	3	10
Chest	No	22	73.3
	Yes	8	26.7
Abdomen	No	20	66.7
	Yes	10	33.3
Back	No	11	36.7
	Yes	19	63.3
Arms	No	26	86.7
	Yes	4	13.3

Table 5

Continued

Variable		Frequency	Percent
Hands	No	27	90
	Yes	3	10
Hip	No	26	86.7
	Yes	4	13.3
Thighs	No	7	23.3
	Yes	23	76.7
Lower legs	No	20	66.7
	Yes	10	33.3

Results of Research Question and Hypotheses

Research Question: What is the level of engagement while playing the videogame among the adolescents with sickle cell disease pain?

Table 6 shows the summary measurement of the level of engagement total score measured with the Game Engagement Questionnaire.

Table 6

Summary Measures of Total Engagement Score

N	30
Mean	27.67
Median	28.50
Standard Deviation	6.272
Minimum	10
Maximum	36

Table 7

Presence Self-assessment Manikin

Scores after Playing the Videogame

Score	Frequency	Percent
1	19	63.3
2	8	26.7
3	1	3.3
5	1	3.3
6	1	3.3

The Cronbach's alpha coefficient for the 19-item in level of engagement instrument 0.82. As indicated in Table 8, the Cronbach's alpha for the deleted items were below or at 0.82, except for Items 13 & 19 (“My thoughts go fast” and “I feel like I just can’t stop playing”), where Cronbach's alpha coefficient, for these two items if deleted, exceeded the 0.82. In addition, the

corrected item correlation for Items 13 & 19 in Table 8 were less than the acceptable cut-off point 0.20 (r = 0.15 for Item 13 & r = 0.13 for Item 19). Deleting these two items for the engagement instrument resulted in reliability coefficient 0.83. In addition to using the game engagement questionnaire to measure the engagement level, an important element of engagement was measured after playing the videogame by using the presence self-assessment manikin scale. Table 7 shows the Presence Self-assessment Manikin Scores after Playing the Videogame. The presence self-assessment manikin is a 1 to 9 point pictorial scale.

Table 8

Item-Total Statistics for the Engagement Instrument

Item	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
1. I lose track of time	26.03	35.34	0.48	0.81
2. Things seem to happen automatically	26.27	34.13	0.53	0.80
3. I feel different	26.13	33.64	0.64	0.80
4. I feel happy	25.83	36.49	0.49	0.81
5. The game feels real	26.43	33.15	0.60	0.80
6. If someone talks to me I don't hear	26.80	35.89	0.36	0.81
7. I get excited	25.87	36.39	0.46	0.81

Table 8

Continued

Item	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
8. Time seems to standstill or stop	26.67	34.85	0.43	0.81
9. I feel spaced out	26.40	34.59	0.46	0.81
10. Playing seems automatic	26.03	34.52	0.55	0.80
11. My thoughts go fast	26.03	37.89	0.15	0.83
12. I lose track of where I am	26.73	35.18	0.31	0.82
13. I play without thinking about how	26.17	36.35	0.26	0.82
14. Playing makes me feel calm	25.93	37.24	0.28	0.82
15. I play longer than I meant to	26.37	33.96	0.49	0.81
16. I really get into the game	25.77	36.87	0.49	0.81
17. I feel like I just can’t stop playing	26.13	37.78	0.13	0.83
18. I don’t answer when someone talks	26.73	36.13	0.25	0.82
19. I can’t tell that I'm getting tired	26.27	34.48	0.42	0.81

Hypothesis 1. Upon using videogames for the reduction of pain intensity, adolescents with sickle cell pain will report less pain.

As indicated in Table 9, the mean and median of the self-reported pain score changes downward as the adolescents continue playing videogames up to 45 minutes.

Table 9

Summary Measures of Pain Score at Baseline, 15, 30, and 45 Minutes of Playing Videogames.

Pain	Median	Mean	Std. Deviation	N
Pain 0	5.00	5.17	0.75	30
Pain 15	4.00	4.13	0.94	30
Pain 30	3.00	3.37	0.96	30
Pain 45	2.00	2.90	0.91	30

Results from this table indicate a significant reduction in pain levels after playing the videogame, shown in Figure 1. Multivariate repeated measure analysis of variance was used to determine the change in pain score overtime. The results indicated that there was a significant reduction in pain while using the videogames ($F = 29.28$, $p < 0.0001$). Table 10 shows the comparison of pain scores from baseline and subsequent pain measures. As indicated in Table 10, the reduction in pain between the baseline and the subsequent times were statistically significant.

Table 10

Pain Score Comparisons between Baseline and 15, 30, and 45 Minutes of Playing Videogames.

Pain	Sum of Squares	df	Mean Square	F	p-value
Pain 15 vs. Pain 0	32.033	1	32.033	71.64	<0.0001
Pain 30 vs. Pain 0	97.200	1	97.200	97.87	<0.0001
Pain 45 vs. Pain 0	154.133	1	154.133	140.278	<0.0001

In addition, the comparison of the pain scores between the two adjacent measures indicated a significant self-reported pain reduction during a 45-minute videogame session (Table 11).

Table 11

Pain Score Comparisons between Adjacent Measures of Baseline, 15, 30, and 45 Minutes

Pain	Sum of Squares	Df	Mean Square	F	p-value
Pain 0 vs. Pain 15	32.033	1	32.033	71.643	<0.0001
Pain 15 vs. Pain 30	17.633	1	17.633	26.404	<0.0001
Pain 30 vs. Pain 45	6.533	1	6.533	8.826	0.006

Figure 1 shows the change in self-reported pain score overtime.

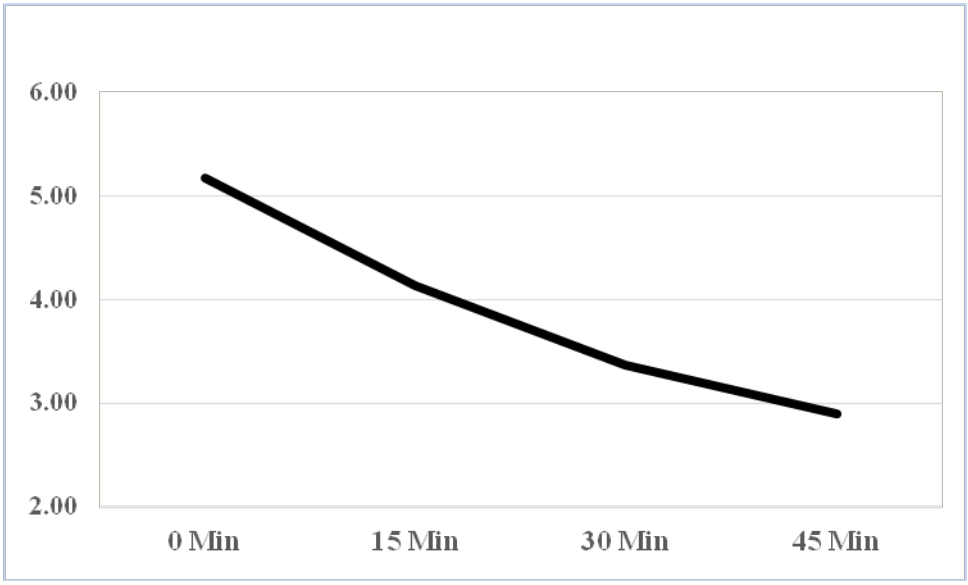

Figure 1. Change in Mean Pain Scores Overtime

Hypothesis 2. Engagement level will be negatively correlated with self-reported pain level.

The Game Engagement Questionnaire consisted of a 19 item questionnaire with choices of answers as No (coded as 0), Maybe (coded as 1), and Yes (Coded as 2). A higher total score is associated with a higher level of engagement.

Table 12 shows the correlation coefficient between the total engagement score and the self-reported pain score at the baseline, 15, 30, and 45 minutes. As indicated in Table 12, the total engagement score and pain score are inversely related. As the pain level decreased the inverse relationship between engagement level and pain score became stronger. However, these inverse relationships shown in Table 12 were not statistically significant.

Table 12

Correlation Between Total Engagement Score And Self-reported Pain Level at Baseline, 15, 30 and 45 minutes

Pain	Total Engagement Level
Pain 0	$r = -0.10$, $p = 0.606$
Pain 15	$r = -0.17$, $p = 0.358$
Pain 30	$r = -0.21$, $p = 0.272$
Pain 45	$r = -0.24$, $p = 0.211$

Summary of Research Findings

The study hypotheses and research question were designed to examine the level of engagement induced by playing a videogame. Additionally, this study proposes how the distractive properties of engagement can lower the level of pain in adolescents 12-21 years old with sickle cell disease. Several significant results were found while analyzing the data for this study. Playing the videogame was associated with lower pain scores as well as higher engagement levels from both the Game Engagement Questionnaire and presence self-assessment manikin. Moreover, and from comparing adjacent pain score measurements, the results indicate that the longer the videogame is played the more profound the effect. Although it did not yield significant results, the correlation between pain and engagement levels was stronger overtime.

CHAPTER 5

Discussion

In this chapter, an interpretation of research results, recommendations, and implications for nursing practice, and research are discussed. The discussion will be done according to each research question or hypothesis. First, changes in the level of engagement in adolescents with sickle cell pain after playing the videogame will be discussed. Second, changes in the level of pain before, during and after playing the videogame will be discussed. Third, the relationship between the levels of pain and engagement will be discussed. Additionally, a comparison of the key findings with the existing literature about the levels of pain and engagement is presented.

Discussion of Research Findings

The current work measures the effectiveness of a videogame as a developmentally appropriate non-pharmacological modality on pain in adolescents 12-21 years of age with sickle cell pain.

The following research question and hypotheses were addressed:

Research question 1: What is the level of engagement among the adolescents with sickle cell disease?

Engagement is the level of distraction induced by multisensory stimulation while maintaining a level of attachment to the stimulant. The videogame utilized in this research, LittleBigPlanet 2, is an example of a multisensory stimulation which has been proposed to divert participants' thoughts from the sensation of pain. The game engagement questionnaire used in this study, adopted from Brockmyer et al (2009), included 19 items pertaining to the engagement experience completed at the completion of the videogame. Cronbach's alpha coefficient analysis was applied to measure the internal consistency of all 19 items and yielded an adequate score of

0.82. In comparison to the Cronbach's alpha results 0.85 from the Brockmyer et al (2009) which was done on 18-26 only-male 107 participants, results from the current study indicate that this instrument is consistent across both age groups from both studies and with the use of two different interventions. Participants answered with "Yes" to most of the items in the Game Engagement Questionnaire instrument indicating that they were successfully immersed in the virtual environment of the videogame. Examples of the items with the highest number of positive results include "I feel happy" (90%, n=27), "I get excited" (86.7%, n=26), "I really get into the game" (96.7%, n=29), "playing seems automatic" (76.7%, n=23), and "I lose track of time" (73.3%, n-22). In addition to completing the Game Engagement Questionnaire instrument, the presence self-assessment manikin was used to measure the level of presence which is also, as discussed before, an essential element of engagement. Similar to the Game Engagement Questionnaire, the presence self-assessment manikin scale was completed by participants at the completion of the videogame. Results from the presence-self assessment manikin scale were consistent with the positive results from the Game Engagement Questionnaire instrument. As shown in Table 7, 63.3% of participants (n=19) indicated that they experienced the highest level of presence while playing the videogame by answering with a score of 1 while 26.7% of participants (n=8) answered with a score of 2 on the 9 point pictorial scale. These findings are also consistent with the literature which propose that videogames and virtual reality can induce a high level of immersion (Schneider, Lang, Shin, and Bradley, 2004; Serrano, Botella, Banos, and Alcaniz, 2013). Considering that the participants were experiencing high levels of pain while playing the videogame, these results indicate that the intervention was successful in inducing an immersion level enough to be expressed on the used scale. This high level of immersion

achieved during the study also emphasizes the high potential of using videogames as a distraction technique for the management of pain in adolescents with sickle cell disease.

Hypotheses 1: Upon using videogames for the reduction of pain intensity, adolescents with sickle cell pain will report less pain.

The level of pain was measured before, during and after playing the video game at exactly 0, 15, 30 and 45 minute time-point. Pain was measured using the built-in faces scale described earlier. The mean pain score was 5.17 at 0 time-point and 2.90 at the 45 minutes time-point which was the completion of the videogame. Findings from this study indicate that the reduction of the level of pain rated by participants at 0, 15, 30 and 45 time-points yielded statistically significant results at a p value of < 0.001.

Additionally, data from this study indicated that there is a correlation between the amount of time the videogame was played and a decrease in pain level. Therefore, it was evident that the more time the videogame is played the more effective the intervention was. From looking at comparisons of baseline pain scores with each time-point separately, it was evident that pain was decreasing with time as participants were playing the videogame which yielded to statistically significant results ($p < 0.001$). Moreover, a comparison between each time-point and the adjacent time-point starting with baseline and ending with the 45 minute time-point was done which also showed statistically significant results. These results are consistent with prior literature that used similar interventions (Hawkins, Liossi, Ewart, Hatira, & Kosmidis, 1998; Dahlquist et al. 2009; Pölkki, Pietil, Vehvilinen-Julkunen, Laukkala, & Kiviluoma, 2008; Chan, Chung, Wong, Lien & Yang, 2006; Wiederhold, Gao, Sulea, Wiesderhold, 2014). Therefore, as videogames and other distraction techniques become more of a routine in the treatment of pain in adolescents, recognition that the longer the time, the better the benefit from the used intervention will be.

Hypothesis 2: Engagement level will be negatively correlated with self-reported pain level.

The current study is one of the first to discuss the relationship between pain and engagement level in videogaming in adolescents with sickle cell disease experiencing acute pain. Furthermore, it was found that, even though the correlations were not statistically significant, there was negative association between the level of pain and engagement. Therefore, the higher the engagement level yields a lower pain score. Looking at the results from table 12, it is noticeable that the correlation was getting stronger with each following time-point; p=0.211 at 45 minutes time-point compared to 0.606 at baseline or 0 minutes time-point. These results are also consistent with the assumption that with longer the exposure to a multisensory stimulant the more profound the effect will be.

Another important observation was the change in the body language of participants with time as they play the videogame. It was noticed by the investigator that, as they get more engaged with the videogame, participants' faces were more relaxed and their bodies were less tense. This observation was also evident by watching the participants react to the videogame environment either by smiling or by expressing a reflex in either an arm or a leg as they try to go though obstacles in the videogame. This observation also confirms that the videogame used was successful in being an effective distraction technique.

Limitations of the study

Studies with a one-group repeated measure quasi-experimental design are limited in the credibility of the findings compared to studies with true experimental design. In this study design, subjects gave their pain scores before and after the intervention which makes them as their own control in the study. Additionally, this study used a non-randomized convenience

sampling design which limits the generalizability of the findings to other patients or settings. The number of participants enrolled in the study was small. The small number of participants can further limit the generalizability of the findings. Future research should include a higher number of participants to address this limitation.

In addition to the aforementioned limitations, the level of engagement was only measured after the intervention using both the Game Engagement Questionnaire and presence self-assessment manikin which made it difficult to do statistical comparisons with pain scores at different time-points. Future research should include measurements of engagement levels both prior to, if possible, and after playing the videogame. Additionally, the use of a control group and randomization will improve the credibility and generalizability of the results.

Implications for clinical practice and education

The current study offers clinical empirical data that demonstrates the use of videogames as a cognitive behavioral strategy helps adolescents with their sickle cell disease pain. Although this study recommends using videogames as an adjuvant strategy to pharmacological therapy, the use of videogames as cognitive behavioral strategy to control pain has the potential decrease the amount of opioid analgesics used over time. Therefore, using these cognitive behavioral strategies and adapting them as self-care behaviors decreases the associated long-term side effects from the frequent use of these drugs.

Moreover, and due to the positive reports on the use of videogames and cognitive behavioral strategies from this and other studies, nurses, advanced practice nurses as well as primary care providers should advocate the use of such strategies. It is also important to emphasize the importance of increasing the awareness of families on the effectiveness of using cognitive behavioral strategies, such as videogames, to manage pain. Increasing awareness will

help shift the families' perspective from negative, viewing videogames as a waste of time, to positive, viewing videogames as measure to help manage pain. In addition, the necessary education should be provided to adolescents and their families on how to balance between the use of pharmacological and non-pharmacological approaches.

Implications for future research

Research investigating the applications of videogames for pain management is still in its inception. If tailored toward specific patient populations, pain types, and age groups, videogames could enhance the depth of engagement or immersion achieved by playing these videogames which on the other hand will play an essential role in the treatment of pain. The investigators of this study advise that further research is needed to address the specificity of videogames and the groups of patients that would benefit the most from these strategies. Additionally, the effectiveness of other cognitive therapies such as music and guided imagery should continue to be studied and perhaps used in conjunction with videogames. Furthermore, future research should also focus on the specificity of these interventions and their benefits in patients with acute as well as chronic pain.

Even though results from this study provide excellent evidence toward the effect of using videogame as a distraction approach sickle cell disease pain, there is a high need to conduct similar studies in a multi-cohort controlled setting. Additionally, future research should focus on the influences of other variables such gender, previous videogaming experience, socioeconomic status and its effect on access to videogames. Moreover, future studies should measure the amount of pain medications used over time while using videogames in a controlled setting as well as utilizing a cost-benefit analysis between cohorts.

Conclusion

In addition to the aforementioned literature, results from this study are also consistent with prior studies that used similar approaches and technologies in different populations such as burns care (Schmitt et al. 2011), cancer pain (Schneider & Workman, 2000), and painful medical procedures (Gold et al. 2005). In addition to the benefits and application of videogames, their use as a distraction modality has been proven to show positive and significant results in the treatment of acute pain. Pain from burns, cancer, medical procedures, and post-operative pain are just a few examples of how videogames have been explored previously. Additionally, some of the reviewed literature also argued that using videogames and virtual reality may improve the effect of analgesics during medical painful procedures (Hoffman, et al., 2000, 2001 & 2011; Keefe, et al. 2012). The purpose of this study was not to replace traditional pain management but to explore using videogames as an adjunct option for adolescents with sickle cell disease experiencing acute pain. Results from this study show promising findings related to pain management that can be more accessible to adolescents with sickle cell pain at home and in the hospital setting.

A consideration is the high costs of gaming systems, equipment and videogames. These costs continue to decrease which makes them increasingly accessible to a larger number of patients. Costs of video game systems from a recent internet search are $399 for Playstation 4, $349.99 for Xbox One, $299.95 for Xbox 360, $215.99 for PlayStation 3 and $108.59 for Nintendo Wii (Video Game Consoles Review 2014, Best Gaming Consoles - TopTenREVIEWS, 2014). The decrease in cost and increase in accessibility to these system as well as the adolescents' awareness of these technologies also emphasizes the potential of using these

systems not just in the hospital or clinic setting but also makes them more readily accessible in their home.

APPENDIX A: HIC AND IRB APPROVALS

WAYNE STATE UNIVERSITY

IRB Administration Office
87 East Canfield, Second Floor
Detroit, Michigan 48201
Phone: (313) 577-1628
FAX: (313) 993-7122
http://irb.wayne.edu

NOTICE OF EXPEDITED APPROVAL

To: Talal Ali
Family, Comm Mental Health
2424 Somerset Blvd APT 106

From: Dr. Deborah Ellis or designee C. Zoloudek/BB.
for Chairperson, Behavioral Institutional Review Board (B3)

Date: July 29, 2014

RE: IRB #: 073214B3E

Protocol Title: Using Video Games for Decreasing Pain Caused by Acute Painful Crisis in Adolescents with Sickle Cell Disease

Funding Source:

Protocol #: 1407013219

Expiration Date: July 28, 2015

Risk Level / Category: 45 CFR 46.404 - Research not involving greater than minimal riskResearch not involving greater than minimal risk

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The above-referenced protocol and items listed below (if applicable) were **APPROVED** following *Expedited Review* Category (#7)* by the Chairperson/designee *for* the Wayne State University Institutional Review Board (B3) for the period of 07/29/2014 through 07/28/2015. This approval does not replace any departmental or other approvals that may be required.

- Revised Protocol Summary Form (received in the IRB Office 7/29/2014)
- Protocol (received in the IRB Office 7/10/2014)
- A waiver of requirement for written documentation of informed consent has been granted according to 45 CFR 46 116(d). This waiver satisfies: 1) the research involves no more than minimal risk to the participants. Participants will play video games and answer questionnaires. Standard of care will not be disrupted. The research activity is unlikely to cause physical or psychological harm. There is an adequate plan to minimize a breach of confidentiality; 2) the research involves no procedures for which written consent is normally required outside of the research context. Written consent is not normally required to reply to surveys and play video games; 3) the consent process is appropriate and 4) an information sheet disclosing the required and appropriate additional elements of consent disclosure will be provided to participants.
- Consent/Parental Permission to Be Contacted about Participating in a Research Study (Advocate Health Care)
- Information Sheet (Advocate Health Care)
- Assent to Participate in Research (U. of Illinois - Chicago, dated 5/9/2014)
- Research Information and Consent for Participation in Social Behavioral Research - Parental Permission (U. of Illinois - Chicago, dated 5/9/2014)
- Research Information and Consent for Participation in Social Behavioral Research - Informed Consent (U. of Illinois - Chicago, dated 5/9/2014)
- Information Sheet (U. of Illinois - Chicago, dated 6/20/2014)
- Study Flyer - UIC
- Data Collection Tools: Game Engagement Questionnaire (Advocate Health Care), Presence Self-assessment Manikin (Advocate Health Care), Appendix B Demographic questionnaire (Advocate Health Care), Appendix H: Presence Self-assessment Manikin (UIC), Appendix B Demographic questionnaire (UIC, 4/10/2014), and Appendix M Eligibility Checklist (UIC, dated 4/8/2014)

APPENDIX A: HIC AND IRB APPROVALS

- Federal regulations require that all research be reviewed at least annually. You *may* receive a *"Continuation Renewal Reminder"* approximately two months prior to the expiration date; however, it is the Principal Investigator's responsibility to obtain review and continued approval ***before*** the expiration date. Data collected during a period of lapsed approval is unapproved research and can never be reported or published as research data.
- All changes or amendments to the above-referenced protocol require review and approval by the IRB **BEFORE** implementation.
- Adverse Reactions/Unexpected Events (AR/UE) must be submitted on the appropriate form within the timeframe specified in the IRB Administration Office Policy (http://www.irb.wayne.edu//policies-human-research.php).

NOTE:

1. Upon notification of an impending regulatory site visit, hold notification, and/or external audit the IRB Administration Office must be contacted immediately.
2. Forms should be downloaded from the IRB website at **each** use.

*Based on the Expedited Review List, revised November 1998

APPENDIX A: HIC AND IRB APPROVALS

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Approval Notice
Amendment to Research Protocol and/or Consent Document – Expedited Review
UIC Amendment # 1

August 19, 2014

Lewis Hsu, MD
Pediatrics
840 S. Wood Street
M/C 856
Chicago, IL 60612
Phone: (312) 996-6102 / Fax: (312) 413-9484

RE: **Protocol # 2014-0277**
"Using Video Games for Decreasing Pain Caused by Acute Painful Crisis in Adolescents with Sickle Cell Disease"

Dear Dr. Hsu:

Members of Institutional Review Board (IRB) #2 have reviewed this amendment to your research under expedited procedures for minor changes to previously approved research allowed by Federal regulations [45 CFR 46.110(b)(2)]. The amendment to your research was determined to be acceptable and may now be implemented.

Please note the following information about your approved amendment:

Amendment Approval Date: August 18, 2014
Amendment:
Summary: UIC Amendment #1, dated 15 August 2014 and submitted to OPRS 18 August 2014, is an investigator-initiated amendment adding Wayne State University as a research site (Appendix K; IRB approval 7/28/2014 - 7/28/2015).
Approved Subject Enrollment #: 30
Performance Sites: UIC, Wayne State University
Sponsor: None
Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
08/18/2014	Amendment	Expedited	08/18/2014	Approved

APPENDIX A: HIC AND IRB APPROVALS

2014-0277 Page 2 of 2 August 19, 2014

Please be sure to:

→ Use your research protocol number (2014-0277) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the enclosure,
"UIC Investigator Responsibilities, Protection of Human Research Subjects"
(http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf)

Please note that the UIC IRB #2 has the right to seek additional information, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact the OPRS at (312) 996-1711 or me at (312) 355-2764. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Betty Mayberry, B.S.
IRB Coordinator, IRB # 2
Office for the Protection of Research Subjects

Enclosure: None

cc: Usha Raj, Pediatrics, M/C 856
Privacy Office, Health Information Management Department, M/C 772

APPENDIX A: HIC AND IRB APPROVALS

Advocate Health Care
Institutional Review Board
3075 Highland Parkway, 4th Fl.
Downers Grove, IL 60515
IRBMail@AdvocateHealth.com

APPROVAL

May 29, 2014

Talal Ali, RN, MSN
Advocate Children's Hospital – Oak Lawn
au0023@wayne.edu

Dear Investigator:

On 05/29/14 the IRB reviewed the following protocol:

Type of Review:	Initial – Expedited		
IRB ID:	5805	Approval period:	05/29/14 – 05/28/15
Title:	Using Video Games for Decreasing Pain Caused by Acute Painful Crisis in Adolescents with Sickle Cell Disease		
Investigator:	Talal Ali, RN, MSN		
Funding:	N/A		
Document reviewed:	Application forms 211, 226, protocol; survey, demographic and rating measures; parental/subject approach consent; participant information sheet		

The study was approved with a waiver of written consent and HIPAA Authorization under Expedited criterion 3(7b) (Research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies). Potential subjects and the parents of minors will be asked to sign a "Permission to Contact" form in order to receive further information about the study. No identifying information will be recorded from actual study subjects.

Within 25 business days of study close or 6 weeks before the expiration date of 05/28/15, whichever is earlier, you are to submit a completed "FORM: Continuing Review (HRP-212)" and required attachments to request continuing approval or closure.

If continuing review approval is not granted on or before the expiration date, all study activities will need to cease. In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

Sincerely,

Joal Hill

Joal Hill, JD, MPH, PhD
Chairman, Advocate Institutional Review Board

cc:

The AHC IRB is organized under the authority of, and in accordance with, regulations of the United States Department of Health and Human Services, Food and Drug Administration (Title 21 Code of Federal Regulations [CFR] Part 56 [Institutional Review Board], and Title 45 CFR Part 46 [Protection of Human Subjects]).

APPENDIX B: DEMOGRAPHIC QUESTIONNAIRE

Appendix B Demographic questionnaire.

I would like to start by asking you some background information about you and your family. Please answer the following questions. You can ask your mother/father/guardian or data collector if you need help:

1- What is your age? ☐

2- Are you a Boy ☐ or a Girl ☐ ?

3- What is the reason for your admission to the hospital?

_____

4- How do you best describe yourself: (Pick one)

- ☐ White/Caucasian/non-hispanic
- ☐ Asian American
- ☐ Native American
- ☐ African-American
- ☐ Hispanic
- ☐ Other

Do you receive free or reduced lunch at school?

☐ Yes ☐ No

5- Who works and supports your family:
Father: ☐ Mother: ☐ Both: ☐ Other: ☐

6- Do you play videogames at home? ☐ Yes ☐ No.

APPENDIX B: DEMOGRAPHIC QUESTIONNAIRE

ɔpendix B Demographic questionnaire.

If your answer is YES, what gaming system do you have? (Select one)

Playstation 2	☐	XBOX 360	☐
Playstation 3	☐	Nintendo Wii	☐
XBOX	☐	Other	☐ _____

7- How often do you play videogames at home?

☐ Once a day ☐ Three time a day

☐ Twice a day ☐ More than three times a day

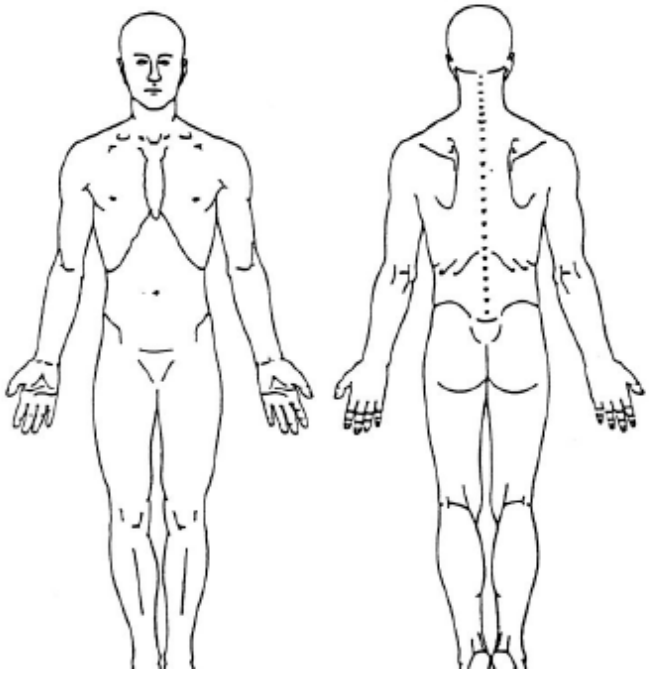
☐ None

8- What do you do when you have pain at home? (List all the things that you do)

- -
- -
- -

9- What is the location of your pain: (Use attached diagram to point at all places that hurt)

Mark the picture with an X where your pain is located



APPENDIX C: INFORMATION SHEET (UNIVERSITY OF ILLINOIS CHILDREN'S HOSPITAL)

Investigators:

Lewis Hsu, PhD, MD
Professor of Pediatrics
University of Illinois,College of Medicine

Talal Ali, BSN RN
PhD candidate
Wayne State University, College of Nursing

Santosh Saraf, MD
Assistant professor of medicine
University of Illinois,College of Medicine

Purpose of the study:

Pain in adolescents with sickle cell disease has been identified by parents as one of the most common reasons for hospitalization, stress and discomfort in adolescents. In addition to the use of pain medications, the use of therapies such as relaxation music, virtual reality, and massage have the potential to helping adolescents decrease the level of their pain. An example of these therapies is the use of videogames in the hospital or when at home. You are being asked to be in this research study to see if using videogames can help decrease your pain level.

This research study is being conducted by University of Illinois pediatric faculty and a Wayne State University/ College of Nursing PhD student.

The game:

The game that will be used is developed by Multimedia Molecule and published by Sony entertainment and released. The rating of the game is (E) which means for everyone 6 years of age and older. LittleBigPlanet 2 (www.littlebigplanet.com) is a playstation 3 game in which players control characters referred to as Sackboy for males and Sackgirl for females. The characters in the game can be customized and modeled in different colors and clothing according to your liking. The game is fully 3-dimensional in 2-dimensional environments. The video game play includes your Sack person going through obstacles and adventures in addition to activities such as running and jumping and manipulating objects by hanging onto them or by dragging or pushing them. While playing the game, and in order to go through some obstacles or gates successfully, you will be completing puzzles and incomplete words in the game related to your health.

Study Procedure:

If you take part in the study, you will be given a brief demographic questionnaire which will take up to 5 minutes to complete. Before you start playing the video game, you will be given a tutorial sheet to help

you with the basic commands to play the game which will take you up to 5 minutes to review. Before you start playing the game, you will be asked to rate your pain level using a pain scale within the game. Game play will take approximately 45 minutes to be completed. While playing the videogame, you will be asked to provide a pain rating every 15 minutes. At the end of the game, you will be asked to give a second pain rating and fill out two questionnaires about your game experience which will take up to 5 minutes. The total time needed for you to participate in this study is one hour.

Benefits:

As a participant in this research study, there may be no direct benefit for you; however, information from this study may benefit other people now or in the future.

Risks:

There are no known risks at this time from participation in this study. However, breach of privacy (others will know that you are participating in research) and confidentiality (accidental disclosure of identifiable data) may occur.

Costs:

There is not direct or indirect cost to you.

Compensation:

For taking part in this research study, you will be compensated for your time and participation by getting a 10 dollar gift card that can be used at any Target store location upon completion of the study task.

Confidentiality:

All information collected about you during the course of this study will be kept without any identifiers.

Voluntary Participation /Withdrawal:

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part, you can change your mind later and withdraw from the study. You are free to not answer any questions or withdraw at any time. Your decision will not affect your relationships with the University of Illinoi at Chicago or its affiliates

Questions:

If you have any questions about this study now or in the future, you may contact Talal Ali, PhDc, RN at 248-882-2911 or email: au0023@wayne.edu; Lewis Hsu, MD at 312-996-6143 or email: LewHsu@uic.edu; or Santosh Saraf, MD at 312-996-5680 or email: ssaraf@uic.edu.

Participation:

By completing the questionnaire/interview and providing your initials on this information sheet, you are agreeing to participate in this study. If you have any further questions you may contact the UIC Office for the Protection of Research Subjects at 312-996-1711 or email: uicirb@uic.edu.

APPENDIX C: INFORMATION SHEET (ADVOCATE CHILDREN'S HOSPITAL)

Investigators:

Talal Ali, BSN RN
PhD candidate
Wayne State University
College of Nursing

Jason Canner, DO
Pediatric Hematology Oncology
Advocate Children's Hospital

Fran Majca, MA, BSN, RN, CPON
Pediatric Oncology Nurse
Advocate Children's Hospital

Purpose of the study:

Pain in adolescents with sickle cell disease has been identified by parents as one of the most common reasons for hospitalization, stress and discomfort in adolescents. In addition to the use of pain medications, the use of therapies such as relaxation music, virtual reality, and massage have the potential to helping adolescents decrease the level of their pain. An example of these therapies is the use of videogames in the hospital or when at home. You are being asked to be in this research study to see if using videogames can help decrease your pain level.

This research study is being conducted by Advocate Children's Hospital pediatric staff and a Wayne State University/ College of Nursing PhD student.

The game:

The game that will be used in the study is developed by Multimedia Molecule and published by Sony entertainment and released in the market (Target, Bestbuy, Walmart…etc). The rating of the game is (E) which means for everyone 6 years of age and older. LittleBigPlanet 2 (www.littlebigplanet.com) is a Playstation 3 game in which players control characters referred to as Sackboy for males and Sackgirl for females. The characters in the game can be customized and modeled in different colors and clothing according to your liking. The game is fully 3-dimensional in 2-dimensional environments. The video game play includes your Sack person going through obstacles and adventures in addition to activities such as running and jumping and manipulating objects by hanging onto them or by dragging or pushing them. While playing the game, and in order to go through some obstacles or gates successfully, you will be completing puzzles and incomplete words in the game related to your health.

Study Procedure:

If you take part in the study, you will be given a brief demographic questionnaire which will take up to 5 minutes to complete. Before you start playing the videogame, you will be given a tutorial sheet to help you with the basic commands to play the game which will take you up to 5 minutes to review. Before you start playing the game, you will be asked to rate your pain level using a pain scale within the game.

Game play will take approximately 45 minutes to be completed. While playing the videogame, you will be asked to provide a pain rating every 15 minutes. At the end of the game, you will be asked to give a second pain rating and fill out two questionnaires about your game experience which will take up to 5 minutes. The total time needed for you to participate in this study is one hour.

Benefits:

As a participant in this research study, there may be no direct benefit for you; however, information from this study may benefit other people now or in the future.

Risks:

There are no known risks from participation in this study.

Costs:

There is no direct or indirect cost to you.

Compensation:

For taking part in this research study, you will be compensated for your time and participation by getting a 10 dollars gift card that can be used at any Target store location upon completion of the study task.

Confidentiality:

All information collected about you during the course of this study will be kept without any identifiers.

Voluntary Participation /Withdrawal:

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part, you can change your mind later and withdraw from the study. You are free to not answer any questions or withdraw at any time. Your decision will not change any present or future relationships with Advocate Health or its affiliates.

Questions:

If you have any questions about this study now or in the future, you may contact Talal Ali, RN at 248-882-2911 Jason Canner, DO at 708-684-3113 or Fran Majca, RN, BSN, CPON at 708-684-4247.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team: Talal Ali, RN at 248-882-2911 Jason Canner, DO at 708-684-3113 or Fran Majca, RN, BSN, CPON at 708-684-4247.

This research has been reviewed and approved by an Institutional Review Board (“IRB”) and will be monitored by the IRB of Advocate Health Care. An IRB is a committee, independent of the [sponsor and]

investigators, that reviews and oversees research studies to protect the rights and safety of participants. You may talk to them at 630-929-6149 or email

IRBMail@advocatehealth.com if:

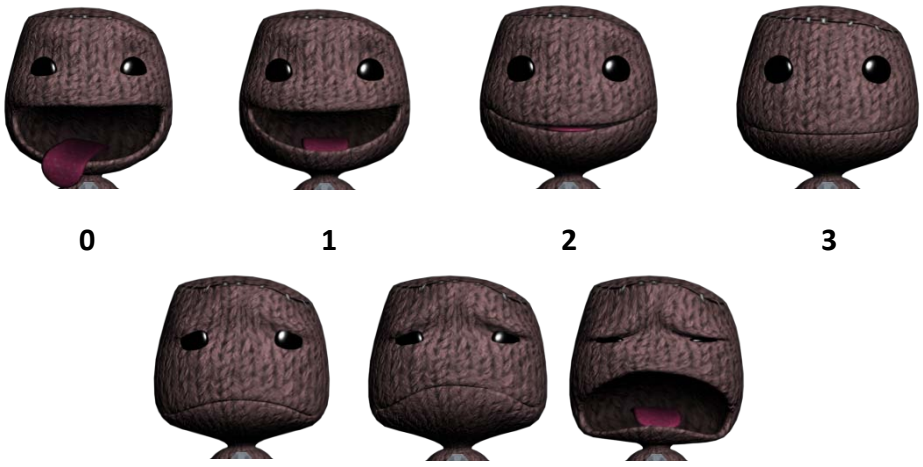
- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research**.**

Participation:

By completing the questionnaire/interview and providing your initials on this information sheet, you are agreeing to participate in this study.

APPENDIX D: MEASUREMENT TOOL

Integrated faces scale in the game



The integrated faces from the videogame: These faces will be available for participants to choose from in the game. Children will be able to change the facial expression as they are playing the videogame by using the playstation 3® controller. Seven faces will be used in the study and will be scored accordingly from face 0 (no pain) to face 6 (worst pain).

APPENDIX F: STAFF SUMMARY SHEET (ALL SITES)

Summary sheet

Purpose of the study

Various degrees and types of pain can be debilitating to children and adolescents, affecting all aspects of their lives. In order to manage their pain effectively, patients can rely on non-pharmacological approaches separately or as adjunct therapy with other pharmacological interventions. One of the primary non-pharmacological interventions examined in the literature includes the use of distraction which will be the scope of this pilot study. Distraction is a class of cognitive coping strategies that divert attention from a noxious stimulus through passively redirecting the subject's attention or by actively involving the subject in the performance of a distractor task. The purpose of this study is to evaluate the effectiveness of using videogames on pain and as a form of non-pharmacological pain management tool in adolescents 12-17 years of age with sickle cell pain. Additionally, the level of engagement induced when playing the videogame and relationship to pain will be measured.

Sample

A sample of hospitalized adolescents (12-21 years of age) with sickle cell disease related pain will be asked to participate in this study. For appropriate statistical analysis, 30 participants will be enrolled in this study.

Inclusion criteria:

- Adolescents at University of Illinois Children's Hospital experiencing sickle cell related pain with a score of 4 and above on a 0-10 Likert scale.

- Participants must have a normal developmental milestone.
- Participants must speak the English language fluently.

Exclusion criteria:

- Adolescents with vision disability.
- Adolescents with neuropathic disorders, paralyzed or having disorders that can limit their movement and interaction with the videogame such as cerebral palsy.
- Adolescents with cognitive impairment.
- Adolescents who are unable to participate because of the severity of their illness.
- Adolescents who are not able to provide an assent or consent from their parent(s).

Procedure

The teen and parent/guardian will be approached by the assigned registered nurse and will be offered an opportunity to participate in the study before they are approached by the study personnel. If they are interested in the study, the teen and parent/guardian will be approached by the PI or research assistant and given a copy of the information sheet. Research personnel will be available if participants have any questions or concerns. You or your child will be asked to sign a consent or assent in order to participate. Those adolescents interested will be invited to participate in the study. The survey instruments and data collection sheets will be coded and colored for data collection purposes. No patient identifiers will be used where documents will have a study code ID number that will correspond with participants in the study. The PI will **not** look at the patients' medical records but will obtain information regarding patient's reason for hospitalization and chief complaints from the charge nurse or assigned registered nurse.

If they agree to participate in the study, participants will be given a brief demographic questionnaire which will take up to 5 minutes to complete and a tutorial sheet to help them with the basic commands to play the game which will take up to 5 minutes to review. Any questions that the teen, parent and nurse have will be answered by the PI or research assistant. Participants will be prompted to rate their pain using the integrated faces scale in the game. Participants will play the game until they finish the pre-built level that was designed for the proposed study, it will take up to 45 minutes to finish. The PI or research assistant will leave the room as the study participant starts playing the game and will enter the room within 15 and 30 minutes to check if participants have any concerns or questions.

At the conclusion of the game or after 45 minutes, participants will be asked to rate their pain using the integrated faces scale. In addition, participants will be asked to fill out two short engagement questionnaires to assess the level of engagement induced while playing the game which will take up to 5 minutes to complete. Study procedures will be concluded by completing the 28 item immersion/engagement questionnaire. A Target gift card (for the amount of $10) will be given to each participant as compensation for their time upon completion of the study.

APPENDIX G: GAME ENGAGAMENET QUESTIONNAIRE

Game engagement questionnaire Participant ID_____

Please answer the following questions based on your experience playing the videogame:

1- I lose track of time:

Yes **Maybe** **No**

2- Things seem to happen automatically:

Yes **Maybe** **No**

3- I feel different:

Yes **Maybe** **No**

4- I feel happy:

Yes **Maybe** **No**

5- The game feels real:

Yes **Maybe** **No**

6- If someone talks to me, I don't hear:

Yes **Maybe** **No**

7- I get excited:

Yes **Maybe** **No**

8- Time seems to standstill or stop:

Yes **Maybe** **No**

9- I feel spaced out:

Yes **Maybe** **No**

10- I don't answer when someone talks:

Yes **Maybe** **No**

APPENDIX G: GAME ENGAGAMENET QUESTIONNAIRE

Game engagement questionnaire Participant ID_____

11- I can't tell that I'm getting tired:

Yes **Maybe** **No**

12- Playing seems automatic:

Yes **Maybe** **No**

13- My thoughts go fast:

Yes **Maybe** **No**

14- I lose track of where I am:

Yes **Maybe** **No**

15- I play without thinking about how:

Yes **Maybe** **No**

16- Playing makes me feel calm:

Yes **Maybe** **No**

17- I play longer than I meant to:

Yes **Maybe** **No**

18- I really get into the game:

Yes **Maybe** **No**

19- I feel like I just can't stop playing:

Yes **Maybe** **No**

APPENDIX H: PRESENCE SELF-ASSESSMENT MANIKIN

ID _____

Date/Time _____

_____

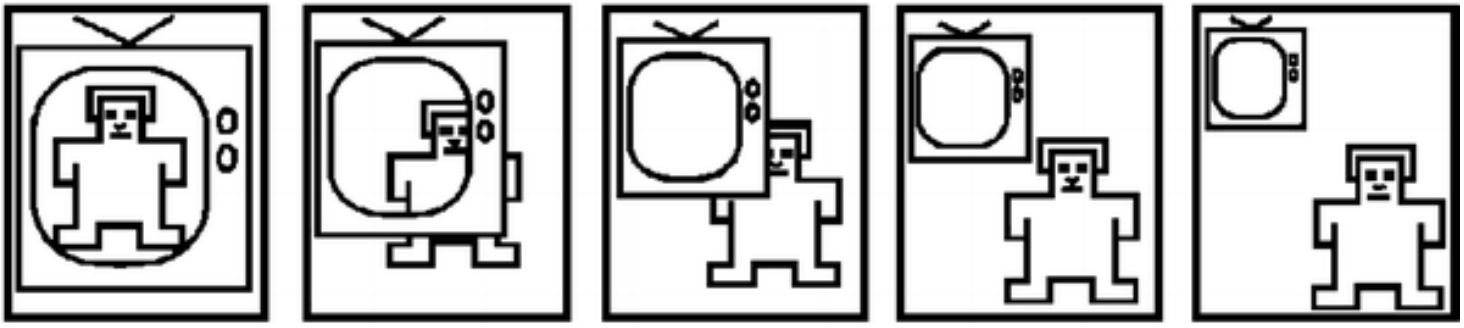
What mission did you just complete?

_____

Please answer the following questions in regard to your feelings during your last session.

Feelings of presence

Please use the figures below to indicate your feelings or emotional response to the game. The pictures go from a person who feels he or she is INSIDE THE PICTURE, A PART OF THE STORY, A PART OF THE ACTION on the left end, to a person who feels he or she is OUTSIDE THE PICTURE, REMOVED OR SEPARATED FROM THE STORY, NOT PART OF THE ACTION on the right end. Please circle the number for the picture, or the space between any two pictures, that best represents how you felt during the game experience.



1 2 3 4 5 6 7 8 9

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Agargün, M. Y., Öner, A. F., & Akbayram, S. (2001). Hypnotic intervention for pain management in a child with sickle cell anemia. *Sleep and Hypnosis, 3*(3), 127-128.

Ahmadi, M. (2001). Virtual reality may help children undergoing chemotherapy. *Journal of the National Cancer Institute*, 93, 675–676.

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ABSTRACT

USING VIDEO GAMES FOR DECREASING PAIN CAUSED BY ACUTE PAINFUL CRISIS IN ADOLESCENTS WITH SICKLE CELL DISEASE

by

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May 2015

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Purpose: The most common symptom of sickle cell disease is pain, which occurs as the cells clump compromising further blood flow to distal organs. Despite the advancement in pain management, many children and adolescents' pain remains under treated. The purpose of this study is measure the effectiveness of a videogame as a developmentally appropriate non-pharmacological modality on pain in adolescents 12-21 years of age with sickle cell crisis.

Methods: A one-group repeated measure quasi-experimental design was used to evaluate the effectiveness of using videogames on pain in a sample of adolescents 12-21 years of age. Using a repeated measures design permits intensive scrutiny of within-patient variability. Quasi-experimental study designs have been developed to provide alternative means of examining causality in situations not conducive to experimental controls. A sample of 30 hospitalized adolescents (12-21 years of age) diagnosed with sickle cell disease pain were enrolled. Recruitment of participants was undertaken at University of Illinois Children's Hospital and Advocate Children's Hospital.

Results: The Cronbach's alpha coefficient for the 19-item in level of engagement instrument was 0.82. The presence self-assessment manikin scores selected by participants after playing the videogame were 63.3% for the score of 1, 26.7% for the score of 2 and 3.3% for the scores of 3, 5 and 6. The decrease in pain level from baseline to after playing the videogame was statistically significant ($F = 29.28$, $p < 0.0001$). Additionally, the decrease in pain level from each time point and the adjacent time point was statistically significant; pain 0 minute vs pain 15 minutes ($p < 0.0001$), pain 15 minutes vs pain 30 minutes ($p < 0.0001$) and pain 30 minutes vs pain 45 minutes ($p < 0.006$). Although the data analysis did not yield statistically significant results, an inverse relationship has been found between the levels of pain and engagement.

Conclusion: Results from this study were consistent with prior literature that used similar technologies with different populations such as burn care, painful medical procedures and cancer pain. The use of videogames as a distraction modality has been proven to show positive and significant results in the treatment of acute pain. Results from this study show promising findings related to pain management that can be more accessible to adolescents with sickle cell pain at home and in the hospital setting.

AUTOBIOGRAPHICAL STATEMENT

EDUCATION

PhD in Nursing, Wayne State University, Detroit, MI- 2007-2015
Area of concentration: Hematology/ oncology, pediatrics, and cancer pain management. Thesis: Sickle Cell Pain Management
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Area of concentration: Pediatric hematology/oncology and neurosurgery.
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