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A Biopsychosocial-Spiritual Model of Chronic Pain in Adults with Sickle Cell Disease

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Abstract

Chronic pain in adults with sickle cell disease (SCD) is a complex multidimensional experience that includes biological, psychological, sociological, and spiritual factors. To date, three models of pain associated with SCD (i.e., biomedical model; biopsychosocial model for SCD pain; Health Belief Model) are published. The biopsychosocial (BPS) multidimensional approach to chronic pain developed by Turk and Gatchel is a widely used model of chronic pain. However, this model has not been applied to chronic pain associated with SCD. In addition, a spiritual/religious dimension is not included in this model. Because spirituality/religion is central to persons affected by SCD, this dimension needs to be added to any model of chronic pain in adults with SCD. In fact, data from one study suggest that spirituality/religiosity is associated with decreased pain intensity in adults with chronic pain from SCD. A BPS-Spiritual model is proposed for adults with chronic pain from SCD since it embraces the whole person. This model includes the biological, psychological, sociological, and spiritual factors relevant to adults with SCD based on past and current research. The purpose of this paper is to describe an adaptation of Turk and Gatchel's model of chronic pain for adults with SCD and to summarize research findings that support each

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component of the revised model (i.e., biological, psychological, sociological, spiritual). The paper concludes with a discussion of implications for the use of this model in research.

Keywords

sickle cell disease; chronic pain; multidimensional; biopsychosocial; spiritual

Introduction

Chronic pain in adults with sickle cell disease (SCD) is a complex multidimensional experience that includes biological, psychological, sociological, and spiritual factors (Anie, Steptoe, & Bevan, 2002; Benjamin, 2008; Cooper-Effa, Blount, Kaslow, Rothenberg, & Eckman, 2001; Gil, Carter, Porter, Scipio, & Bediako, 2004; Gil, Phillips, Webster, Martin, Abrams...Janal, 1995; Harrison, Edwards, Koenig, Bosworth, Decastro...Wood, 2005). The biopsychosocial (BPS) multidimensional approach to chronic pain developed by Turk and Gatchel (2002) is a widely used model of chronic pain. However, this model has not been applied to chronic pain associated with SCD and a spiritual/religious dimension is not included in this model. Because spirituality/religion is central to the lives of many patients, including those with chronic pain and SCD, this dimension needs to be added to any model of chronic pain in adults with SCD. In fact, data from one study suggest that spirituality/religiosity is associated with decreased pain intensity in adults with chronic pain from SCD (Harrison et al., 2005). The purpose of this paper is to describe an adaptation of Turk and Gatchel's model of chronic pain for adults with SCD and to summarize research findings that support each component of the revised model. The paper concludes with a discussion of implications for the use of this model in research.

Background and Literature Review

Sickle cell disease is an inherited blood disorder and the most common genetic disorder. It is caused by the substitution of the amino acid valine for glutamic acid at the sixth position of the beta globin chain (Ballas, 2002; Marengo-Rowe, 2006). The mutation results in abnormal hemoglobin (Hb S) that causes deoxygenated red blood cells, which change shape and block small blood vessels leading to a cascade of problems such as chronic anemia, chronic ischemia, organ damage, and acute and chronic sickle cell pain (Pace, 2007). Complications from this chronic illness make SCD a major healthcare and societal problem.

SCD is commonly found in people of African and Mediterranean descent, but can occur in any ethnic group and affects millions of people worldwide (Aliyu, Kato, Taylor, Babadoko, Mamman...Gladwin, 2008). In the United States (U.S.), SCD may affect approximately 100,000 people, the majority of whom are African American (Hassell, 2010). The prevalence of SCD may be underestimated because no national registry for SCD exists and statistics are mainly provided for African American and Hispanic persons with SCD.

Sickle cell pain is the hallmark feature of SCD (Ballas, 2005). The sickling process causes recurrent vascular occlusion, infarctive tissue damage, and a secondary inflammatory response that often results in both acute and chronic pain. Both types of pain often exist at the same time within a given individual, which makes pain in SCD unique among pain syndromes (Benjamin, Dampier, Jacox, Odesina, Phoenix...Treadwell, 1999). Of note, the majority of people with SCD manage their pain at home (Ballas, 2005; Benjamin et al., 1999; Booker, Blethyn, Wright, & Greenfield 2006; Smith, W., Penberthy, Bovbjerg, McClish, Roberts, ...Roseff, 2008).

Most of the research on pain from SCD has focused on children with acute pain associated with sickle cell crisis. Consequently, a lack of research exists on the occurrence and characteristics of chronic pain, especially in adults with SCD. Patients with SCD who experience chronic pain are often underserved and their pain is under-treated. This under-treatment may result in increased healthcare costs associated with emergency room visits, hospitalizations, and lost work productivity (Benjamin, Swinson, & Nagel, 2000). In 2004, 83,149 adults were hospitalized for SCD with approximately \$488 million in associated costs (Agency for Healthcare Research and Quality [AHRQ], 2004).

A review of the literature on the multidimensional characteristics of chronic pain in adults with SCD revealed that chronic pain in SCD can be due to many factors (Taylor, Stotts, Humphreys, Treadwell, & Miaskowski, 2010). The most common causes are recurrent pain episodes due to vaso-occlusion of the microcirculation and destruction of bones, joints, and visceral organs (Benjamin et al., 1999). However, factors other than biological factors, such as psychological and sociological factors are associated with chronic pain in adults with SCD (e.g., SCD genotype, HbF levels, co-morbidity, depression, stress; Benjamin et al., 1999; Edwards, Telfair, Cecil, & Lenoci, 2001; Gil et al., 2004; Smith, W., et al., 2008).

Spirituality is an important factor in the chronic pain experience of adults with SCD that has received little attention. In one study of adults with SCD (Harrison et al., 2005), those individuals with higher levels of spirituality/religiosity reported lower pain intensity and were better able to cope with their pain. Because of the complexity of chronic pain in adults with SCD, a multidimensional perspective is needed which embraces the whole person by focusing on biological, psychological, sociological, and spiritual factors (Anie et al., 2002; Benjamin, 2008; Cooper-Effa, et al., 2001; Gil et al., 2004; Harrison et al., 2005).

Previously Used Models of Pain in SCD

To date three models associated with pain in SCD are published (i.e., biomedical model; Maxwell, Streetly, & Bevan, 1999; BPS model for SCD pain; Smith, W., Bovbjerg, Penberthy, McClish, Levenson... Aisiku, 2005; Health Belief Model; Leavell & Ford, 1983; Rosenstock, 1974). Of the three models, the BPS Model for SCD pain is the only model that focuses on the biological, psychological, and sociological factors associated with pain in SCD. It was developed as a framework to study SCD pain and is based on the Health Utilization Model (Andersen, Kravits, & Anderson, 1971), the Health Belief Model (Rosenstock, 1974), Engel's BPS model of illness (Engel, 1977), and research on pain and responses to pain in SCD.

The BPS model of SCD pain hypothesizes that three categories of variables (i.e., disease-related, psychosocial, readiness) act together over time to explain pain and the response to pain (i.e., disability, distress, healthcare utilization) in SCD (Smith, W., et al., 2005). Disease related variables include SCD genotype, hematocrit, fetal hemoglobin (HbF) level, SCD complications and comorbidities, treatment variables (e.g., hydroxyurea, opiates, antidepressants), and pain location. Psychosocial variables include stress, mental health status, coping behaviors, social interactions, cognitive dysfunction, and functional and socioeconomic status. Readiness variables refer to an individual's readiness to utilize care and include perceived threats that result from non-utilization of healthcare and perceived benefits and barriers to healthcare utilization (Smith, W., et al., 2005). None of the models previously used for pain in SCD address spirituality. Furthermore, none of the models focus specifically on chronic pain.

BPS Model of Chronic Pain

The BPS multidimensional approach to chronic pain developed by Turk and Gatchel (2002) is a widely used model of chronic pain proposed in response to the prevalence of chronic pain and the need for a more holistic approach to chronic pain management. The BPS model of chronic pain is based on Engel's (1977) conceptualizations of the interactive processes involved in health and illness (Figure 1; Gatchel, 2004). The overall goal of the BPS model of chronic pain is to help the patient become an active participant in life management skills and learn new ways of thinking about and coping with chronic pain (Turk & Gatchel, 2002).

The key elements of the BPS model of chronic pain are biological, psychological, and social processes (Gatchel, 2004; Turk & Gatchel, 2002). Biological and psychological factors consist of central and peripheral processes and genetic predispositions. Central and peripheral processes are influenced by efferent and afferent feedback between biological and psychological systems, which in turn affect the immune system. Social factors interact with the biological and psychological system and consist of the following elements: activities of daily living (ADLs), environmental stressors, interpersonal relationships, family environment, social support/isolation, social expectations, cultural factors, medico-legal/insurance issues, previous treatment experiences, and work history. The BPS model of chronic pain hypothesizes that chronic pain is an integrated experience as a result of biological, cognitive, sensory, affective, genetic, and social factors (Gatchel, 2004; Turk & Gatchel, 2002).

Adapting Turk and Gatchel's (2002) BPS model of chronic pain for patients with SCD has several advantages. First, unlike the other three models, Turk and Gatchel's model focuses on chronic pain and has proven utility in other chronic pain populations (Angst, Verra, Lehmann, Brioschi, & Aeschlimann, 2009; Geisser, Wiggert, Haig, & Colwell, 2005; Hanley, Jensen, Ehde, Hoffman, Patterson...Robinson, 2004; Lamb, Hansen, Lall, Castelnuovo, Withers...Underwood, 2010; Peters, Vlaeyen, & Weber, 2005). In one study of patients with chronic pain (Angst et al., 2009), patients in an interdisciplinary treatment program (e.g., physiotherapy, individual psychotherapy, participation in a pain coping group, information and education about pathophysiology of pain mechanisms and management of chronic disabling pain, regular medical consultations, drug therapy) reported decreases in mean pain severity and improvement in social functioning compared to patients receiving standard care (i.e., inpatient rehabilitation and drug therapy). In another study of patients with chronic low back pain (Lamb et al., 2010), the use of cognitive behavior therapy and advice resulted in less pain severity as compared to advice alone. Second, the BPS model of chronic pain is designed to address the various mechanisms associated with chronic pain. Third, this model of chronic pain clearly demonstrates the inter-relationships among the biological, psychological, and sociological dimensions of chronic pain. Fourth, additional factors relevant to chronic pain in adults with SCD in Turk and Gatchel's model were omitted from previously published models (e.g., previous treatments, environmental stressors, cultural factors). Given the complexity of chronic pain in SCD, a model is needed that is specific to this problem. Because of its advantages over other previously used models associated with pain in adults with SCD (Maxwell et al., 1999; Smith, W., et al., 2005; Leavell & Ford, 1983; Rosenstock, 1974) this model was adapted for these patients.

Although, the BPS model of chronic pain (Turk & Gatchel, 2002) has been used in various chronic pain populations, it has not been applied to chronic pain associated with SCD. More importantly, a spiritual/religious dimension is not included in the BPS model of chronic pain. Because spirituality/religion is central to the lives of persons affected by SCD, this dimension needs to be added to any model of chronic pain in adults with SCD.

Dimensions of the BPS Model of Chronic Pain in Adults with SCD Figure 2 illustrates the revision of Turk and Gatchel's (2002) model for chronic pain in adults with SCD. The next sections of this paper summarize the current evidence for each component of the model and identify areas for future research.

Spirituality

It is a widely accepted belief that people are made up of mind, body, and spirit (Astin, 1998; Holt & McClure, 2006; Sulmasy, 2002). With this recognition, the importance of addressing spirituality in the healthcare of patients has increased in recent years (Balboni, Vanderwerker, Block, Paulk, Lathan...Prigerson, 2007; Cooper-Effa et al., 2001; Grant, Murray, Kendall, Boyd, Tilley...Ryan, 2004; Harrison et al., 2005; Koenig, 2004; McCord, Gilchrist, Grossman, King, McCormick...Srivastava, 2004). One study of participants with cancer (Balboni et al., n = 156) reported that nearly 70% of the participants found religion to be very important and nearly 50% performed private religious/spiritual activities (e.g., prayer) at least daily. In another study (McCord et al., 2004), approximately 85% of the patients reported that they wanted their spiritual issues and beliefs addressed by their physician and healthcare providers in the case of serious illness.

Nevertheless, no universal consensus exists among researchers on how to define spirituality or the distinction between spirituality and religion/religiousness. For example, spirituality is defined as the essence of an individual's personal search to cope with and find meaning and purpose in his or her life through a transcendent or connected association with a higher being (i.e., God) or elements in the universe (Dunn, 2004; Sulmasy, 2002). Spirituality is also described as a process in which people search for the sacred through a larger religious context, where the sacred includes God, the divine, transcendent, and aspects of life outside the ordinary (Hill & Pargament, 2003). Similarly, religion is defined as a set of beliefs representative of an individual's search for transcendent meaning in a particular way, generally on the basis of a belief in a deity. Religiousness/religiosity involves the practices individuals use to express their religion/spirituality (Koenig, 2004; Sulmasy, 2002, 2006).

A tendency exists for researchers to polarize spirituality and religiosity into independent constructs (Koenig, 2004). However, an important consideration is how patients define the terms. Among medical patients, a huge overlap occurs between spirituality and religiousness (Balboni et al., 2007; Koenig, 2004). Nearly 90% of medical patients consider themselves to be both spiritual and religious with similarities existing between the two (Koenig, 2004). Likewise, data suggest that persons with SCD have used the terms spirituality and religion interchangeably (Cotton, Grosseohme, Rosenthal, McGrady, Roberts...Tsevat, 2010; Jenerette & Lauderdale, 2008). Therefore, for the purposes of this manuscript, spirituality and religiosity will be used interchangeably.

A growing body of research suggests that spiritual and religious coping strategies (e.g., use of prayer, attending religious services, seeking counsel from clergy, reading the Bible, listening to spiritual/religious programs and music) are important aspects of chronic pain management (Cooper-Effa, et al., 2001; Dunn, 2004; Glover- graf, Marini, Baker, & Buck, 2007; Harrison et al., 2005; Rashiq & Dick, 2009; Rippentrop, Altmaier, Chen, Found, & Keffala, 2005). In one study of persons with chronic non-cancer pain (Rashiq & Dick, 2009, n = 65, 365), decreased risk of chronic non-cancer pain was associated with the presence of an important role in life for spirituality or faith. In another study of persons with chronic pain (Glover-Graf et al., 2007), prayer was the second most commonly used method (i.e., 61%) of coping with chronic pain.

Few studies exist on the role of spirituality/religiosity in persons with SCD (Adegbola, 2007; Cooper-Effa et al., 2001; Cotton et al., 2009; Harrison et al., 2005; Yoon & Black,

2006). In one pilot study that investigated religious/spiritual coping in adolescents with SCD (Cotton et al., 2009, n = 48), approximately 70% of participants reported that prayer helped them cope with painful episodes. In another study that investigated the pharmacologic and complementary therapies used by caregivers for the pain management of children with SCD, prayer was the most commonly used modality.

Only three studies have evaluated the impact of spirituality and religious coping in adults with SCD (Adegbola, 2007; Cooper-Effa et al., 2001; Harrison et al., 2005). In one study (Harrison et al., 2005), participants who attended church one or more times per week reported lower pain intensity ($p < .0004$). In contrast, Cooper-Effa et al. (2001) found that spiritual well-being (i.e., religiosity as a specific relationship with God, spirituality as a sense of life purpose and satisfaction) was not correlated with pain severity. Instead, spiritual well-being helped adults with SCD cope better with pain through perceptions of life control and through social support. These studies did not focus specifically on chronic pain in SCD.

Summary

Current research suggests that approximately 70% of patients feel that spirituality is an important part of their lives. Furthermore, data suggest that at least 95% of patients want their healthcare providers to address their spiritual needs. Controversy exists over how spirituality is defined, but rather than a focus on defining spirituality, researchers should concentrate on how patients define the term themselves. Research suggests that 90% of medical patients view themselves as both religious and spiritual and use the terms interchangeably. Patients with chronic illnesses (e.g., chronic pain) in particular rely on their spirituality/religion to cope with their illness. Few studies exist on the role of spirituality/religion in persons with chronic pain in SCD. At least one study in adults with SCD found an association between attending church and a decrease in pain intensity. In order to address the multidimensional aspects of chronic pain in adults with SCD, attention must be given to the spiritual/religious needs of these individuals. More studies are needed that investigate the role of spirituality/religiosity in chronic pain in adults with SCD.

Biologic factors associated with chronic pain in adults with SCD

A number of biological factors (e.g., comorbid conditions, age, gender, racial differences) impact the chronic pain experience of adults with SCD (Hofkamp, Henrickson, & Wegener, 2007). While some biological factors are common to all types of chronic pain, some are unique to persons with SCD. The unique biological factors associated with chronic pain in adults with SCD are genotype, levels of fetal hemoglobin (HbF), race, age, gender, and comorbid conditions (Ballas, 2002; Ballas, 2005; Dampier, Setty, Eggleston, Brodecki, O'Neal...Stuart, 2004; Driscoll, 2007; Platt, Thorington, Brambilla, Milner, Rosse...Kinney, 1991; Smith, W., et al., 2008). Individuals with SCD share common pathophysiologic pain mechanisms that are influenced by biological factors (i.e., genotype, HbF levels; Platt et al., 1991; Steinberg, Barton, Castro, Pegelow, Ballas...Terrin, 2003).

Pathophysiology of chronic pain in SCD—The underlying mechanism for pain in SCD is the polymerization of sickled hemoglobin, which is the primary process responsible for vaso-occlusion (Ballas, 2002; Ballas, 2005; Pace, 2007). In SCD, polymerization occurs when deoxygenated sickle hemoglobin molecules (monomers) adhere to each other and form sickle hemoglobin polymers (multiple monomers). The repeated process of polymerization and depolymerization of sickle hemoglobin distorts the shape of and damages red blood cells (RBCs). As a result of the sickling of RBCs and associated hypoxia, polymorphonuclear leukocytes release cytokines, which cause sickled and unsickled RBCs, platelets, and leukocytes to adhere to vessel walls and to each other, causes damage to the

vascular endothelium, inflammation, and results in increased sickling (Ballas, 2005; Setty & Stuart, 1996; Turhan, Weiss, Mohandas, Collier, & Frenette, 2002). This cycle results in tissue damage, which causes the release of inflammatory mediators that results in activation of peripheral nociceptors (Ballas, 2005). In addition, interactions between RBCs and the vascular endothelium lead to the release of vasoconstrictors, which further prevent blood flow, and lead to increased sickling, vaso-occlusion, and pain (Ballas, 2002; Ballas, 2005; Pace, 2007).

Pain mechanisms—The pain mechanisms associated with SCD are generally categorized as nociceptive, neuropathic, or inflammatory (Ballas, 2005). All three of these pain mechanisms can cause acute, chronic, or mixed pain in SCD. However, it is important to note that sickle cell pain is variable in nature and patients can experience nociceptive and/or neuropathic pain (Ballas, 2005; Pace, 2007).

Nociceptive pain in SCD can be visceral or somatic (Ballas, 2005; Niscola, Sorrentino, Scaramucci, de Fabritiis, & Cianiulli, 2009). It can occur during an acute vaso-occlusive episode (i.e., pain crises) or be more chronic in nature (e.g., pain associated with leg ulcers; Ballas, 2005; Niscola et al., 2009). Neuropathic pain is caused by abnormal somatosensory processing in the peripheral or central nervous system and may occur in the presence or absence of obvious central or peripheral nerve injury (Ballas, 2005; Pace, 2007).

Neuropathic pain in SCD is characterized by sensations of burning, shooting, or lancinating pain, tingling, or numbness (Ballas, 2005). In persons with SCD, neuropathic pain is associated with vaso-occlusive episodes, pain secondary to therapy (e.g., hyperalgesia secondary to opioid withdrawal, loose prosthesis, postoperative chronic pain), and pain due to comorbid conditions (e.g., trauma, arthritis, and ulcers; Ballas, 2005; Compton, Athanasos, & Elashoff, 2003; Niscola et al., 2009).

SCD is referred to as a chronic inflammatory disorder (Okpala, 2006). When RBCs sickle due to hypoxia, vascular occlusion begins, which causes infarctive tissue damage. This process in turn initiates a secondary inflammatory response (Ballas, 2005). The sympathetic nervous system may be activated, which causes the release of norepinephrine and results in increased tissue ischemia. Markers of inflammation, which are increased during both vaso-occlusive episodes and steady state SCD, include leukocytes, platelets, C-reactive protein, interleukin, fibrinogen, and activated circulating vascular endothelial cells (Okpala, 2006). During the inflammatory phase of a vaso-occlusive episode, individuals may have persistent, severe pain, which lasts four to five days (Jacob, 2001). This destructive cycle of recurrent infarctive tissue damage and secondary inflammatory responses makes pain in SCD unique in its acuteness and severity (Ballas, 2005).

Genotype—Four commonly occurring genotypes are associated with SCD (i.e., Hb SS, Hb SC, Hb S β^0 [sickle beta zero], Hb S β^+ [sickle beta plus] Platt et al., 1991). Although, the experience of chronic pain in adults with SCD is variable, genotype is one of the most important risk factors for disease severity, including the frequency and severity of pain (Ashley-Koch, Yang, & Only, 2000; Pace, 2007; Reese & Smith, 1997).

Hb SS or sickle cell anemia (SCA) is the most common form of SCD (Ashley-Koch et al., 2000). Approximately 63% of adults with SCD have Hb SS (Pace, 2007). In persons with Hb SS, both beta hemoglobin subunits contain Hb S. Therefore, their primary hemoglobin is Hb S, instead of Hb A. Persons with Hb SS have more than 90% Hb S and typically higher rates of pain crises (0.8 pain crises per year), as well as more severe pain, disease complications, and higher mortality than persons with Hb SC and Hb S β^+ thalassemia (Anie et al., 2000; Ballas, 2002; Driscoll, 2007; Pace, 2007; Platt et al., 1991).

In a longitudinal study ($N = 3578$) that evaluated the characteristics of sickle cell pain (Platt et al., 1991), the largest percentage of the sample (i.e., 67%) was persons with Hb SS. One percent of these participants reported more than six pain episodes per year. Participants with HbSS who had 3 to 10 pain episodes per year represented 32.9% of all pain episodes. In addition, participants with Hb SS who were over 20 years of age and had more than three pain episodes per year had a higher mortality rate than those with less frequent episodes and different genotypes (Platt et al., 1991). Persons with Hb SS had a median life expectancy of 45 years (Platt, Brambilla, Rosse, Milner, Castro...Klugg, 1994). Further research is needed to evaluate current life expectancy of individuals with SCD.

Approximately 29% of persons with SCD have Hb SC in which one Hb S gene and another variant hemoglobin gene, Hb C, is inherited (Driscoll, 2007). Like Hb S, Hb C is caused by a mutation at the sixth position of the beta-globin chain. However, lysine is substituted for glutamic acid. Hb C causes dehydrated RBCs, which form crystals (Mohandas & Gallagher, 2008). Fifty percent of the hemoglobin in persons with Hb SC is Hb S (Driscoll, 2007). In a cross-sectional study that examined the relationship between pain, coping, and quality of life (QOL) in adults with SCD ($N = 96$, Anie et al., 2002), participants with Hb SC had higher hemoglobin levels than participants with Hb SS (10.2 versus 8.77, respectively). Higher hemoglobin levels in persons with Hb SC were associated with less sickling of the RBCs, less vaso-occlusion, and lower pain intensity scores than in participants with Hb SS.

The average rate of pain crises in persons with Hb SC is 0.04 per year (Platt et al., 1991). Although individuals with Hb SS typically have more severe pain than those with Hb SC, in one study (Platt et al., 1991) some individuals with Hb SC had more severe pain than those with Hb SS. This finding may be due to the fact that individuals with Hb SC have an increased risk for thromboembolic complications compared to individuals with Hb SS (Platt et al., 1991). In addition, factors other than biology may influence the pain experience of persons with SCD. Persons with Hb SC had a median life expectancy of 65 years (Platt et al., 1994).

Approximately 8% of persons with SCD have Hb S β^0 thalassemia, in which one sickle gene and one beta-thalassemia gene is inherited (Pace, 2007). Like persons with Hb SS, the beta hemoglobin subunits in these individuals do not produce any normal hemoglobin. Therefore, their primary hemoglobin is Hb S (Ashley-Koch et al., 2000). Hb S accounts for more than 80% of hemoglobin in persons with S β^0 thalassemia (Driscoll, 2007). In addition to the presence of Hb S, persons with thalassemia have RBCs that are smaller and paler than normal RBCs (Park, 2004).

Individuals with S β^0 thalassemia may have severe disease, similar or identical to those with Hb SS. Consequently, much of the information on Hb SS pertains to S β^0 thalassemia (Ashley-Koch et al., 2000). Platt et al. (1991) found that patients with S β^0 thalassemia comprised the second largest group of patients who had 3 to 6 pain episodes per year, with an average of 1.0 pain crisis per year. In another study that performed daily assessments of pain in 232 adults with SCD (Smith, W., et al., 2008), participants with S β^0 thalassemia and Hb SS had the highest probability of a day with pain ($n = 73\%$). No data exist on the life expectancy of persons with S β^0 thalassemia. More research is needed on the life expectancy of these individuals.

Approximately 1% of persons with SCD have Hb S β^+ thalassemia, in which one sickle gene and one beta-thalassemia gene is inherited from each parent (Pace, 2007). However, unlike S β^0 thalassemia, the beta globin chain in these individuals produces normal hemoglobin, but in reduced quantities. Individuals with Hb S β^+ thalassemia have 60% Hb S and typically experience fewer complications than individuals with Hb SS and/or Hb S β^0 thalassemia.

(Ballas, 2002; Platt et al., 1991). These individuals experience an average of 0.4 pain crises per year (Platt et al., 1991). However, as with individuals with Hb SC, some patients with Hb S β^+ thalassemia have more severe pain than those with Hb SS (Platt et al., 1991). As with S β^0 thalassemia, more research is needed on the life expectancy of persons with Hb S β^+ thalassemia.

Levels of fetal hemoglobin (HbF)—Associations exist between levels of HbF in persons with SCD and pain and genotype. HbF is a widely recognized modulator of disease severity in SCD (Ballas, 2002). In fact, HbF levels may be the most important risk factor for disease severity in SCD. Persons with SCD and increased HbF have less sickling and less painful episodes than those with lower HbF levels (Ballas, Barton, Waclawiw, Swerdlow, Eckman...Bonds, 2006; Platt et al., 1991).

Race—Associations may exist between race, levels of HbF, and severity of chronic pain in SCD (Ballas, 2002; Center for Arab and Genetic Studies, 2007; Pace, 2007; Steinberg et al., 2003). According to the Center for Arab and Genetic Studies (2007), significantly higher levels of HbF and a milder course of SCD characterized by fewer pain crises were found in Arab-Indians versus African patients who had lower levels of HbF and more severe disease expression. More research is needed on racial/ethnic differences in the pain experiences of adults with SCD in the United States.

Age—Increased life expectancy of adults with SCD is a fairly recent phenomenon. Therefore, most of the research on pain with SCD has focused on children with acute pain. The limited amount of research on adults with chronic pain in SCD suggests a relationship between age and chronic pain in SCD (Dampier, Setty, et al., 2004; Franck, Treadwell, Jacob, & Vichinsky, 2002; Platt et al., 1991; Smith, W., et al., 2008). One study (Platt et al., 1991) found that participants 25 to 34 years of age had the highest prevalence of pain. Another study (Smith, W., et al., 2008) found that 25 to 44 year old participants had a higher probability of a pain day compared to participants who were younger and older.

Gender—Previous research suggests that women and men with SCD differ in their experience of chronic pain (Dampier, Setty, et al., 2004; Franck et al., 2002; McClish, Levenson, Penberthy, Roseff, Bovbjerg...Smith, 2006). Women may experience more painful episodes with a longer duration, have more painful sites, and have higher pain intensity scores than men. However, Anie et al. (2002) found no differences in pain intensity scores between women and men. In a longitudinal study of 226 adults with SCD (McClish et al., 2006), women scored worse (i.e., worse pain) on the bodily pain subscale of the SF-36 than men (women 43.9 versus men 53.8, $p = 0.006$). These findings are consistent with other previous studies of gender differences in chronic pain (Miaskowski, 2004; Rustøen, Wahl, Hanestad, Lerdal, Paul...Miaskowski, C. 2004).

Comorbid conditions—Comorbid conditions need to be evaluated to determine their contribution to chronic pain in adults with SCD. In one study (Smith et al., 2008), the probability of having a pain day was associated with several self-reported comorbid conditions. For example, participants with avascular necrosis had the highest probability of a pain day with or without a vaso-occlusive episode.

Avascular necrosis, leg ulcers, and gallstones are common causes of chronic pain in adults with SCD (Driscoll, 2007; Vicari, Gil, Cavalheiro, & Figueiredo, 2008; Walker, Hambleton, & Serjeant, 2000). Avascular necrosis occurs in 50% of persons with Hb SS. Roughly 10% to 25% of these adults have leg ulcers and 50% have gallstones (Driscoll, 2007; Walker et al., 2000). Avascular necrosis occurs in nearly 60% of persons with Hb SC by age 60 years

(Driscoll, 2007). Gallstones occur in about 20% of these individuals. However, this frequency may be underestimated by ultrasound (Walker et al., 2000).

Summary

Numerous biological factors can affect the chronic pain experience of adults with SCD. The genotype and HbF levels of adults with SCD appear to impact the phenotypic expression of chronic pain in these individuals more than other biological factors. That is not to say that other less well studied biological factors, such as age, gender, and comorbid conditions are not important considerations in these patients. The biological mediators (e.g., recurrent vaso-occlusive episodes, levels of HbF) associated with chronic pain in SCD differentiate it from other pain states. Furthermore, the mortality associated with the frequency of recurrent vaso-occlusive episodes makes chronic pain in SCD unique among other chronic pain conditions. The biological mechanisms of chronic pain in adults with SCD warrant further research, particularly on how these mechanisms differ from other types of chronic pain.

Psychological factors and chronic pain in adults with SCD

Mental health is an important part of overall health and therefore is a key component in the experience of chronic pain. As pain becomes more chronic in nature, the psychological state of the individual becomes increasingly more vulnerable to a wide range of conditions (e.g., depression, anxiety, catastrophizing, poor coping strategies; Turk & Monarch, 2002). Mental function (e.g., cognition, memory, concentration) and pain behaviors (e.g., active and passive coping strategies) can negatively or positively affect the experience of chronic pain (Munoz & Esteve, 2005).

Some of the psychological factors that have been studied in adults with chronic pain from SCD include emotional distress, personal beliefs, catastrophizing, and coping strategies (Anie et al., 2002; Benjamin et al., 1999; Booker et al., 2006; Edwards et al., 2001; Pace, 2007; Smith, W., et al., 2008). While research shows that chronic pain is associated with disruptions in memory (Dick & Rashid, 2007; Munoz & Esteve, 2005), no studies have investigated the impact of chronic pain on the memory of adults with SCD.

Emotional distress—Emotional distress is a major component of most chronic pain syndromes including chronic pain from SCD (Ballas, 2005). Studies of pain and mood in adults with SCD have found a positive relationship between pain intensity and negative mood (e.g., depressed, unhappy, angry/hostile, frustrated, worried/anxious; Gil et al. 2004; Porter, Gil, Carson, Anthony & Ready, 2000). Approximately 40% to 50% of adults with SCD experience depression, which is the most common psychological reaction to chronic pain in SCD (Edwards et al., 2001; Hasan, Hashmi, Alhassen, Lawson, & Castro, 2003; Schaeffer, Gil, Burchinal, Kramer, Nash...Strayhorn, 1999). In one study of 50 adults with SCD (Hasan et al., 2003), 44% of the participants scored within the mild to severe range on the Beck Depression Inventory. Participants more likely to be depressed were those with poor pain control and a history of frequent vaso-occlusive episodes.

Personal beliefs—Personal beliefs are another psychological factor associated with chronic pain in adults with SCD (Booker et al., 2006; Edwards et al., 2001). Personal beliefs can affect pain severity and can be a barrier to pain management and healthcare utilization in adults with SCD. In a qualitative study on pain management in 10 Afro-Caribbean adults with SCD (Booker et al., 2006), participants reported that they felt mistrusted and disbelieved by their healthcare providers. Some of these participants managed their pain at home, including pain due to vaso-occlusive episodes, for fear of being labeled as drug seeking. In another longitudinal study of 147 African American adults with SCD (Edwards et al., 2001), self efficacy, which is a personal belief in one's ability to engage successfully

in specific behaviors that lead to specific desired outcomes, was inversely related to the severity of physical and psychological symptoms (e.g., pain severity and anxiety, respectively). Adults with higher levels of self-efficacy had lower pain intensity. This finding is similar to data from patients with fibromyalgia, chronic low back pain, and arthritis (Barlow, Williams, & Wright, 1996; Buckelew, Murray, Hewett, Johnson, & Huyser, 1995; Lackner, Carosella, & Feuerstein, 1996).

Catastrophizing—Research suggests that persons with SCD may catastrophize more than persons with other chronic pain conditions (e.g., rheumatoid arthritis spinal, cord injury, osteoarthritis; Citero, Levenson, McClish, Bovbjerg, Cole...Smith, 2007). In fact, catastrophizing in adults with SCD and chronic pain, which is an orientation toward negative thinking, was associated with: increased pain intensity, a higher number of recurrent vaso-occlusive episodes, more healthcare utilization and work absences, depression and anxiety, decreased social activities, and decreased health-related quality of life ([HRQOL]; Anie et al., 2002; Citero et al., 2007; Gil et al., 1995; Gil et al., 2004).

Coping strategies—Several studies have reported on the coping strategies used by adults with chronic pain and SCD (Anie et al., 2002; Dampier, Ely, Brodecki, & O' Neal, 2002; Dampier, Ely, Eggleston, Brodecki, & O'Neal, 2004; Gil, Carson, Sedway, Porter, Schaeffer... Orringer, 2000; Thompson, Gil, Abrams, & Phillips, 1996; Cooper-Effa et al., 2001; Harrison et al., 2005).

These coping strategies can be categorized as active coping (e.g., ignoring pain sensations, calming self-statements, increasing activity, diverting attention, reinterpreting pain sensation), passive adherence coping (e.g., resting, taking fluids, heat/cold, massage), and affective coping (e.g., catastrophizing, praying and hoping, isolation). These coping strategies were positively associated with the number of recurrent pain episodes, pain intensity, and healthcare utilization (Anie et al., 2002; Dampier et al., 2004; Gil et al., 2000, Gil et al., 2002; Thompson et al., 1996).

Gil et al. (2000) found that daily use of coping skills was associated with more successful home management of SCD pain and fewer major healthcare contacts. Participants used more coping attempts on days that they reported increased pain. In another study (Anie et al., 2002), active coping was associated with an increased number of pain episodes, while passive coping was associated with increased pain intensity. These studies did not establish the cause of the reported pain response. It may be that patients with worse pain used more active and passive coping strategies. In other studies of chronic pain patients, participants who used higher levels of passive coping had decreased pain intensity (Conner, Tennen, Zautra, Affleck, Armeli...Fifield, 2006; Mercado, Carroll, Cassidy & Cote, 2005). However, other research on chronic pain found no association between active coping and pain intensity (Elander, Robinson, Mitchell, & Morris, 2009; McCracken & Eccleston, 2003).

Summary

Chronic pain in adults with SCD is influenced by an array of psychological factors. An understanding of the psychological dimension of chronic pain in adults with SCD has important implications for pain management. For example, the ability of these individuals to cope with chronic pain may be impeded by their current mental state. Therefore, focusing on adaptive coping responses may ameliorate some of the symptoms of chronic pain in SCD. Only recently have clinicians begun to examine the role that psychological factors play in chronic pain in SCD. More research is needed that inter-relates the biological, psychological, sociological, and spiritual factors associated with chronic pain in adults with SCD.

Sociological factors and chronic pain in adults with SCD

The interplay between sociological factors and disease is an important consideration in the management of chronic pain. Sociological factors (e.g., social support, socioeconomic status, access to healthcare, patient-provider relationship) have even been viewed as fundamentally related to disease because of their relationship to access to resources. These sociological factors affect many disease outcomes through multiple mechanisms (Link & Phelan, 1995). For these reasons, the sociological factors associated with chronic pain in adults with SCD must be given substantial consideration.

Within the BPS model of chronic pain, many sociological factors are involved in the experience of chronic pain from SCD (e.g., activities of daily living (ADLs), socioeconomic status of the affected individual, cultural factors, access to healthcare, patient-provider relationship, and social/family support; Anie et al., 2002; Pace, 2007; Smith, B., et al., 2005). Although not clearly explained in the model, as with the biological and psychological dimensions, these factors act synergistically with each other and overlap with the other dimensions.

ADLs—The relationship between ADLs and the sociological dimension of chronic pain has to do with the lack of participation in social activities caused by interruptions to an individual's social, work and sex life, mobility, and sleep due to pain (Raphael, Southall, Gnanadurai, Treharne, & Kitas, 2002). In adults with SCD, chronic pain, acute recurring vaso-occlusive episodes, and mixed pain can interfere with ADLs (e.g., decreased physical mobility and activity, impaired social functioning, sleep disturbance; Anie et al., 2002; Bodhise, Dejoie, Brandon, Simpkins, & Ballas, 2004; Haque & Telfair, 2000; Schaeffer et al., 1999). In one study (Anie et al., 2002), participants who reported more frequent pain were more impaired in their social and physical functioning.

Environmental stressors—Evidence exists to support the fact that chronic pain in adults with SCD occurs in the context of a stressful day, where stress is defined as an external demand placed on a biopsychosocial system (Gil et al., 2004; Porter et al., 2000; Porter, Gil, Sedway, Ready, Workman...Thompson, 1998; Thompson, Gil, Abrams, & Phillips, 1992, 1996). Gil et al. (2004) found that higher levels of stress were significantly associated with higher levels of same day pain ($p < .0001$) and pain two days later ($p = .05$). A reverse relationship was noted through the use of reverse-model analyses, in which SCD pain and other pain (e.g., headache, menstrual pain) predicted higher levels of stress on the subsequent two days. These findings suggest bidirectional effects, such that increased pain may lead to increased stress, which in turn may lead to more pain.

Socioeconomic status (SES)/Social Expectations—Data from chronic pain populations demonstrates an inverse relationship between SES (e.g., income, employment, educational attainment, housing accommodations) and chronic pain severity and pain related disability (Smith, B., Elliott, Chambers, Smith, W., Hannaford...Penny, 2001; McWilliams, Cox, & Enns, 2003). In the US, many persons with SCD are of low SES (Anie et al., 2002). A small body of research found an inverse relationship between SES and pain severity, pain episodes, and a negative relationship between SES and pain control in adults with chronic pain from SCD (Barrett, Wisotzek, Abel, Rouleau, Platt...Eckman, 1988; Haque & Telfair, 2000; Hasan et al., 2003). In one study (Hasan et al., 2003), participants with family incomes of less than \$10,000 had poorer pain control. Of note, these participants reported more depressive symptoms. In another cross sectional study of 1298 persons with SCD (Haque & Telfair), the SES of the participants was measured indirectly by means of a community distress index (CDI) score. The variables in the CDI were income, education, poverty, unemployment, and not being in the labor force. Participants with higher CDI

scores lived in rural areas and those with lower CDI scores lived in urban areas. The results suggested that adults who lived in rural areas (worse SES) were likely to have a lower medical index score (e.g., fewer pain episodes). However, these findings conflict with data from another study (Telfair, Haque, Etienne, Tang, & Strasser, 2003), in which adults in rural areas scored higher on the Medical Problem Index scale (e.g., more painful episodes requiring hospitalization) than those who lived in urban areas. In at least one other study of adults with various types of chronic pain (Hoffman, Meier, & Council, 2002), participants who lived in rural areas reported greater pain intensity, pain of longer duration, and greater frequency of chronic pain than those who lived in urban areas.

Access to healthcare (Medicolegal/Insurance Issues)—Adequate access to quality healthcare for adults with chronic pain from SCD is an issue that deserves attention (Benjamin, 2008; Telfair et al., 2003). Access to healthcare for these adults appears to be negatively influenced by a variety of factors (e.g., race/ethnicity, attitudes and biases of healthcare providers, SES, geographic location; Benjamin, 2008; Booker et al., 2006; Telfair et al., 2003; Pack-Mabien, Labbe, Herbert, & Haynes, 2001). The impact of these factors on access to healthcare reflects the overlap among variables in the sociological dimension of chronic pain in SCD.

In one study (Haque & Telfair, 2000), adults with more medical problems (e.g., pain episodes) tended to avoid seeking healthcare services. In addition, healthcare utilization rates were lower for participants in rural areas, perhaps because these individuals lived farther from a clinic than those who lived in urban areas. In another study of 662 rural and urban individuals with SCD in Alabama (Telfair et al., 2003), participants who lived in rural areas had lower healthcare utilization rates than those who lived in urban areas. However, these results were not statistically significant. Of note, in both of these studies, clinics and health services for adults were limited and disproportionate to those offered for children. These findings emphasize the need for more research on the relationship between access to care and chronic pain in adults with SCD.

Patient-Provider relationship (Interpersonal Relationships)—The quality of the patient-provider relationship (e.g., trust, communication) is important in the experience of chronic pain (Hirsh, Atchison, Berger, Waxenberg, Lafayette-Lucey...Robinson, 2005). Unrelieved pain can lead to mistrust of clinicians and influence how persons with chronic pain from conditions such as SCD cope with their pain (Benjamin, 2008). Most of the studies that examined the patient-provider relationship and chronic pain in SCD focused on pain management, patient coping, and prescribing practices. For example, clinicians' fears of patient addiction to prescribed analgesics have led to pain medication being withheld from adults with SCD-related pain (Pack-Mabien et al., 2001). More studies are needed that evaluate the association between the patient-provider relationship and the multidimensional experience of chronic pain in adults with SCD.

Social support—High levels of perceived social support can reduce pain severity in patients with chronic pain (Feldman, Downey, & Schaffer-Neitz, 1999). This assistance could be in the form of resources, coping assistance, social networks, and family support. Research on the relationship between social support and chronic pain in adults with SCD is very limited. Furthermore, data are inconsistent about the effects of social support on chronic pain in this population.

In a study that used the Social Functioning Scale to measure social support (Barrett et al., 1988), adults with SCD who were asymptomatic had stronger social support networks. In another study (Fox & Ingram, 1999), social support groups were helpful for patients with SCD pain. However, in another study (Lenoci, Telfair, Cecil, & Edwards, 2001), social

support, as measured by feeling supported, was not correlated with pain severity in adults with SCD. This finding may be due to poor reliability of the Feeling Supported subscale of the Chronic Illness Assessment Interview for Sickle Cell Disease ([CIAI-SCD]; i.e., Chronbach's $\alpha = 0.14$).

Family support—Persons with chronic pain who have a supportive family have significantly less pain intensity than those who have a non-supportive family (Feldman et al., 1999; Jamison & Virts, 1990). No studies have evaluated the relationship between family support and chronic pain in adults with SCD. However, Smith, W. and colleagues (2005) hypothesized that a lack of family support may affect an individual's ability to cope with chronic pain in SCD. In addition, persons with SCD and low family support may report more distress as a response to pain compared to those with high family support (Smith, W., et al., 2005).

Most studies of family support and SCD were conducted with children and did not focus on the relationship between family support and pain, but rather on the impact of SCD on family functioning or how parents cope with a child who has SCD. In one study (Haque & Telfair, 2000), adults with more medical problems, such as pain episodes, reported more interference with daily activities (e.g., relationship with family members). Two studies (Burlew, Telfair, Colangelo, & Wright, 2000; Thompson et al., 1992) found no effect of family support on pain severity or on the number of painful episodes in adolescents and adults, respectively. However, a significant inverse relationship was found between family support and anxiety and depression. A more supportive family environment was significantly associated with decreased anxiety and depression.

Summary

In order to understand the chronic pain experience of adults with SCD, it is important to consider factors such as the impact of ADLs on social life, the support from family and others, access to healthcare, patient-provider relationships, and SES. As with other research on pain in SCD, few studies have examined the relationships among chronic pain and sociological factors in adults with SCD. More research is needed to appreciate the multidimensionality of chronic pain in this population and the interplay between the sociological dimension and biological and psychological dimensions found in the BPS model.

Summary and Conclusions

SCD is a debilitating and stigmatizing disease complicated by acute and chronic pain. In the U.S. SCD affects primarily African Americans and is associated with significant economic burden. However, since no national registry exists for persons with SCD, the number of persons affected and the impact of this chronic illness on society may be underestimated. Adults with SCD have increased survival rates, but present with unique challenges due to chronic pain. Research findings suggest that chronic pain in adults with SCD is poorly understood by clinicians and undertreated.

Chronic pain in adults with SCD is multifactorial (i.e., biological, psychological, sociological, spiritual). Therefore, a multidimensional model is needed to improve the understanding of chronic pain in this population. Previously used models of pain in SCD have focused on biopsychosocial factors related to pain in SCD, but have neglected to include spirituality, thus failing to address the whole person. Research suggests spirituality is an important element of person and that many patients with chronic illnesses, including chronic pain, use spirituality/religion to cope with their pain. Furthermore, data suggest that many patients want their healthcare providers to address their spiritual needs.

Controversy exists over the definition of spirituality as some researchers use it interchangeably with religion, while others differentiate it from religion. Despite the lack of a unified definition for spirituality, considerable overlap exists between the two constructs. As many as 90% of patients consider themselves to be both spiritual and religious and use the terms interchangeably. Therefore, an important consideration for researchers and healthcare providers is how patients define and use the terms. Like many other patients, research supports that in patients with SCD and chronic pain a substantial overlap exists in spirituality and religion and that spirituality is expressed through religion.

The BPS model of chronic pain is a generic model that demonstrates the interrelationships among the biological, psychological, and sociological dimensions of chronic pain. Although a disease-specific BPS model of SCD pain was published (Smith, W., et al., 2005), the BPS model of chronic pain has several advantages over the former model. Namely, the BPS model of chronic pain addresses the various mechanisms associated with chronic pain. Furthermore, additional factors relevant to chronic pain in adults with SCD (i.e., previous treatment, environmental stressors, cultural factors) omitted from previously published models are included in this model. However, like previously published models of SCD pain (Leavell & Ford, 1983; Maxwell et al., 1999; Rosenstock, 1974; Smith, W., et al., 2005), the BPS model of chronic pain does not address spirituality.

Similar to the overlap between spirituality and religion, considerable overlap occurs within and between the biological, psychological, sociological, and spiritual dimensions of chronic pain in SCD. In fact, spirituality intersects with the psychological and sociocultural dimension of chronic pain in adults with SCD as a method of coping and social support. Although spirituality may be viewed as a sociological and/or psychological factor, it is a widely accepted belief that people are made up of mind, body, and spirit. Therefore it is necessary to add spirituality as a separate dimension to the BPS model of chronic pain and develop a BPS-Spiritual model of chronic pain in adults with SCD.

Implications for Nursing and Future Research

The management of chronic pain in adults with SCD requires a multidimensional approach focused on biological, psychological, sociological, and spiritual needs. Nurses and healthcare providers have begun to put more emphasis on the biopsychosocial factors related to chronic pain in this population. However, attention to spiritual/religious needs is lacking. Adapting a BPS-Spiritual model of chronic pain for adults with SCD may allow nurses and healthcare providers to better understand and manage the experience of chronic pain in adults, as well as, in children. Research shows that biopsychosocial factors play an important role in children's and adolescents' adaptation to SCD. The proposed BPS-Spiritual model is applicable to the pediatric SCD population as data suggest that adolescents with SCD have used religious/spiritual coping. In addition, data suggest that parents commonly use the spiritual practice of prayer to help their children cope with SCD pain (Beyer & Simmons, 2004; Cotton et al., 2009; Yoon & Black, 2006; Dampier et al., 2002). Furthermore, the model is applicable to the inpatient, as well as, outpatient setting (Bediako, Lattimer, Haywood, Ratanawongsa, Lanzkron...Beach, 2010; Benjamin et al., 2008; Harrison et al., 2005; Smith, W., et al., 2005). Few studies have examined some of the factors involved in the proposed BPS-Spiritual model (e.g., pain mechanisms, memory, sleep, SES, social support/family support, access to healthcare, patient provider relationship, spirituality/religiosity) and their relationship to chronic pain. More research is needed that investigates these relationships in adults with chronic pain from SCD.

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Figure 1.

A conceptual model of the biopsychosocial interactive processes involved in health and illness. From "Comorbidity of Chronic Pain and Mental Health Disorders: The Biopsychosocial Perspective," by R. J. Gatchel, *American Psychologist*, 59(8), 795–805. Copyright © 2004 by the American Psychological Association. Reproduced with permission.

Figure 2.

A conceptual model of the Biopsychosocial-Spiritual Model of Chronic Pain in Adults with Sickle Cell Disease by L.V. Taylor. Copyright © 2010. Adapted from A conceptual model of the biopsychosocial interactive processes involved in health and illness. From "Comorbidity of Chronic Pain and Mental Health Disorders: The Biopsychosocial Perspective," by R. J. Gatchel, *American Psychologist*, 59(8), 795–805. Copyright © 2004 by the American Psychological Association. Adapted with permission.