HHS Public Access

Author manuscript

Med Clin North Am. Author manuscript; available in PMC 2017 January 01.

Published in final edited form as:

Med Clin North Am. 2016 January ; 100(1): 183–197. doi:10.1016/j.mcna.2015.08.013.

Managing Chronic Pain in Special Populations with Emphasis on Pediatric, Geriatric, and Drug Abuser Populations

Kyle M. Baumbauer[1,2,4], **Erin E. Young**[1,3,4], **Angela R. Starkweather**[1], **Jessica W. Guite**[5], **Beth S. Russell**[7], and **Renee C. Manworren**[1,6]

[1]School of Nursing and the Center for Advancing Management of Pain, University of Connecticut, Storrs, CT

[2]Department of Neuroscience, University of Connecticut Health Center, Farmington, CT

[3]Department of Genetics and Genome Sciences, University of Connecticut Health Center, Farmington, CT

[4]Institute for Systems Genomics, University of Connecticut Health Center, Farmington, CT

[5]Department of Pediatrics, University of Connecticut School of Medicine, Hartford Hospital/The Institute of Living, and the Division of Pain Medicine, Connecticut Children's Medical Center, Hartford, CT

[6]Division of Pain and Palliative Medicine, Department of Pediatrics, Connecticut Children's Medical Center, Hartford, CT

[7]Human Development & Family Studies, University of Connecticut, Storrs, CT

Synopsis

Chronic pain represents a significant health and societal concern. In the adult population chronic pain can lead to loss of productivity, earning potential, and decreased quality of life. Research has typically focused on otherwise healthy adults with chronic pain conditions; however there appear to be distinct groups with increased vulnerability for the emergence of chronic pain. These groups may be defined by developmental status and/or life circumstances that increase the risk of injury or for which treatment of pain is less effective. Within the pediatric, geriatric, and drug abuser populations, chronic pain also represents a significant health issue, which can lead to increased absenteeism during school age years, as well as decreased quality of life and increased risk of additional adverse health conditions later in life. Currently, little is known about the mechanisms that encourage the development of chronic pain in these groups, and, consequently, pediatric, geriatric, and substance abuse patients represent challenging cohorts to manage. We focus on known anatomic, physiologic, and genetic mechanisms underlying chronic pain in these

Corresponding Author: Renee C. Manworren, PhD, APRN, BC, PCNS-BC, FAAN, Division of Pain and Palliative Medicine, Department of Pediatrics Connecticut Children's Medical Center, 100 Retreat Avenue, 5th floor, Hartford, CT 06106, (860) 837-5217, Rmanworren@connecticutchildrens.org.

populations, and highlight the need for a multimodal approach from multiple healthcare professionals for management of chronic pain in those with the most risk.

Keywords

chronic pain; pain management; multimodal treatment; pediatric pain; geriatric pain

Introduction

Pain serves as an evolutionarily adaptive tool to warn of tissue damage and allow for subsequent tissue repair. For unknown reasons, in some individuals the normally adaptive pain system is hijacked in some individuals and chronic pain ensues. Numerous laboratories are currently examining the neural and non-neural mechanisms that both initiate and support the persistence of pain in human and non-human models. Meanwhile, clinicians face the daunting task of treating patients with chronic pain based on incomplete information regarding the causative mechanisms and limiting options to facilitate resolution of pain. Multimodal treatment plans involve the use of analgesics that target the pharmacological mechanisms underlying analgesia and nociception in conjunction with psychological and physical therapy. Although research indicates these interventions reduce pain and improve function, a significant number of patients continue to suffer. Moreover, healthcare professionals face growing frustration in treating chronic pain patients with chronic pain due in no small part to challenges involved in ascertaining personalized pain management strategies for those at greatest need. Identifying those individuals at the greatest risk for developing treatment resistant chronic pain may lead to the development of novel strategies to mitigate suffering and disability.

The incidence of chronic pain is 20–25% worldwide and fewer than half of patients report experiencing adequate relief (Gold & Gebhart, 2010). This prevalence can be substantially higher in the most vulnerable populations. For example, pediatric and geriatric patients are particularly susceptible to the development of chronic pain, as well as individuals who are prone to substance abuse. The purpose of this review is to highlight potential mechanisms of vulnerability for chronic pain during periods in which this risk may be most readily revealed – the extremes of age: pediatrics and geriatrics. We propose anatomical, physiological, and genetic mechanisms that may contribute to chronic pain susceptibility, and describe unique strategies for managing pain in geriatric and pediatric patients.

Pediatric Chronic Pain

While chronic pain diagnoses are less frequent in pediatric populations compared to adults, their prevention and management may influence lifelong health outcomes. Chronic pediatric pain can have debilitating medical, emotional, social, functional, and economic consequences for youth and their families. (Bursch, Walco, & Zeltzer, 1998; Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001; Palermo, 2000; L. S. Walker, Garber, & Greene, 1993; Zernikow et al., 2012). Up to 40% report significant effects on school attendance, social engagement, appetite, sleep, and health service utilization which can continue into adulthood (Fearon & Hotopf, 2001; Hotopf, Carr, Mayou, Wadsworth, &

Wessely, 1998; Hotopf, Mayou, Wadsworth, & Wessely, 1999; Hotopf, Wilson Jones, Mayou, Wadsworth, & Wessely, 2000; Lynn S. Walker, Dengler-Crish, Rippel, & Bruehl, 2010). Moreover, periods of rapid development may represent times of enhanced vulnerability for chronic pain. Research from both human and animal models indicate that early life pain exposure may alter neurodevelopment and increase the likelihood of long-term, maladaptive changes on neurally-mediated behaviors (e.g., pain, cognition, social interactions and emotional experiences) (Schneider, 2013). Pediatric chronic pain prevalence estimates vary by pain location with a high degree of variability in both location and prevalence of pain. (King et al., 2011) For example, headache is most prevalent and reported in 8–83% of children, followed by abdominal pain (4–53%), musculoskeletal pain (4–40%), and back pain (14–24%).

Children as young as 3 years of age may be able to provide a self-report of pain intensity with simple developmentally appropriate and validated tools. (Herr, Coyne, McCaffery, Manworren, & Merkel, 2011). When elicited, children and adolescents with chronic pain commonly report moderate to severe pain intensity, which often much greater than expected. This discordance reflects the attenuation of overt behavioral signs of pain as pain becomes chronic. Social cues may trigger the pediatric patient's behavioral expression of pain, but there are no reliable or recommended observational measures of pediatric chronic pain (Herr et al., 2011; McGrath et al., 2008; von Baeyer & Spagrud, 2007; Stinson, Kavanagh, Yamada, Gill, & Stevens, 2006). By consensus, pediatric pain management experts recommend assessment of pain intensity, physical functioning, emotional functioning, role functioning, symptoms and adverse events related to treatment and pain, global judgment of satisfaction with treatment, and sleep (McGrath et al., 2008). Obtaining self-report pain intensity ratings over time may be more valuable than single ratings and both paper and electronic pain diaries have been tested for developmental appropriateness and validity in children as young as 6 years (McGrath et al., 2008). At least two measures of physical functioning have been validated for children and adolescents with chronic pain, the Functional Disability Index and the Peds QL. The Peds QL is also a valid measure of emotional, social, and school functioning for children 2 to 18 years of age (McGrath et al., 2008). There are several other well-validated measures for emotional function, such as the Children's Depressive Inventory and the Revised Child Anxiety and Depression Scale. Role functioning can be assessed by school attendance and with the PedsMIDAS. Additional measures, including measures of satisfaction with treatment and sleep, have emerging validity or are in development (Zempsky et al., 2013). Assessment of pain quality, timing, location, aggravating and alleviating factors may provide vital information for diagnosis and treatment. In addition, risk factors, such as pain catastrophizing and caregiver burden, may be valuable for developing a family-centered multimodal pain management plan.

Opioids are rarely used in multimodal pediatric chronic pain management plans. Traditional analgesics and other pharmacologic therapies that are routinely used in adults may be trialed in the pediatric patient, however few pharmacologic therapies are FDA approved and indicated for the treatment of chronic pediatric pain. A vital and uniquely pediatric component of the multimodal treatment plan for pediatric patients with chronic pain is pharmacologic strategies for managing acute procedurally based pain, such as topical dermal anesthetics prior to needle procedures. Optimal management for the discomfort and distress

of even these short procedures should be coupled with coping strategies and biobehavioral therapies. These anxiety provoking procedures are often necessary during the child's initial diagnostic work-up, but repeated and exhausted diagnostic testing is often not medically indicated and may actually be a barrier to pain treatment by delaying appropriate therapies and allowing catastrophizing to perseverate.

As pain in children and adolescents recurs, persists and becomes chronic, resources for effective coping may be depleted. Therefore, the resulting disability associated with pediatric chronic pain [i.e., "pain-associated disability syndrome" (Bursch, Walco, & Zeltzer, 1998)] frequently becomes the primary focus of intervention. At the most basic level, the management of pain requires patients to contend with unpleasant physical and emotional experiences; those who manage these experiences adaptively utilize self-regulatory skills to modulate the intensity and duration of a given moment, often relying on psychological and behavioral coping skills to do so (Gross, 1998; Tennen, Affleck, Armeli, & Carney, 2000). Coping is best described as the set of cognitive and behavioral efforts taken to manage distressing circumstances, which requires the perception of a situation as stressful and the effortful or planned steps to manage resulting emotions (emotion focused coping) and/or the situation itself (problem focused coping; (Lazarus & Folkman, 1984). Hence coping with an uncomfortable sensation requires that the individual attend to the stimuli sufficiently to interpret the experience as unpleasant and to take steps to reduce the discomfort.

While pediatric treatment plans are multimodal (e.g., include medical, physical, psychological and behavioral components), lack of engagement in treatment can result in school absenteeism, increased use of emergency departments, and hospital admissions. Increased parenting stress and interference in parent's regular roles/activities is a common challenge for families with a child with chronic pain. Hence, caregiver burden and parenting stress are markedly heightened in these families and subsequently pose risks to adaptive family functioning. Prior research has shown that threatening beliefs about pain such as pain catastrophizing influence the types of strategies used to cope with pain (Van Slyke, 2001; Guite, 2001; Lynn S. Walker, Smith, Garber, & Claar, 2005; Caes, Vervoort, Eccleston, Vandenhende, & Goubert, 2011). Parental catastrophizing about their child's pain further contributes to the child's disability as well as to parenting stress (Goubert, Eccleston, Vervoort, Jordan, & Crombez, 2006; Caes et al., 2011; Vowles, Cohen, McCracken, & Eccleston, 2010). Our previous work documents significant agreement in adolescent-parent dyad reports of pain catastrophizing (Guite et al., 2014). Moreover, we have found that parental protective responses to their child's pain is associated with disability indirectly through pain catastrophizing at an initial clinic visit and two months later (Welkom, Hwang, & Guite, 2013).

Social cognitive models of development (Bandura, 1991; Bandura, 2001) posit that a sense of competence in exerting control over circumstances results in patients' beliefs that they can take effective steps to mitigate their discomfort, stressing the importance of social reinforcement to develop a sense of personal efficacy in the face of pain. Recent advancements in cognitive behavioral therapies that target coping skills to improve distress tolerance have demonstrated consistent benefit in pediatric patients with chronic pain

(Davis, Zautra, Wolf, Tennen, & Yeung, 2015; Lynch-Jordan, 2015; Morley, Eccleston, & Williams, 1999; Reiner, Tibi, & Lipsitz, 2013). Cognitive behavioral mindfulness interventions aim to bolster pediatric patients' abilities to self-monitor their physical and psychological state, maintain a non-judgmental interpretive frame for their experiences, and to slow impulsive responses to discomfort (Carlson, 2014; Day, Jensen, Ehde, & Thorn, 2014).

Geriatric Chronic Pain

The risk for chronic pain conditions increases with age, making the geriatric population particularly vulnerable. National surveys of pain in older adults from North America, Europe, Asia and Australia found that over 50% of respondents reported bothersome pain in the last month (Patel, Guralnik, Dansie, & Turk, 2013; Leadley, Armstrong, Lee, Allen, & Kleijnen, 2012; Henderson, Harrison, Britt, Bayram, & Miller, 2013; Jackson, Chen, Iezzi, Yee, & Chen, 2014). The estimated incidence of chronic pain in adults is 4.69 per 100 person-years, and the prevalence of chronic pain in individuals over 85 years is as high as 79% (Shi, Hooten, Roberts, & Warner, 2010). Pain in older adults is significant problem worldwide; and is associated with reduced activity, falls, mood disorders, sleep disturbances, isolation and substantial disability; factors that compromise quality of life and well-being. Persistent pain may lead to frailty, compromising general health and functional status (Shega et al., 2012; Shega et al., 2013). Although pain management can be successfully implemented for the majority of older adults, pain remains undertreated in the oldest old, African Americans and ethnic minorities as well as individuals with cognitive impairment (Malec & Shega, 2015). Overall, older adults are less likely to receive analgesics compared to young adult patients despite the significant ramifications to general health and well-being (Hwang et al., 2014).

Neurophysiological changes associated with aging appear to influence pain processing, with evidence to support a general increase in pain threshold and reduced pain tolerance from deterioration of the pathways involved in endogenous inhibition. An age-related increase in pain threshold to thermal stimuli may be related to loss in the structure and function of the peripheral (Aδ fibers) and CNS pathways implicated in the processing of noxious information (Hadjistavropoulos et al., 2014). Experimental pain studies provide some evidence of reduced sensitivity to mild pain with advancing age, particularly for thermal pain (Gibson & Farrell, 2004). Other types of pain stimuli (i.e. mechanical, electrical) are more equivocal with reports of no change or decreased thresholds in older adults (Lautenbacher, 2012). In contrast, results from ten independent studies showed reduced pain tolerance as a function of age, irrespective of stimulus method (Gibson & Farrell, 2004; Lautenbacher, 2012). In addition, temporal summation of noxious heat is enhanced in the CNS of older adults compared to younger individuals (Edwards & Fillingim, 2001). Age-related impairment in opioid and non-opioid mechanisms of the endogenous pain inhibitory systems have been described, showing less than a third of the strength of induced effects on sensitivity when compared with younger adults (Riley, King, Wong, Fillingim, & Mauderli, 2010; Morley et al., 1999). Collectively, these studies suggest that aging increases vulnerability to persistent severe pain owing to reduced pain tolerance and impaired endogenous pain-modulating capacities.

In concert with age-associated changes in somatosensory function, chronic comorbidities often contribute to pain including musculoskeletal disorders, diabetes, and cancer, particularly with advanced stages of chronic disease. In addition, pain may result from treatments, such as surgery and chemotherapy (Reid, Eccleston, & Pillemer, 2015). In medically complex populations, such as older adults who are incarcerated, severe frequent pain is common and associated with difficulty in performing activities of daily living and limited independence (Williams et al., 2014). Risk factors for chronic pain include advancing age, lower socioeconomic status, lower educational level, obesity, tobacco use, history of injury, strenuous job, childhood trauma and psychological comorbidity, especially depression and anxiety (Reid et al., 2015). The identification of risk factors that may influence long-term outcomes may be one avenue of informing the type and intensity of therapeutic modalities. For instance, at the initial presentation of musculoskeletal pain in older adults, three brief items have been shown to predict lack of patient improvement at six months; degree of interference from pain, pain in multiple body sites, and duration of pain (Mallen et al., 2013). An assessment of risk factors for persistent pain or poor clinical outcomes should be incorporated in the clinical examination and used to develop a multi-modal treatment approach.

A comprehensive pain history and physical exam focused on cognitive, motor and sensory assessments as well as diagnostic tests when indicated, provides a foundation for the development of treatment approaches for the older adult (Hadjistavropoulos et al., 2014). This should include administering standardized pain assessment tools, identifying the impact of pain on mood and functioning as well as attitudes and beliefs about pain (Makris, Abrams, Gurland, & Reid, 2014). Input may be sought from family and/or caregivers when possible to assist in the sharing of information and implementation of the plan of care. In older adults with cognitive impairment or nonverbal individuals, pain assessment should include attempts at self-report, review of painful conditions, evaluation of pain behaviors, and family/caregiver interviews. Well-established general principles for the management of pain have been published, including those of the American Geriatrics Society and American Pain Society (2009).

Specific physiological changes in older adults need to be considered when selecting appropriate analgesic therapy (Hadjistavropoulos et al., 2014). Older adults have reduced intravascular volume and muscle mass that may alter drug distribution resulting in increased plasma levels relative to younger individuals. This can result in increased volume of distribution of fat-soluble opioids (i.e.. fentanyl) because of great fat-to-lean body mass ratio while decreased total body water can result in increased plasma levels of hydrophilic opioids (i.e. morphine). Renal clearance (glomerular filtration, tubular reabsorption, and secretion) decrease at a rate of 6–10% per decade beginning at age 30 years. Thus reduced renal function without underlying kidney disease is common in older adults. In addition, hepatic clearance is reduced due to decreased hepatic blood flow. Nonsteroidal anti-inflammatory drugs are not recommended by the American Geriatrics Society, especially long-term use because of the high risk of adverse effects on the gastrointestinal, cardiovascular and renal systems. Taken together, dosage reduction (25–50%) of medications used to treat pain in older adults are typically necessary, particularly at initiation of treatment (Gupta & Avram, 2012).

Although respiratory depression is rare in opioid-naïve patients who are prescribed initial low dose opioid therapy, the risk increases with older age, opioid dose and underlying pulmonary conditions, particularly sleep apnea and chronic obstructive pulmonary disease. In addition the concomitant use of other central nervous system depressants, such as alcohol, benzodiazepines or barbiturates, with opioids can significantly increase the risk of respiratory depression. Research on addiction and misuse in older adults is sparse, however, the prevalence is thought to be much lower than younger populations. An approach of "universal precautions" is recommended for any patient prescribed opioids, including the administration of opioid risk stratification tools and adherence monitoring (Steinman, Komaiko, Fung, & Ritchie, 2015).

Multi-modal approaches to pain management are encouraged including cognitive behavioral therapy, self-management programs, rehabilitation, and exercise programs. While there are a growing number of well-designed studies evaluating pharmacological and non-pharmacological therapies there are a number of factors that limit the generalizability of findings. Longitudinal designs are needed to evaluate short- and long-term outcomes with diverse study populations that include participants in the oldest-old category (>80 years). Data regarding treatment adherence including long-term safety and efficacy of different modalities, particularly multi-modal approaches, are needed as well as identification of optimal strategies for the delivery of non-pharmacological approaches. Understanding the neurophysiological changes that influence pain in later life, including those with cognitive impairment, is important for ensuring adequate and ethical treatment at the end of life. Studies to test innovative treatment approaches will help to inform the delivery of multi-modal treatment approaches that entail less adverse effects. Research on cost, quality and safety outcomes of multidisciplinary approaches for the management of pain are needed to inform policy decisions and standards of care.

Substance Abusers: A Special Population

Recent evidence suggests that approximately 10% of the population over 12 years of age report recent substance use (SAMHSA, 2011) with an estimated 5.1 million of these individuals indicating misuse specifically of prescription pain relievers. The estimated societal cost of drug misuse and/or diversion exceeds $500 billion annually (NDIC, 2010; NCASA, 2011). Recent reviews of opioid abuse in the chronic pain population indicates that the potential risk factors for substance abuse in this population include genetic variation in opioid receptor and drug metabolism-associated genes, demographic factors (including age), pain severity and drug related factors (i.e., physician reported aberrant use behavior), family history of substance use, and psychiatric comorbidity (Sehgal, Manchikanti, & Smith, 2012). Other studies have consistently identified familial substance use and co-morbid mental health diagnoses (e.g., affective disorders including depression) as significant predictors of addiction in chronic pain samples and, further, that peer influence and substance use is of particular salience to models of use in younger samples (Ewing et al., 2015; Fergusson, Boden, & Horwood, 2008; Jamison et al., 2010; Wasan et al., 2007). Impulsivity and sensation-seeking personality traits have also been consistently identified as risk factors for substance abuse across the lifespan (Acton, 2003; McNamee et al., 2008; Staiger, Kambouropoulos, & Dawe, 2007; Young, McCabe, Cranford, Ross-Durow, & Boyd, 2012)

and hold considerable value as intervention targets to stem the rates of substance abuse among chronic pain patients.

The most prevalent motivation for medical misuse of opioids (84.2%) is “to relieve pain” (McCabe, West, & Boyd, 2013). Pain relievers are more commonly used for nonmedical uses than any other class of prescription medications (Viana et al., 2012; A. M. Young, Glover, & Havens, 2012) and nonmedical use of prescription analgesics - specifically opioid analgesics like oxycodone - has substantially increased in recent years (National Drug Intelligence Center, 2010; Substance Abuse and Mental Health Services Administration, 2010) (Miech, Bohnert, Heard, & Boardman, 2013). Drug misuse is reported in approximately 40% of pain patients with half (20%) of those identified as substance abusers and a much smaller proportion (2–5%) identified as addicts (Gourlay, Heit, & Almahrezi, 2005). However, healthcare professionals may overestimate the prevalence of those patients who seek prescription medication in response to addiction vs. those that are seeking medication to relieve chronic pain (Baker, 2005). Furthermore, healthcare professionals may perceive the development of an addiction as being a “flip of the switch” phenomenon, but evidence suggests a slow developmental trajectory (Ballantyne & LaForge, 2007; Manworren, 2014). As a result of both societal and healthcare specific beliefs about addiction, substance abusers/addicts may feel stigmatized and may be less likely to disclose their addiction (Arnstein, 2010; McCaffery, 2011). However, the World Health Organization has identified pain relief as a fundamental human right. When diagnosed with a comorbid chronic pain condition, the medical management of these patients is particularly challenging given their prior history of substance abuse. The American Society for Pain Management Nursing Position Statement on Pain Management in Patients with Substance Use Disorders clearly supports maintenance of dignity, respect, and high quality pain management in this population (Oliver et al., 2012) despite their increased risk for subsequent misuse.

Beyond an understanding of the broad predictors of substance use and addiction in the chronic pain population, medical professionals are wise to consider the developmental and social context in which patients will employ recommended pain management plans. Compared to adult populations, choices about adolescent nonmedical drug use are especially informed by sociocultural contexts (Maccoun, 2006; Olthuis, Darredeau, & Barrett, 2013). Currie & Wild (2012) posit that adolescents may choose analgesics because they believe analgesics are safer given pervasive marketing for pain medication in American culture. Consideration for the cognitive development of children and adolescents provides crucial elements to comprehensive models for substance use: Beyond personality traits including anxiety, impulsivity, and novelty seeking tendencies, normative changes in future-oriented thinking, risk assessment, and perspective taking all contribute to adolescents’ vulnerability to substance abuse – a vulnerability that is heightened during the normative neuroproliferation and subsequent synaptic pruning in the frontal lobes seen in to the early 20s (Schepis, Adinoff, & Rao, 2008; Stanger, Budney, & Bickel, 2013; Stanger, Elton, et al., 2013).

Genetics as a fundamental vulnerability across the lifespan

Chronic pain can be described as a condition of complex etiology reflecting the interaction of environmental (e.g. illness, injury, etc.) and genetic factors over the lifespan. With this in mind, genetic susceptibility to develop chronic pain is, arguably, one of the primary determinants of vulnerability across age, developmental status, and lifetime experience. Understanding the genetic underpinnings of chronic pain susceptibility may allow for prevention and earlier diagnosis as well as the development of novel therapeutic interventions specifically targeting the fundamental mechanisms of vulnerability.

Twin studies and genetic association studies have both been used to shed light on the inherited nature of chronic pain risk. The former provides evidence for heritability by determining how much of the variability in pain occurrence is due to genetics and how much is due to non-genetic factors while the latter designed to identify and/or test the influence of individual genes on susceptibility to a given chronic pain condition. Twin studies offer the opportunity to evaluate polygenic inheritance without *a priori* hypotheses, which is a useful tool in the formation of subsequent specific empirical questions about mechanism. Data from twin studies estimate specific heritability for low back pain and neck pain to be ~60% and ~50% respectively (MacGregor, Andrew, Sambrook, & Spector, 2004). Other chronic pain conditions, including migraine (Wessman, Terwindt, Kaunisto, Palotie, & Ophoff, 2007), pelvic pain (Zondervan, Cardon, Kennedy, Martin, & Treloar, 2005), irritable bowel syndrome (Lembo, Zaman, Jones, & Talley, 2007; Levy et al., 2001), chronic widespread pain (Kato, Sullivan, Evengard, & Pedersen, 2006), and osteoarthritis (Page, Hoaglund, Steinbach, & Heath, 2003; Spector & MacGregor, 2004) also exhibit significant heritability from 30–75%. While these methods do not indicate a specific gene or set of genes that convey inherited risk for chronic pain, they do confirm that risk for these chronic conditions is heritable and encourage further investigation into the mechanisms by which risk is inherited.

Findings from candidate gene studies have shed light on the contribution of specific genetic variations to the risk of developing chronic pain. Reports from both animal models and clinical populations have identified genetic variations that convey chronic pain risk. Single nucleotide polymorphisms (SNPs) within a number of genes have been associated with risk or protection against the development of chronic pain, though some of the specific mechanisms remain to be fully elucidated. SNPs within the Catechol-O-methyltransferase (*COMT*) gene known to play a role in inactivation of dopamine, norepinephrine, and epinephrine, have been linked with altered experimental pain sensitivity as well as susceptibility to chronic musculoskeletal and neuropathic pain (Belfer & Segall, 2011; Diatchenko et al., 2005). Variation within *ADRB2*, encoding the beta 2 adrenergic receptor, has been associated with variability in self-reports of the extent and duration of pain in patients with CWP, a finding in agreement with a previously reported association between *ADRB2* haplotypes and an increased risk for TMD pain. Associations have also been revealed between polymorphisms within the serotonin transporter gene *(SLC6A4*), specifically the associated serotonin transporter linked promoter region (5-*HTTLPR*), and risk for developing fibromyalgia (Buskila & Neumann, 2005). Along these same lines, a single SNP within *HTR2A*, the gene encoding the serotonin receptor 2A, has also been

associated with an increased risk of CWP diagnosis (Nicholl et al., 2011) and post-surgical pain burden (Aoki et al., 2010). Variations in signaling within both the serotonin and catecholamine systems have been linked with risk for depression, anxiety, and other psychological health issues, which may have implications for efficacy of treatment strategies targeting the negative cognitive and emotional aspects of chronic pain (Elder & Mosack, 2011; Helton & Lohoff, 2015) and/or pain modulation.

Genetic polymorphisms unrelated to neurotransmission have also been associated with chronic pain susceptibility. Many of these genes are involved in ion channel function and directly affect the dynamics of the cellular response to noxious stimulation. *SCN9A* encodes the alpha subunit of the voltage-gated sodium channel NaV1.7 and evidence suggests a role for *SCN9A* in determining risk for chronic pain conditions, including sciatica, osteoarthritis, chronic pancreatitis, and phantom limb pain, as well as variation in pain responding within normal populations(Reimann et al., 2010). Rare gain-of-function mutations of this gene have been implicated in primary erythromelalgia and paroxysmal extreme pain disorder while loss of function variants result in the congenital insensitivity to pain (CIPA) characterized by an inability to feel pain (Cox et al., 2010; Drenth & Waxman, 2007; Reimann et al., 2010). These findings indicate a fundamental role for sodium channel function in the transmission of pain signals and confirm that this process must remain in delicate balance in order to prevent maladaptive changes conducive to chronic pain development. Others have found that a single SNP within *KCNS1*, the gene encoding a voltage-gated potassium channel (subfamily S, member 1), increased risk for chronic pain in 5 separate clinical cohorts from patient populations with a high prevalence of pain reporting (Costigan et al., 2010). Variation within two genes related to calcium channel function, *CACNA2D3* (encodes the alpha 2 delta 3 subunit of the voltage dependent calcium channel) and *CACNG2* (encodes the gamma 2 subunit of voltage dependent calcium channel) have been shown to play a role in susceptibility to chronic back pain following lumbar discectomy and chronic post-mastectomy pain, respectively (Neely et al., 2010; Nissenbaum et al., 2010).

The responses to every injury, every surgery, every illness are shaped by the context of our genetic makeup. This framework shapes our physical and emotional experience to a painful experience and sets the stage for long-term changes that may be adaptive (recovery and return to normal function) or maladaptive (development of chronic pain and dysfunction). Taken together, these findings suggest that the future of personalized medicine may include genetic testing as part of the decision-making process between patient and physician. The ultimate goal would be to develop a comprehensive list of “chronic pain genes” to be used for risk assessment in healthcare settings. This would be particularly important when the treatment plan includes procedures with high risk for developing chronic pain (e.g. amputation, chemotherapy, surgical procedures, etc.). The frustration reported by medical professionals regarding the treatment of chronic pain patients as well as the stigmatization of chronic pain patients as “difficult” could be decreased by further elucidation of the underlying mechanisms of chronic pain vulnerability.

Conclusion

The geriatric, pediatric, and substance abuser populations represent groups with difficult to manage chronic pain. The therapeutic approach in each group should be multimodal, but include components that meet the unique needs of patients. Further research is required to fully understand how chronic pain develops and evolves in each of these patient groups. In particular, as our understanding of the physiological and genetic mechanisms underlying chronic pain in these understudied populations improves, advances in treatment options will also improve. Undoubtedly, treatment will still continue to utilize a multimodal approach and cooperative efforts between all healthcare professionals involved in the pain management team.

References

Acton GS. Measurement of impulsivity in a hierarchical model of personality traits: implications for substance use. Subst Use Misuse. 2003; 38(1):67–83. [PubMed: 12602807]

American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain on older persons. Journal of the American Geriatric Society. 2009; 57(8):1331–1346.

Aoki J, Ikeda K, Murayama O, Yoshihara E, Ogai Y, Iwahashi K. The association between personality, pain threshold and a single nucleotide polymorphism (rs3813034) in the 3'-untranslated region of the serotonin transporter gene (SLC6A4). J Clin Neurosci. 2010; 17(5):574–578. [PubMed: 20303273]

Arnstein P. Is my patient drug-seeking or in need of pain relief? Nursing. 2010; 40(5):60–61. [PubMed: 20386408]

Baker K. Chronic pain syndromes in the emergency department: identifying guidelines for management. Emerg Med Australas. 2005; 17(1):57–64. [PubMed: 15675906]

Ballantyne JC, LaForge KS. Opioid dependence and addiction during opioid treatment of chronic pain. Pain. 2007; 129(3):235–255. [PubMed: 17482363]

Bandura A. Social cognitive theory of self-regulation. Organizational Behavior and Human Decision Processes. 1991; 50(2):248–297.

Bandura A. Social cognitive theory; An agentic perspective. Annual review of psychology. 2001; 52:1–26.

Belfer I, Segall S. COMT genetic variants and pain. Drugs Today. 2011; 47(6):457–467. [PubMed: 21695287]

Bursch B, Walco GA, Zeltzer L. Clinical assessment and management of chronic pain and pain-associated disability syndrome. J Dev Behav Pediatr. 1998; 19(1):45–53. [PubMed: 9524306]

Bursch B, Walco GA, Zeltzer LK. Clinical assessment and management of chronic pain and pain-associated disability syndrome. Journal of Developmental and Behavioral Pediatrics. 1998; 19(1): 45–53. [PubMed: 9524306]

Buskila D, Neumann L. Genetics of fibromyalgia. Curr Pain Headache Rep. 2005; 9(5):313–315. [PubMed: 16157058]

Caes L, Vervoort T, Eccleston C, Vandenhende M, Goubert L. Parental catastrophizing about child's pain and its relationship with activity restriction: The mediating role of parental distress. Pain. 2011; 152(1):212–222. [PubMed: 21126822]

Carlson, M. CBT for chronic pain and psychological well-being: A skills training manual integrating DBT, ACT, behavioral activation and motivational interviewing. Hoboken, NJ: Wiley-Blackwell; 2014.

Costigan M, Belfer I, Griffin RS, Dai F, Barrett LB, Coppola G, Woolf CJ. Multiple chronic pain states are associated with a common amino acid-changing allele in KCNS1. Brain. 2010; 133(9): 2519–2527. [PubMed: 20724292]

Cox JJ, Sheynin J, Shorer Z, Reimann F, Nicholas AK, Zubovic L, Parvari R. Congenital insensitivity to pain: novel SCN9A missense and in-frame deletion mutations. Hum Mutat. 2010; 31(9):E1670–1686. [PubMed: 20635406]

Currie CL, Wild TC. Adolescent use of prescription drugs to get high in Canada. Can J Psychiatry. 2012; 57(12):745–751. [PubMed: 23228233]

Davis MC, Zautra AJ, Wolf LD, Tennen H, Yeung EW. Mindfulness and cognitive–behavioral interventions for chronic pain: Differential effects on daily pain reactivity and stress reactivity. Journal of Consulting and Clinical Psychology. 2015; 83(1):24–35. [PubMed: 25365778]

Day MA, Jensen MP, Ehde DM, Thorn BE. Toward a theoretical model for mindfulness-based pain management. J Pain. 2014; 15(7):691–703. [PubMed: 24985483]

Diatchenko L, Slade GD, Nackley AG, Bhalang K, Sigurdsson A, Belfer I, Maixner W. Genetic basis for individual variations in pain perception and the development of a chronic pain condition. Human Molecular Genetics. 2005; 14(1):135–143. [PubMed: 15537663]

Drenth JP, Waxman SG. Mutations in sodium-channel gene SCN9A cause a spectrum of human genetic pain disorders. J Clin Invest. 2007; 117(12):3603–3609. [PubMed: 18060017]

Edwards RR, Fillingim RB. Effects of age on temporal summation and habituation of thermal pain: clinical relevance in healthy older and younger adults. J Pain. 2001; 2(6):307–317. [PubMed: 14622810]

Elder BL, Mosack V. Genetics of depression: an overview of the current science. Issues Ment Health Nurs. 2011; 32(4):192–202. [PubMed: 21355753]

Ewing BA, Osilla KC, Pedersen ER, Hunter SB, Miles JN, D'Amico EJ. Longitudinal family effects on substance use among an at-risk adolescent sample. Addict Behav. 2015; 41:185–191. [PubMed: 25452064]

Fearon P, Hotopf M. Relation between headache in childhood and physical and psychiatric symptoms in adulthood: national birth cohort study. British Medical Journal. 2001; 322(12 May):1145. [PubMed: 11348907]

Fergusson DM, Boden JM, Horwood LJ. The developmental antecedents of illicit drug use: evidence from a 25-year longitudinal study. Drug Alcohol Depend. 2008; 96(1–2):165–177. [PubMed: 18423900]

Gibson SJ, Farrell M. A review of age differences in the neurophysiology of nociception and the perceptual experience of pain. Clin J Pain. 2004; 20(4):227–239. [PubMed: 15218407]

Gold MS, Gebhart GF. Nociceptor sensitization in pain pathogenesis. Nat Med. 2010; 16(11):1248–1257. [PubMed: 20948530]

Goubert L, Eccleston C, Vervoort T, Jordan A, Crombez G. Parental catastrophizing about their child's pain. The parent version of the Pain Catastrophizing Scale (PCS-P): a preliminary validation. Pain. 2006; 123(3):254–263. [PubMed: 16644128]

Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. Pain Med. 2005; 6(2):107–112. [PubMed: 15773874]

Gross JJ. The emerging field of emotion regulation: An integrative review. Review of General Psychology. 1998; 2(3):271–299.

Guite, JW. The relation of psychological and biomedical factors to children's experience of abdominal pain. (doctoral dissertation). Nashville, TN: Vanderbilt University; 2001.

Guite, Jessica W.; Kim, Sohee; Chen, Chia-Pei; Sherker, Jennifer L.; Sherry, David D.; Rose, John B.; Hwang, Wei-Ting. Pain beliefs and readiness to change among adolescents with chronic musculoskeletal pain and their parents before an initial pain clinic evaluation. The Clinical Journal of Pain. 2014; 30(1):27–35. [PubMed: 23446077]

Gupta DK, Avram MJ. Rational Opioid Dosing in the Elderly: Dose and Dosing Interval When Initiating Opioid Therapy. Clinical Pharmacology & Therapeutics. 2012; 91(2):339–343. [PubMed: 22205194]

Hadjistavropoulos T, Herr K, Prkachin KM, Craig KD, Gibson SJ, Lukas A, Smith JH. Pain assessment in elderly adults with dementia. Lancet Neurol. 2014; 13(12):1216–1227. [PubMed: 25453461]

Helton SG, Lohoff FW. Serotonin pathway polymorphisms and the treatment of major depressive disorder and anxiety disorders. Pharmacogenomics. 2015; 16(5):541–553. [PubMed: 25916524]

Henderson JV, Harrison CM, Britt HC, Bayram CF, Miller GC. Prevalence, causes, severity, impact, and management of chronic pain in Australian general practice patients. Pain Med. 2013; 14(9): 1346–1361. [PubMed: 23855874]

Herr K, Coyne PJ, McCaffery M, Manworren R, Merkel S. Pain assessment in the patient unable to self-report: position statement with clinical practice recommendations. Pain Manag Nurs. 2011; 12(4):230–250. [PubMed: 22117755]

Hotopf M, Carr S, Mayou R, Wadsworth M, Wessely S. Why do children have chronic abdominal pain, and what happens to them when they grow up? Population based cohort study. British Medical Journal. 1998; 316(7139):1196–1200. [PubMed: 9552994]

Hotopf M, Mayou R, Wadsworth M, Wessely S. Childhood risk factors for adults with medically unexplained symptoms: results from a national birth cohort study. American Journal of Psychiatry. 1999; 156(11):1796–1800. [PubMed: 10553745]

Hotopf M, Wilson Jones C, Mayou R, Wadsworth M, Wessely S. Childhood predictors of adult medically unexplained hospitalisations. Results from a national birth cohort study. British Journal of Psychiatry. 2000; 176:273–280. [PubMed: 10755076]

Hwang U, Belland LK, Handel DA, Yadav K, Heard K, Rivera-Reyes L, Morrison RS. Is all pain is treated equally? A multicenter evaluation of acute pain care by age. Pain. 2014; 155(12):2568–2574. [PubMed: 25244947]

Jackson T, Chen H, Iezzi T, Yee M, Chen F. Prevalence and correlates of chronic pain in a random population study of adults in Chongqing, China. Clin J Pain. 2014; 30(4):346–352. [PubMed: 23887340]

Jamison RN, Ross EL, Michna E, Chen LQ, Holcomb C, Wasan AD. Substance misuse treatment for high-risk chronic pain patients on opioid therapy: a randomized trial. Pain. 2010; 150(3):390–400. [PubMed: 20334973]

Kashikar-Zuck S, Goldschneider KR, Powers SW, Vaught MH, Hershey AD. Depression and functional disability in chronic pediatric pain. Clinical Journal of Pain. 2001; 17:341–349. [PubMed: 11783815]

Kato K, Sullivan PF, Evengard B, Pedersen NL. Importance of genetic influences on chronic widespread pain. Arthritis Rheum. 2006; 54(5):1682–1686. [PubMed: 16646040]

King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, MacDonald AJ. The epidemiology of chronic pain in children and adolescents revisited: A systematic review. Pain. 2011; 152(12):2729–2738. [PubMed: 22078064]

Lautenbacher S. Experimental approaches in the study of pain in the elderly. Pain Med. 2012; 13(Suppl 2):S44–S50. [PubMed: 22497747]

Lazarus, RS.; Folkman, S. Stress, appraisal, and coping. Springer Pub. Co.; 1984.

Leadley RM, Armstrong N, Lee YC, Allen A, Kleijnen J. Chronic diseases in the European Union: the prevalence and health cost implications of chronic pain. J Pain Palliat Care Pharmacother. 2012; 26(4):310–325. [PubMed: 23216170]

Lembo A, Zaman M, Jones M, Talley NJ. Influence of genetics on irritable bowel syndrome, gastro-oesophageal reflux and dyspepsia: a twin study. Aliment Pharmacol Ther. 2007; 25(11):1343–1350. [PubMed: 17509102]

Levy RL, Jones KR, Whitehead WE, Feld SI, Talley NJ, Corey LA. Irritable bowel syndrome in twins: heredity and social learning both contribute to etiology. Gastroenterology. 2001; 121(4):799–804. [PubMed: 11606493]

Lynch-Jordan AM, Sil S, Cunningham NR, Joffe N, Slater SK, Tran ST, Crosby LE. Measuring treatment response in an outpatient pediatric pain program. Clinical Practice in Pediatric Psychology. 2015; 3(1):1–11.

Maccoun RJ. Competing accounts of the gateway effect: the field thins, but still no clear winner. Addiction. 2006; 101(4):473–474. discussion 474–476. [PubMed: 16548926]

MacGregor AJ, Andrew T, Sambrook PN, Spector TD. Structural, psychological, and genetic influences on low back and neck pain: a study of adult female twins. Arthritis Rheum. 2004; 51(2): 160–167. [PubMed: 15077255]

Makris UE, Abrams RC, Gurland B, Reid MC. Management of persistent pain in the older patient: a clinical review. JAMA. 2014; 312(8):825–836. [PubMed: 25157726]

Malec M, Shega JW. Pain management in the elderly. Med Clin North Am. 2015; 99(2):337–350. [PubMed: 25700587]

Mallen CD, Thomas E, Belcher J, Rathod T, Croft P, Peat G. Point-of-care prognosis for common musculoskeletal pain in older adults. JAMA Intern Med. 2013; 173(12):1119–1125. [PubMed: 23699833]

Manworren RC. Pediatric nursing knowledge and attitude survey regarding pain. Pediatr Nurs. 2014; 40(1):50. [PubMed: 24757922]

McCabe SE, West BT, Boyd CJ. Motives for medical misuse of prescription opioids among adolescents. J Pain. 2013; 14(10):1208–1216. [PubMed: 23954519]

McCaffery M. Stigma and misconceptions related to addictive disease. American Nurse Today. 2011; 6(6)

McGrath PJ, Walco GA, Turk DC, Dworkin RH, Brown MT, Davidson K, PedImmpact. Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. J Pain. 2008; 9(9):771–783. [PubMed: 18562251]

McNamee RL, Dunfee KL, Luna B, Clark DB, Eddy WF, Tarter RE. Brain activation, response inhibition, and increased risk for substance use disorder. Alcohol Clin Exp Res. 2008; 32(3):405–413. [PubMed: 18302723]

Miech R, Bohnert A, Heard K, Boardman J. Increasing use of nonmedical analgesics among younger cohorts in the United States: a birth cohort effect. J Adolesc Health. 2013; 52(1):35–41. [PubMed: 23260832]

Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. Pain. 1999; 80(1–2):1–13. [PubMed: 10204712]

Neely GG, Hess A, Costigan M, Keene AC, Goulas S, Langeslag M, Penninger JM. A genome-wide Drosophila screen for heat nociception identifies alpha2delta3 as an evolutionarily conserved pain gene. Cell. 2010; 143(4):628–638. [PubMed: 21074052]

Nicholl BI, Holliday KL, Macfarlane GJ, Thomson W, Davies KA, O'Neill TW, European Male Ageing Study, G. Association of HTR2A polymorphisms with chronic widespread pain and the extent of musculoskeletal pain: results from two population-based cohorts. Arthritis Rheum. 2011; 63(3):810–818. [PubMed: 21305503]

Nissenbaum J, Devor M, Seltzer Z, Gebauer M, Michaelis M, Tal M, Darvasi A. Susceptibility to chronic pain following nerve injury is genetically affected by CACNG2. Genome Res. 2010; 20(9):1180–1190. [PubMed: 20688780]

Oliver J, Coggins C, Compton P, Hagan S, Matteliano D, Stanton M, Turner HN. American Society for Pain Management nursing position statement: pain management in patients with substance use disorders. Pain Manag Nurs. 2012; 13(3):169–183. [PubMed: 22929604]

Olthuis JV, Darredeau C, Barrett SP. Substance use initiation: the role of simultaneous polysubstance use. Drug Alcohol Rev. 2013; 32(1):67–71. [PubMed: 22612987]

Page WF, Hoaglund FT, Steinbach LS, Heath AC. Primary osteoarthritis of the hip in monozygotic and dizygotic male twins. Twin Res. 2003; 6(2):147–151. [PubMed: 12724001]

Palermo TM. Impact of recurrent and chronic pain on child and family daily functioning: A critical review of the literature. Journal of Developmental and Behavioral Pediatrics. 2000; 21(1):58–69. [PubMed: 10706352]

Patel KV, Guralnik JM, Dansie EJ, Turk DC. Prevalence and impact of pain among older adults in the United States: findings from the 2011 National Health and Aging Trends Study. Pain. 2013; 154(12):2649–2657. [PubMed: 24287107]

Reid MC, Eccleston C, Pillemer K. Management of chronic pain in older adults. BMJ. 2015; 350:h532. [PubMed: 25680884]

Reimann F, Cox JJ, Belfer I, Diatchenko L, Zaykin DV, McHale DP, Woods CG. Pain perception is altered by a nucleotide polymorphism in SCN9A. Proc Natl Acad Sci U S A. 2010; 107(11):5148–5153. [PubMed: 20212137]

Reiner K, Tibi L, Lipsitz JD. Do mindfulness-based interventions reduce pain intensity? A critical review of the literature. Pain Med. 2013; 14(2):230–242. [PubMed: 23240921]

Riley JL 3rd, King CD, Wong F, Fillingim RB, Mauderli AP. Lack of endogenous modulation and reduced decay of prolonged heat pain in older adults. Pain. 2010; 150(1):153–160. [PubMed: 20546997]

Schepis TS, Adinoff B, Rao U. Neurobiological processes in adolescent addictive disorders. Am J Addict. 2008; 17(1):6–23. [PubMed: 18214718]

Schneider M. Adolescence as a vulnerable period to alter rodent behavior. Cell Tissue Res. 2013; 354(1):99–106. [PubMed: 23430475]

Sehgal N, Manchikanti L, Smith HS. Prescription opioid abuse in chronic pain: a review of opioid abuse predictors and strategies to curb opioid abuse. Pain Physician. 2012; 15(3 Suppl):ES67–ES92. [PubMed: 22786463]

Shega JW, Andrew M, Kotwal A, Lau DT, Herr K, Ersek M, Dale W. Relationship between persistent pain and 5-year mortality: a population-based prospective cohort study. J Am Geriatr Soc. 2013; 61(12):2135–2141. [PubMed: 24320761]

Shega JW, Dale W, Andrew M, Paice J, Rockwood K, Weiner DK. Persistent pain and frailty: a case for homeostenosis. J Am Geriatr Soc. 2012; 60(1):113–117. [PubMed: 22150394]

Shi Y, Hooten WM, Roberts RO, Warner DO. Modifiable risk factors for incidence of pain in older adults. Pain. 2010; 151(2):366–371. [PubMed: 20696524]

Spector TD, MacGregor AJ. Risk factors for osteoarthritis: genetics. Osteoarthritis Cartilage. 2004; 12(Suppl A):S39–S44. [PubMed: 14698640]

Staiger PK, Kambouropoulos N, Dawe S. Should personality traits be considered when refining substance misuse treatment programs? Drug Alcohol Rev. 2007; 26(1):17–23. [PubMed: 17364832]

Stanger C, Budney AJ, Bickel WK. A developmental perspective on neuroeconomic mechanisms of contingency management. Psychol Addict Behav. 2013; 27(2):403–415. [PubMed: 22663343]

Stanger C, Elton A, Ryan SR, James GA, Budney AJ, Kilts CD. Neuroeconomics and adolescent substance abuse: individual differences in neural networks and delay discounting. J Am Acad Child Adolesc Psychiatry. 2013; 52(7):747–755. e746. [PubMed: 23800488]

Steinman MA, Komaiko KD, Fung KZ, Ritchie CS. Use of opioids and other analgesics by older adults in the United States, 1999–2010. Pain Med. 2015; 16(2):319–327. [PubMed: 25352175]

Stinson JN, Kavanagh T, Yamada J, Gill N, Stevens B. Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents. Pain. 2006; 125(1–2):143–157. [PubMed: 16777328]

Tennen H, Affleck G, Armeli S, Carney MA. A daily process approach to coping: Linking theory, research, and practice. American Psychologist. 2000; 55(6):626–636. [PubMed: 10892205]

Van Slyke, DA. Parent influences on children's pain behavior. (doctoral dissertation). Nashville: Vanderbilt University; 2001.

Viana AG, Trent L, Tull MT, Heiden L, Damon JD, Hight TL, Young J. Non-medical use of prescription drugs among Mississippi youth: constitutional, psychological, and family factors. Addict Behav. 2012; 37(12):1382–1388. [PubMed: 22781877]

von Baeyer CL, Spagrud LJ. Systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years. Pain. 2007; 127(1–2):140–150. [PubMed: 16996689]

Vowles KE, Cohen LL, McCracken LM, Eccleston C. Disentangling the complex relations among caregiver and adolescent responses to adolescent chronic pain. Pain. 2010; 151(3):680–686. [PubMed: 20833472]

Walker LS, Dengler-Crish CM, Rippel S, Bruehl S. Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood. Pain. 2010; 150(3):568–572. [PubMed: 20615615]

Walker LS, Garber J, Greene JW. Psychosocial correlates of recurrent childhood pain: A comparison of pediatric patients with recurrent abdominal pain, organic illness, and psychiatric disorders. Journal of Abnormal Psychology. 1993; 102(2):248–258. [PubMed: 8315137]

Walker LS, Smith CA, Garber J, Claar RL. Testing a Model of Pain Appraisal and Coping in Children With Chronic Abdominal Pain. Health Psychology. 2005; 24(4):364–374. [PubMed: 16045372]

Wasan AD, Butler SF, Budman SH, Benoit C, Fernandez K, Jamison RN. Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. Clin J Pain. 2007; 23(4):307–315. [PubMed: 17449991]

Welkom JS, Hwang WT, Guite JW. Adolescent pain catastrophizing mediates the relationship between protective parental responses to pain and disability over time. The Journal of Pediatric Psychology. 2013; 38(5):541–550. [PubMed: 23471361]

Wessman M, Terwindt GM, Kaunisto MA, Palotie A, Ophoff RA. Migraine: a complex genetic disorder. Lancet Neurol. 2007; 6(6):521–532. [PubMed: 17509487]

Williams BA, Ahalt C, Stijacic-Cenzer I, Smith AK, Goldenson J, Ritchie CS. Pain behind bars: the epidemiology of pain in older jail inmates in a county jail. J Palliat Med. 2014; 17(12):1336–1343. [PubMed: 25265035]

Young A, McCabe SE, Cranford JA, Ross-Durow P, Boyd CJ. Nonmedical use of prescription opioids among adolescents: subtypes based on motivation for use. J Addict Dis. 2012; 31(4):332–341. [PubMed: 23244552]

Young AM, Glover N, Havens JR. Nonmedical use of prescription medications among adolescents in the United States: a systematic review. J Adolesc Health. 2012; 51(1):6–17. [PubMed: 22727071]

Zempsky WT, O'Hara EA, Santanelli JP, Palermo TM, New T, Smith-Whitley K, Casella JF. Validation of the sickle cell disease pain burden interview-youth. J Pain. 2013; 14(9):975–982. [PubMed: 23701707]

Zernikow B, Wager J, Hechler T, Hasan C, Rohr U, Dobe M. Characteristics of highly impaired children with severe chronic pain: a 5-year retrospective study on 2249 pediatric pain patients. BMC Pediatrics. 2012; 12:54. doi: doi: 1471-2431-12-54 [pii]. [PubMed: 22591492]

Zondervan KT, Cardon LR, Kennedy SH, Martin NG, Treloar SA. Multivariate genetic analysis of chronic pelvic pain and associated phenotypes. Behav Genet. 2005; 35(2):177–188. [PubMed: 15685430]

Key Points

- The developmental status and genetic background of the patient should be considered during chronic pain treatment
- Pediatric, geriatric, and drug abuser patients have unique demands for pain management
- A multimodal treatment approach should be utilized for pain management