



## Pediatric Pain: New Approaches for Our Most Vulnerable Patients

# Psychiatric Considerations in Pediatric Chronic Pain

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**C**hronic pain can greatly affect a patient's daily functioning and significantly impact health-related quality of life (*Pain* 2005;119:1-4). Undertreated or untreated chronic pain in children can be especially burdensome to families by disrupting routines, restricting the child's daily activities, and increasing risk of long-term disability (*Paediatr Drugs* 2002;4:737-46). Therefore, it is not unusual for chronic pain to be highly comorbid with psychiatric disorders. This association is mediated by significant overlap in biological pathways.

First, central and peripheral noradrenergic (NA) and serotonergic (5-HT) pathways are affected in both pain and mood disorders (*Prog Neuropsychopharmacol Biol Psychiatry* 2018;87B:290-7; *J Psychiatry Neurosci* 2001;26:21-9). A pathway involving serotonergic neurons in the dorsal raphe nucleus has been implicated in chronic pain as well as depression (*Nat Neurosci* 2019;22:1612-4). Both NA and 5-HT brainstem-spinal descending systems suppress nociceptive signals from afferent neurons, and the activation of spinal NA and 5-HT receptors has antinociceptive effects. Second, glutamate signaling, particularly signaling through

AMPA receptors, plays a key role in regulating pain, depression, and depression in the context of chronic pain (*Neural Plast* 2015;2015:504691). In addition to NA, 5HT, and glutamate, endocannabinoid signaling plays important roles in regulating both depression and pain. Pain-induced depression may also have unique physiologic and molecular mechanisms, possibly related to endocannabinoid signaling via the CB2 receptor (*Pain* 2009;143:206-12). Additionally, neuroplasticity and neuroinflammation are seen in both depression and chronic pain, and the central nervous system undergoes long-term plastic changes associated with chronic pain and depression (*Neural Plast* 2015;2015:504691). Brain-derived neurotrophic factor, a biomarker of depression (*Curr Pharm Des* 2017;23:3154-63), is elevated in patients suffering from chronic pain (*Neurosci Lett* 2019;706:105-9). The same can be said about inflammatory factors like interleukin-6 and C-reactive protein, which are elevated in both depression (*Transl Psychiatry* 2019;9:127) and fibromyalgia (*Cytokine* 2016;84:25-8). Lastly, neuroimaging studies have revealed similar structural changes in the amygdala, hippocampus, and limbic structures of patients with chronic pain, depres-

sion, and anxiety (*Rev Colomb Psiquiatr* 2018;47:46-55).

### Psychiatric disorders and chronic pain

Studies suggest that youth with psychiatric disorders have higher rates of chronic pain (*Headache* 2019;59:306-38) and that the prevalence of some psychiatric disorders varies depending on the type of chronic pain. Temporal associations were also found between the onset of mental health disorders and the onset of chronic pain. The greatest association was found when onset of mental disorder preceded onset of pain. However, no significant associations were found when onset of pain preceded onset of mental disorders (*J Pain* 2015;16:1054-64). Generally speaking, 40% of adolescents admitted with chronic pain have a comorbid mental health condition, primarily mood disorders (28%) and anxiety disorders (18%) (*Pediatrics* 2013;132:e422-9). Others have estimated that the most common illnesses in the outpatient population are anxiety disorders (*J Pain* 2015;16:1054-64; *Pain Res Manag* 2012;17:93-7).

Studies have shown a mutual maintenance of depression in conjunction with pediatric chronic pain (*Clin J Pain*

2019;35:633-43). Correspondingly, adolescents with chronic pain have a 24.5% lifetime rate of depression, higher than the 14.1% rate of depression without chronic pain (*Pain* 2016;157:1333-8). Depression is also considered a risk factor for both the development and progression of chronic migraine in youth (*Headache* 2019;59:306-38). Overall, psychiatric issues such as depression, anxiety, and self-harm are the most common comorbid conditions with migraine in pediatric patients (*Pediatr Neurol* 2019;97:26-9).

### Anxiety and other disorders

Anxiety also is associated with higher rates of pain (*Pediatr Neurol* 2019;97:26-9), and adolescents with chronic pain have higher lifetime rates of anxiety. This association exhibits a sex bias. Girls with anxiety have a 2.6 times greater prevalence of headaches, a 100 times greater prevalence of stomach aches and headaches together, and a 3.4 times greater prevalence of musculoskeletal pain than girls without an anxiety disorder (*J Am Acad Child Adolesc Psychiatry* 1999;38:852-60). In contrast, boys show no association between anxiety and somatic complaint. However, boys with

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### A Multidisciplinary Approach

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Therapy for Chronic Pain in Children and Adolescents. 2012; *Pain* 2016;157:174-85; *PM R* 2013;5:697-704). Increasing a sense of self-efficacy and gaining skills to manage pain are the ultimate goals. These skills decrease their affective reaction to chronic pain and reduce the catastrophic thoughts that frequently accompany the experience of pain (*Children (Basel)* 2016;3:30; *Pain* 2012;153:1863-70; *J Pediatr Psychol* 2013;38:756-65).

Today, image-guided pediatric chronic interventional pain medicine is a new subspecialty of pain management that uses techniques such as spine injections, joint injections, musculoskeletal injections, and nerve blocks. These treatments are effective for sports injuries, and children require fewer injections than do adult patients who have degenerative changes. However, the outcomes of patients who



The multidisciplinary team concluding the diagnosis and treatment plan with the patient and family.

receive pediatric interventional techniques for chronic pain are dependent on the experience and skill of the operator, especially when these interventions are performed in children who are under sedation or general anesthesia. Therefore, practitioners must be trained in an ac-

credited fellowship program. Moreover, pediatric interventional chronic pain management is a new specialty without sufficient data regarding success rates.

The concept of a multidisciplinary facility for the diagnosis and treatment of complex pain problems has been in-

creasingly embraced by medical professionals (*Pediatrics* 2015;136:115-27). As noted by Vasudevan, "Unlike unimodal, uncoordinated and 'quick fix' pain treatment, multidisciplinary pain programs use a rehabilitation approach in which a 'cure' for the pain or the underlying condition causing the pain is not the goal/aim." (Multidisciplinary Management of Chronic Pain, 2015) In fact, it is counterproductive to imply that patient improvement requires waiting until an explanation and cure can be found. Children living with pain, and their families, can improve their quality of life by replacing pain-related behaviors and negative thinking with behaviors and perspectives that reinforce quality of life. This approach allows individuals with chronic pain to return to a more functional and satisfying life. Thus, chronic pain in the pediatric population is reversible when treated through a multidisciplinary approach. ■

## Psychiatric Considerations

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oppositional defiant disorder or attention deficit hyperactivity disorder were more likely to have stomach aches, and boys with conduct disorder were more likely to have headaches (*J Am Acad Child Adolesc Psychiatry* 1999;38:852-60).

Another study reported that functional neurological disorder and other somatization disorders were present in 6% of children admitted with chronic pain and that 2.4% of those children had post-traumatic stress disorder (*Pediatrics* 2013;132:e422-9). Also, a cohort study found higher levels of post-traumatic stress disorder symptoms in both youth with chronic pain and their parents (*Pain* 2016;157:2277-84).

Chronic pain can also cause changes in the eating habits of adolescents, causing comorbid eating disorders in some cases. However, eating disorders can also precede the development of chronic pain (*J Pediatr Health Care* 2017;31:67-74). Interestingly, a search of the literature did not identify any articles describing comorbidity between chronic pain and psychotic disorders in pediatric and adolescent populations.

One non-negligible comorbidity of chronic pain is suicide. Chronic pain is undoubtedly a risk factor for suicide in adults (*Aging Ment Health* 2016;20:166-94); however, the data are inconclusive in youth. A 2017 study of 186 adolescents found that the occurrence of suicidal ideation was similar among youth with and without chronic pain (*Clin J Pain* 2017;33:21-7). However, in 2011, a much larger study of 9,970 adolescents reported that rates of suicide ideation and attempts were higher among youth who had chronic pain than among those who did not (*J Pain* 2011;12:1032-9). Interestingly, Lewcun et al. (*Psychol Serv* 2018;15:309-15) found that most types of pain were predictive of developing suicidal ideation and that a longer duration of amplified pain could be a risk factor for suicidal ideation. Notably, the comorbidity between suicidality and chronic pain could be mediated by depressive symptoms.

### Guiding principles for treatment

Given the close association between psychiatric disorders and chronic pain, it is critical to screen and treat these disorders concomitantly to achieve positive outcomes. A few principles guide the treatment for children suffering from both psychiatric disorders and chronic pain. The treatment of choice remains a multidisciplinary approach that addresses pain with biological, psychological, and social aspects (*Am Psychol* 2014;69:119-30). The disciplines contributing to this approach are psychiatry and psychology for mental



health disorders; surgery and rheumatology for injections and surgical interventions; anesthesiology for pharmacological and interventional analgesia; and physical and occupational therapy to increase functionality (*Am Psychol* 2014;69:119-30; *Med Clin North Am* 2016;100:55-64; *Rheumatol Int* 2017;37:29-42). Involvement of these disciplines has proven to be superior to usual care for increasing functionality and decreasing pain and disability in patients with chronic pain (*BMJ* 2015;350:h444).

From a risk assessment perspective, it is imperative to screen for suicidal ideation in this population. From a pharmacological perspective, it is recommended that practitioners use the “start low and go

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slow” approach because most treatment modalities have been extrapolated from adults with few guidelines for the pediatric population. Moreover, several medications used to treat the target symptoms may increase suicidal ideation. In recent years, the opioid crisis shed light on the need for adequate non-opioid treatment options. Thus, several non-opioid psychiatric drugs could be used off-label to treat pain and psychiatric disorders simultaneously.

First, antidepressants are often used for analgesic, antidepressant, and anxiolytic effects (*Prog Neuropsychopharmacol Biol Psychiatry* 2018;87B:290-7). Tricyclic

antidepressants (TCAs) and selective serotonin and noradrenaline reuptake inhibitors (SNRIs) are considered first-line treatments, whereas selective serotonin reuptake inhibitors (SSRIs) are considered second-line treatment and bupropion third-line (*Eur J Neurol* 2010;17:1113-e88). It is important to note that analgesia is achieved at lower doses than those needed to address depression (*Am Psychol* 2014;69:119-30). TCAs are also ineffective for depression in youth (*Prog Neuropsychopharmacol Biol Psychiatry* 2018;87B:290-7). Duloxetine, which has been approved by the Food and Drug Administration for anxiety in youth, is the most-reported drug prescription in the pediatric pain population and in one study was found to be particularly effective for treating isolated peripheral neuralgia with associated depression in teenagers (*Paediatr Anaesth* 2014;24:608-13).

Second, antiepileptics, which are widely used for pain, are also effective for some psychiatric disorders. Gabapentin is particularly useful in generalized anxiety disorder (GAD) with social anxiety disorder and alcohol withdrawal symptoms (*Front Psychiatry* 2019;10:228), and pregabalin is somewhat efficacious for GAD (*Ann Pharmacother* 2012;46:424-9). Valproate and topiramate, two known mood stabilizers, are also used, especially in the management of chronic daily headache. Benzodiazepines have a well-established role in managing anxiety disorders associated with chronic pain and may be considered for short-term therapy in patients with concurrent anxiety disorders and low back pain (*Prog Neuropsychopharmacol Biol Psychiatry* 2018;87 B:290-7).

Third, cannabis is used mainly in palliative settings in the U.S.

Non-psychopharmacological interventions include therapies such as physical therapy, cognitive-behavioral therapy (CBT), biofeedback, yoga (*PM R* 2015;7:S295-S315), and mindfulness.



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CBT effectively decreases the intensity of chronic pain in youth while also reducing distress and the interference of pain in day-to-day activities (*Pain* 2010;148:387-97). CBT is also beneficial for anxiety and depression in adolescents with comorbid inflammatory bowel disease (*J Am Acad Child Adolesc Psychiatry* 2007;46:1290-8).

In conclusion, psychiatric disorders are a non-negligible comorbidity of chronic pain. This association can be explained in part by shared neurobiological pathways between chronic pain and psychiatric diseases and also by the negative physical and psychosocial sequelae of chronic pain. Depression is one of the most common psychiatric comorbidities of chronic pain and is the most common in the inpatient population. In contrast, anxiety is the most common comorbidity for outpatient community youth. This distinction may be explained by the fact that admitted patients have more severe illness and higher disability, making depression a more likely comorbidity. The risk of suicide should be evaluated in all patients. Treatment approaches for youth with chronic pain and psychiatric disorders have been extrapolated from adults; therefore, additional research with randomized controlled trials is required to inform treatment in youth. Finally, addressing comorbid mental health illnesses in patients with chronic pain syndromes will have a positive effect on both the pain and patients' ability to manage their pain, and is integral to improving treatment outcome. ■