Pediatric Chronic Pain: Biopsychosocial Assessment and Formulation

Christina Liossi, DPsych,[a,b] Richard F. Howard, MBChB[b]

Chronic pain in children is an increasingly recognized clinical problem with alarmingly high prevalence rates found in some populations. Although it is not understood why some children experience high levels of pain, the subjective experience of chronic pain (including its site, intensity, quality, unpleasantness, and associated suffering) has long been believed to result from interactions between multiple contributors, including nociceptive, affective, sociocultural, behavioral, and cognitive. Regardless of whether the antecedent of chronic pain is known or unknown, similar patterns of symptoms, behaviors, and disability are often seen. Historically, however, there has been an unhelpful tendency to dichotomize chronic pain as either physical or functional in origin. However, recent studies strongly support a biopsychosocial basis to all pain, revealing its sensory emotional nature by showing that large distributed neural networks are accessed during nociceptive processing. The development and maintenance of chronic pain involve long-term changes in multiple integrated peripheral, spinal, and brain regions interacting in a complex way to shape the individual's experience. Hence, chronic pain from any cause cannot be viewed as a purely physical or psychological phenomenon, nor should it be expected that a unimodal approach to treatment will succeed. It follows that when assessing children and young people with chronic pain, information on a wide range of developmentally relevant dimensions, conveniently classified as biological, psychological, and sociocultural, should be gathered to formulate the potential causes, contributors, and effects of pain to devise an appropriate multimodal management plan.

Chronic pain (CP) is recurrent or persistent pain that extends beyond the expected time of healing (usually ~3 months). CP in children is an increasingly recognized clinical problem with alarmingly high prevalence rates in some populations; it may be a consequence of a chronic disease process, subsequent to an injury or surgery or, often, without any specific, identifiable cause. CP is difficult to manage and is often accompanied by comorbid symptoms and behaviors that can add to overall suffering and discomfort, dramatically reduce quality of life, and even delay or prevent recovery.[1,2]

Recent studies show that regardless of whether the antecedent of CP is known or unknown, similar patterns of symptoms, behaviors, and disability are often seen.[3] In addition to the physical and emotional costs to patients and families, the estimated economic burden of pediatric CP is substantial, and investigators have thus called for better identification, diagnosis, and treatment.[4,5]

WHO GETS PEDIATRIC CHRONIC PAIN?

The prevalence of CP increases with age and more advanced pubertal development, and there is a female

[a]*Department of Psychology, University of Southampton, Southampton, United Kingdom; and* [b]*Department of Anaesthesia and Pain Medicine, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom*

Dr Liossi conducted the initial literature review, and drafted and revised the initial manuscript; Dr Howard further contributed to the literature review and reviewed and revised the manuscript; and both authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: 10.1542/peds.2016-0331

Accepted for publication Jun 7, 2016

Address correspondence to Christina Liossi, DPsych, Department of Psychology, University of Southampton, Southampton, SO17 1BJ. E-mail: cliossi@soton.ac.uk

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Liossi C and Howard RF. Pediatric Chronic Pain: Biopsychosocial Assessment and Formulation. *Pediatrics.* 2016;138(5):e20160331

preponderance.[6,7] High rates are reported for idiopathic pain (eg, headache [23%–51%[8–10]], functional abdominal pain [1.6%–41.2%[7]], back pain [14%–24%], and musculoskeletal pain [4%–40%[11]]), with a median prevalence of 11% to 38% in community surveys.[6] Similarly high prevalence rates are reported for disease-related pain. For example, pain associated with vaso-occlusive episodes is a common consequence of sickle cell disease; episodes can begin as early as 6 months of age,[12] and they can be frequent and severe, with adolescent patients with sickle cell disease reporting greater pain intensity than postoperative pediatric patients.[13] Approximately 20% of children report persistent postoperative pain after major surgeries.[14–16] In pediatric cancer populations, the actual prevalence of chemotherapy-induced peripheral neuropathy is unknown.[17,18] However, the incidence of neurotoxicity reportedly ranges from 3% to 13% in studies of pediatric patients with cancer to ~35% in pediatric patients treated specifically for acute lymphoblastic leukemia.[19] Interestingly, there can be a striking disconnect between clinically active disease and experienced pain. In children with polyarticular arthritis, 76% reported pain on >60% of days, despite apparent successful suppression of inflammation by treatment with methotrexate, tumor necrosis factor-α inhibitors, or both.[20]

WHY A BIOPSYCHOSOCIAL APPROACH?

Although it is not understood why some children experience high levels of pain, the subjective occurrence of CP (and its associated site, intensity, quality, unpleasantness, and related suffering) has long been thought to result from interactions between multiple contributors, including neurosensory (nociceptive), affective, sociocultural, behavioral, and cognitive factors.[21,22] As a result, a biopsychosocial model of CP is widely adopted, although considerable uncertainty remains regarding the exact roles and relative contributions of different elements of the model.[22] Unfortunately, and unhelpfully, this uncertainty has often led to a tendency to dichotomize CP into mostly nociceptive or physical in origin or mostly "psychological," the latter conclusion being frequently resisted and resented by children and families.[23]

Research findings in recent years (particularly results of in vivo neuroimaging studies) have driven a radical reappraisal of the neurophysiology leading to, and maintaining, CP. Importantly, this new knowledge provides stronger theoretical support to an integrative biopsychosocial understanding, assessment, and management of CP in both adults and children. Moreover, it also allows a more convincing narrative to negate dualistic theories and justify a broader and more comprehensive approach.

Assessing morbidity from CP is not just a matter of measuring pain intensity and subsequent suffering. In 2008, the pediatric Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials made recommendations concerning outcome domains (and measures) that are important to assess in children and adolescents who have acute, chronic, or recurrent pain.[24] Seven domains in addition to pain intensity were identified: physical, emotional, and role functioning; sleep; other symptoms and adverse events; economic factors; and patient's global satisfaction with treatment. These domains map to most of the domains that need to be assessed in a biopsychosocial clinical interview.

NEUROSCIENCE OF PAIN

The development and maintenance of CP have been shown to involve long-term changes in multiple, integrated peripheral, spinal, and brain neural pain networks that interact in a complex way to contribute to the individual experience of pain, with large distributed brain "networks" being accessed during nociceptive processing. Melzack[25] first described these brain networks as the pain neuromatrix, now more commonly referred to as the "pain matrix." In children, many of these peripheral, spinal, and brain networks and systems are immature at birth and undergo changes in structure and function during the process of maturation, which add further complexity to the understanding, evaluation, and treatment of pain (other researchers have discussed this topic in more detail[26–29]). A meta-analysis of human data from positron emission tomography, functional MRI, EEG, and magnetoencephalography during an acute pain experience in the adult has confirmed that far from activating a single "pain" center in the brain, pain results in widespread activation of multiple cortical and subcortical regions, including: primary and secondary somatosensory, insular, anterior cingulate, and prefrontal cortices and the thalamus.[30] Although studies investigating pharmacologic analgesia show predominant effects in these brain regions, other regions such as the basal ganglia, cerebellum, amygdala, hippocampus, and areas within the parietal and temporal cortices, have also been found to be activated depending on the precise interplay of the factors involved in shaping pain perception (eg, cognition, mood, pain condition).[31–37] Consequently, the pain matrix is not a clearly distinct entity, leading many researchers in the field to call for a move away from a rigid neuroanatomic concept toward a

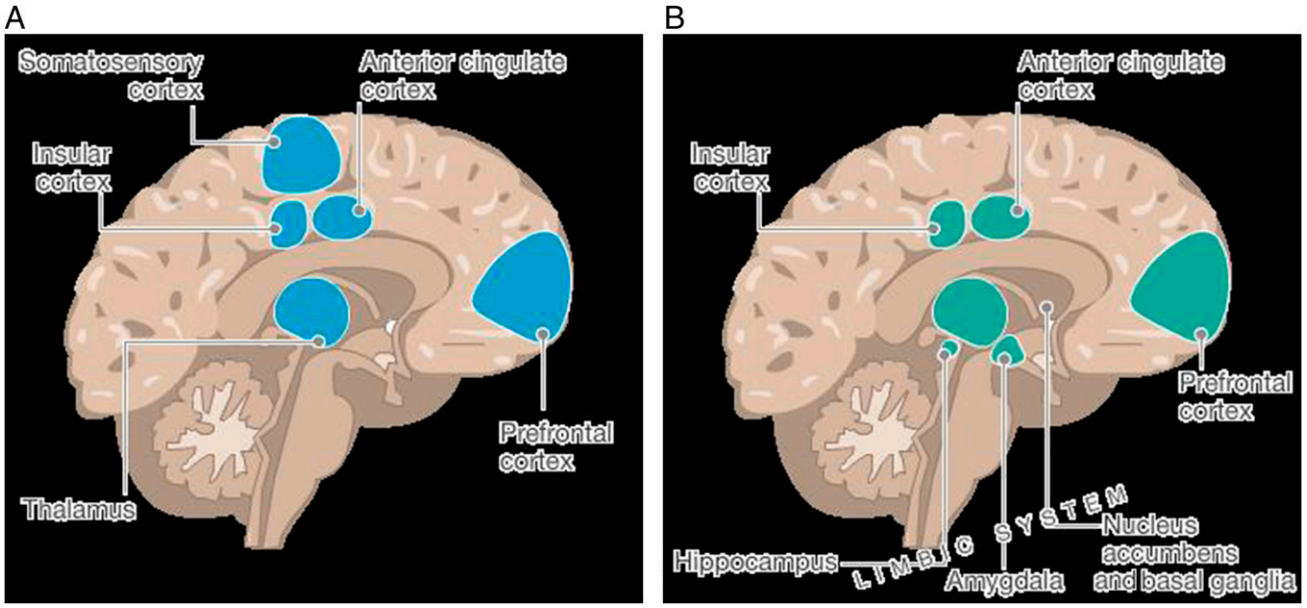

FIGURE 1
Important brain areas involved in pain perception and their respective functions (more information regarding main function is given in the Supplemental Information).

more individually unique neural "pain signature."[37–39]

For CP, the picture is even more complex. Human functional brain imaging studies indicate that CP conditions preferentially engage medial prefrontal cortical areas as well as subcortical limbic regions, especially portions of the dorsal and ventral basal ganglia, amygdala, and hippocampus.[30,37,40] Even though different types of CP, and different perceptions in individual patients, seem to engage distinct cortical and subcortical regions, overall across CP conditions there is generally a shift away from brain regions engaged in processing the sensory component of pain toward regions that encode emotional and motivational subjective states[41–43] (Fig 1). These areas are also strongly associated with functions that include learning, memory, and emotional responses and thereby are believed to relate to the cognitive and emotional problems commonly experienced by patients with CP, such as anxiety and depression,[44] impaired emotional decision-making,[45] working memory,[46] and difficulty in performing classic conditioning tasks.[47] Accumulating evidence suggests that experiences of physical and social pain (ie, social rejection, exclusion, bullying, negative social evaluation, loss of a close relationship), share neurochemical and neural substrates, an observation that provides further support for a biopsychosocial conceptualization of pain and helps explain phenomena such as improved pain control when social support is available and feelings of social isolation when in pain.[48]

Such brain imaging studies have contributed to the understanding of cerebral changes associated with CP, including structural, functional, and neurochemical alterations in patients with CP, compared with matched control subjects; there is clearly a distinct possibility that the changes observed are concurrently an effect and cause of ongoing pain.[49] It has also been noted that in most cases, a correlation exists between specific brain changes and the duration and intensity of CP (ie, the magnitude of the shift from normative data increases as the duration and intensity of pain increase).[50] This linear association suggests that long-term exposure to pain might cause central alterations such as decreased gray matter of the prefrontal cortex, and not vice versa.[51,52] Furthermore, recent studies have shown possible normalization of brain structure and function in response to effective psychological[53,54] and surgical[55,56] interventions for CP, indicating that brain plasticity can be bidirectional even in maturity. Two novel studies recorded broadly similar effects in pediatric patients after interdisciplinary rehabilitation treatment of complex regional pain syndrome (CRPS), a specific type of CP.[57,58] These findings encouraged experts to call for faster diagnosis and multidisciplinary management of CRPS in childhood.[59,60]

Peripheral nociception and the integration of nociceptive information centrally in the spinal cord and brain mature during infancy and childhood. Examples of the clinical consequences of this action in young patients include both a reduced ability to suppress incoming pain signals due to relatively slower development of

descending inhibitory systems from the brain to the spinal cord, as well as a reduced tendency to develop peripheral neuropathic pain after nerve damage.[61,62]

Although the network of brain regions that encode the cognitive, affective, and sensory aspects of adult pain have been well described,[30,37] the cortical and subcortical brain structures involved in infant and child nociceptive processing are less well known. Early indicators, however, point to a similar pattern of activation.[63] In a functional MRI study of pediatric CRPS, stimuli that evoked mechanical or cold allodynia produced patterns of central nervous system activation similar to those reported in adult CRPS.[64]

Brain structural and functional development also underlies the maturation of increasingly sophisticated cognitive abilities, and a similar shift with age from the recruitment of "bottom-up" brain processing regions toward "top-down" (ie, frontal-cortical and frontal-subcortical connections), suggesting progressive functional integration and segregation with age leading to a more mature, and controlled, cognition.[65] At a macroscopic level, brain development typically proceeds first in sensorimotor areas, spreading subsequently and progressively into the dorsal and parietal, superior temporal, and dorso-lateral prefrontal cortices throughout later childhood and adolescence.

Between childhood and adulthood, concurrent with cognitive maturation, there is progressively increased functional activation in task-relevant (lateral and medial frontal, striatal, and parieto-temporal) brain regions that mediate typically later-developing, higher level control functions such as cognitive and motivation control, timing, and attention.[65]

Overall, in brain development, there is a general pattern of functional and structural increase in connectivity and integrative processing, and a changing balance between limbic/subcortical and frontal lobe functions that extend well into young adulthood. This developmental maturation trajectory may explain the development of increasing pain-coping abilities in adolescents versus in children. A mature prefrontal cortex is necessary for good judgment, controlling impulses, solving problems, setting goals, and organizing and planning. The ability of children to use some of these complex coping strategies, such as cognitive reappraisal and acceptance, are correlated with better executive functioning (eg, working memory, cognitive flexibility, self-monitoring),[66] whereas disengagement coping is correlated with poorer executive functioning.

THE ASSESSMENT OF CP

It thus follows that when assessing children and young people with CP, information should be gathered on a wide range of relevant dimensions within a developmental context, to understand the causes, contributors, and effects of pain. Using a biopsychosocial framework, the dimensions are conveniently grouped into biological, psychological, and sociocultural factors.

Clinical history may therefore be compiled from multiple sources, including the young person themselves, parents or caretakers, teachers, and other professionals. In addition to direct questioning, where indicated and during detailed assessment, self-report and other-report scales and questionnaires are a useful adjunct, providing normative information that allows for a comparison versus the young person's peer group and an objective means for monitoring progress (Table 1).

The most commonly reported comorbid symptoms include diminished physical functioning, sleep disturbance, fatigue, and cognitive problems such as difficulties with concentration.[92] Furthermore, CP in children is associated with psychiatric comorbidity, particularly anxiety and mood disorders. Clinically elevated levels of anxiety vary widely across pain conditions, with high rates found among children with noncardiac chest pain (56%–81%),[93,94] abdominal pain (45%),[95] and fibromyalgia (58%),[96] whereas more moderate to low rates have been found among children with CRPS (20%),[97] unexplained pain (18%),[98] and headache (6%).[99] Similarly, elevated depressive symptoms are common in young people with CP[100,101] and have been associated with functional impairment[102] and problems with school functioning.[103] Risk for depression increases with pain frequency,[104] and, conversely, depressive symptoms have been identified as a risk factor for pain frequency, pain persistence, and the development of new pain problems over time.[105–107] Young people with comorbid depression and CP are at an increased risk of thinking about and attempting suicide.[108] Data from the National Longitudinal Study of Adolescent Health, a study of a nationally representative sample of 9970 adolescents in the United States, found that CP was related to suicide ideation/attempt both in the last year (odds ratio: 1.3–2.1) and during the subsequent year (odds ratio: 1.2–1.8).[109]

BIOLOGICAL DOMAIN

The initial evaluation comprises a complete medical and pain history (Table 2). This evaluation includes responses to current and previous medication complemented by physical and neurologic examination that involves observation of the

TABLE 1 Examples of Published Instruments for Assessing Young People Grouped Within the Biological Psychological and Social Domains of Relevance to CP

Domain		Construct	Example Instrument (Age Range, y)
Biological	Pain symptom	Pain intensity	VAS (10), NRS, VRS (>7)
			FPSS-R[67] (4–7), Electronic Pain Diaries[68]
		Pain characteristics	LANSS[69] (not currently standardized for children)
		Pain distribution	Body maps[70]
		Combination: intensity/distribution/quality	Varni/Thompson Pediatric Pain Questionnaire[71] (5–18)
	Comorbid symptoms	Fatigue	PedsQL (MFS) (0–18) (parent and child report)
		Functional status	FDI[72]
		Quality of life	PedsQL[73] (0–18)
		Sleep disturbance	CSHQ[74] (4–10)
Psychological	Emotional functioning	Depression	CDI[75] (7-17)
			RCADS[76] (6-18)
		Anxiety	STAIC[77] (8–12)
			STAI[78] (≥16)
			RCADS[79] (6–18)
		Anger	STAXI–2 C/A[80] (9–18)
			STAXI-2[79] (≥16)
		Combination: anxiety/depression	PI-ED[81] (8–18)
		Anxiety disorders (separation anxiety, generalized anxiety, panic, social phobia, obsessions-compulsions) and depression	RCADS[76] (6–18)
	Cognitions	Coping strategies	PCQ[82] (8–17)
		Catastrophizing	PCS-C[83] (8–17)
		Self-efficacy to manage pain	PSEQ[84] (not currently standardized for children)
Social	Environmental/Social	Family functioning	PSI-SF[85]
		Parental catastrophizing	PCS-P[86]
		Parental anxiety	BAI[78]
			STAI[87]
			HADS[88]
		Parental depression	BDI II[89]
			HADS[88]

Extensive reviews of available assessment tools for children with chronic pain have been published elsewhere.[90,91] BAI, Backache Index; BDI II, Beck Depression Inventory–II; CDI, Children's Depression Inventory; CSHQ, Children's Sleep Habits Questionnaire; FDI, Functional Disability Inventory; FPSS-R, Faces Pain Scale–Revised; HADS, Hospital Anxiety and Depression Scale; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs; MFS, Multidimensional Fatigue Scale; NRS, Numeric Rating Scale; PCQ, Pain Coping Questionnaire; PCS-C, Pain Catastrophizing Scale–Child; PCS-P, Pain Catastrophizing Scale–Parent; PedsQL, Pediatric Quality of Life; PI-ED, Paediatric Index of Emotional Distress; RCADS, Revised Child Anxiety and Depression Scale; STAIC, State-Trait Anxiety Inventory for Children; PSI-SF, Parenting Stress Index/Short Form; STAI, State-Trait Anxiety Inventory; STAXI, State-Trait Anger Expression Inventory; STAXI-2, State-Trait Anger Expression Inventory–2; STAXI–2 C/A, State-Trait Anger Expression Inventory–2 Child and Adolescent; VAS, visual analog scale; VRS, Verbal Rating Scale.

child's general appearance, posture, and gait focusing on, but not limited to, an affected area. Identification of neuropathic pain is important because specific treatments may be indicated (Table 3).[62] Basic vital signs and growth parameters should be obtained during at least the first evaluation. Red flags (Table 4) are key clinical indicators of important pathologic findings that should be investigated and managed if present. Judicious laboratory and radiologic studies are useful if a specific yet undiagnosed disease is suspected.

Physical functioning, fatigue, and sleep disturbance should be evaluated and quantified where possible. Identification of sleep problems in children is particularly important because a growing body of evidence suggests a link between sleep disorders and physical, cognitive, emotional and social development,[111] depression, and physical disability in children with CP.[112,113] Improvement in sleeping habits has been proposed as one of the mechanisms of efficacy in interdisciplinary pain management programs.[114]

PSYCHOLOGICAL DOMAIN

Emotional Functioning

The high rate of comorbidity of mental health conditions along with CP requires assessment for the presence of anxiety and mood disorders. It must be emphasized that high comorbidity does not mean that one causes the other. Psychological distress is both a potential contributing factor and a potential outcome of living with CP. Each condition often involves separate interventions, which require referral to appropriate mental health services.

Pediatricians should be particularly alert to suicide ideation/attempts and comorbid depression in this at-risk population, and they should ascertain the suicidality of depressed adolescents (ie, whether and how often these adolescents think about suicide and whether they have ever attempted suicide). If suicidal ideation or recent suicidal behavior is present in a depressed teenager,

TABLE 2 SOCRATES Mnemonic: A Frequently Recommended Resource to Guide Initial Questioning in CP Assessment

Site	Where is the pain?
Onset	When did the pain start, and how did it first appear?
	Did the pain appear suddenly or developed over time?
	What were you doing when it started?
Character	What words would you use to describe the pain?
	Is it stabbing, sharp, aching, burning, shooting, hot, cold?
Radiation	Does the pain move elsewhere in the body?
Associations	Are there any symptoms, signs, or activities associated with the pain?
	Is it associated with bruising, swelling, nausea, or high temperatures? Does it always come on at certain times; for example, at meal times or when you are doing a particular activity?
Timing	Is the pain spontaneous or evoked?
	Constant, intermittent, or both?
	Background pain?
	Acute exacerbations?
	For how long have you had the pain and has it changed over time?
Exacerbating or relieving factors	What makes the pain better or worse?
	Response to previous treatments?
Severity	How intense is the pain?
	Does it stop you doing any of the things you like or need to do?
	What do you do when you have pain?
	Is there anything you avoid doing as a result of the pain?
	In what ways has your life changed since you developed pain?

TABLE 3 Differences Between Neuropathic and Nociceptive Pain[62,110]

Clinical Characteristic	Neuropathic Pain	Nociceptive Pain
Cause	Lesion or dysfunction of the nervous system	Damage or potential damage to tissues
Descriptors	Sharp, lancinating, shooting, electric-like, stabbing pain	Throbbing, aching, pressure-like pain
Sensory deficits	Common: numbness, tingling, pricking	Uncommon; if present, they have a nondermatomal or nonnerve distribution
Vasomotor signs	Temperature and color changes	Uncommon
Motor deficits	Neurologic weakness may be present if a motor nerve is affected; dystonia or spasticity may be associated with central nervous system lesions and sometimes peripheral lesions (eg, CRPS)	May have pain-induced muscle weakness
Hypersensitivity	Allodynia (ie, pain often evoked by nonpainful stimuli) Hyperalgesia (ie, exaggerated response to painful stimuli)	Uncommon
Character	Distal radiation common	Proximal radiation common
Paroxysms	Exacerbations common and unpredictable	Exacerbations less common and often associated with activity

he or she should be immediately referred to the appropriate mental health services.

Cognitions

Young people and their families hold beliefs about the pain that they experience such as what causes it, how long it will last, whether it is curable, what effects it will have in their lives, what treatments might be relevant, and whether it is understood and believed as "real" by clinicians. Beliefs are powerful and can influence not only pain perception but also treatment adherence and treatment response, and pediatricians may have to actively challenge erroneous beliefs and provide accurate pain education.[115]

Specific cognitions that need to be assessed include pain catastrophizing and coping. Pain catastrophizing, currently conceptualized as both related to a personality-based, dispositional construct and a response that varies in different situations,[116] is characterized by a negative mind-set, magnification, and rumination about pain.[117] Catastrophizing in children is distinct to anxiety and has been identified as a significant predictor of pain, functional disability, and health-related quality of life in children and adolescents with CP[118] and persistent pain and central sensitization into young adulthood.[119]

CP presents a range of stressors and challenges for young people and their families; pediatricians therefore need to assess how the young person copes with each of these factors and not just pain. Coping can be viewed as a collection of purposeful, volitional efforts that are mobilized under stress and directed at the regulation of aspects of the self (ie, emotion, cognition, behavior, physiology), known as secondary control, and interactions with others and the environment, known as primary control .[120,121] Relinquished

TABLE 4 Red Flags in Pediatric CP

Young age at presentation
Systemic upset
Fever
Malaise
Weight loss
Rashes
Lymphadenopathy
Hepatosplenomegaly
Pain that wakes at night
Bone pain
Joint swelling
Impaired growth and development
Neurologic signs
Depression, evidence of suicidal ideation or major psychiatric disorder
Suspicion of child abuse (eg, incongruence between history and presentation or pattern of physical findings)

control refers to the absence of any coping attempt.[122] In general, the degree to which a coping strategy leads to better or worse emotional and behavioral adjustment depends in part on the match between the demands of the stressor and the goals and nature of the coping response.[123] However, overall, studies have shown that secondary control coping (eg, acceptance, cognitive reappraisal, distraction) is associated with lower levels of somatic complaints and symptoms of anxiety and depression,[66,124–126] whereas passive coping (eg, behavioral disengagement, self-isolation, catastrophizing) is related to poorer adjustment.[119,127,128]

SOCIAL DOMAIN

Complex transactional processes and individual factors mediate children's and parents' emotional, cognitive, and behavioral responses to pain, ultimately influencing the child's overall functioning.[129] The 5 characteristics of family functioning commonly assessed in family systems theories[130] relevant in the assessment of the family of a child with CP are organization, cohesion, communication, affective environment, and problem solving.[131] Poorly functioning families can be those that are highly disorganized, with unclear communication and high expressions of conflict or negative affect that only become more disrupted when faced with a stressor. Poorly functioning families can also be characterized by being overly restrictive and ordered, limiting the adaptability of the system to deal with stressors, and limiting individual members' ability to express their emotions or modify maladaptive roles.

In terms of individual factors, parental cognitive responses to pain, such as parental pain catastrophizing or exaggerated negative pain appraisals, have been found to influence both parents' emotional reactions to pain and child functional disability. In addition, higher levels of parents' catastrophic thinking regarding their children's CP are associated with a greater tendency to restrict their children's pain-inducing activities and a greater tendency to prioritize attempts to control their children's pain.[132]

Behaviorally, parental protective responses to children's pain behavior (eg, increasing attention to pain symptoms, excusing the child from responsibilities) have been linked to poorer functional outcomes, serving as the proximal link between parents' internal reactions (eg, cognitions, emotional distress) and child outcomes.[133–135] Conversely, young people of parents with greater levels of psychological flexibility tend to report less physical disability, fewer depressive symptoms, and greater levels of acceptance of their own pain.[136]

Anxiety and mood disorders are prevalent among mothers of children with CP conditions,[137,138] but similar data about fathers are currently lacking. Mothers of children with functional abdominal pain are 4.9 times more likely to have a lifetime history of depressive disorders and 4.8 times more likely to have a lifetime history of anxiety disorders compared with mothers of healthy children.[137] Maternal depression is a risk factor for the socioemotional and cognitive development of children. Depressed mothers generally exhibit less attentiveness and responsiveness to their children's needs, and they are also poor models for negative mood regulation and problem solving. The pediatricians' role in maternal depression is one of screening, followed by guidance for additional evaluation and treatment.

School functioning is often negatively affected in young people with CP,[139] particularly when there is comorbidity with depressive symptoms.[103] Assessment of school functioning should include a number of dimensions,[140,141] namely: (1) school attendance, clarifying if the absence is due to pain or some other reason; (2) cognitive[142] and emotional[143] engagement (eg, self-regulation, studying habits and enjoyment, belonging, and attitudes toward every aspect of school); (3) academic performance (eg, grades across subjects, national standardized test scores, classroom participation); (4) self and teacher perceptions of academic competence[139]; (5) participation in school activities (eg, clubs, school trips); and (6) social functioning in the school setting (eg, social activities, interaction with peers). The limited number of existing studies suggests that young people with CP may have fewer friends, are more isolated, and may be subjected to increased rates of victimization by

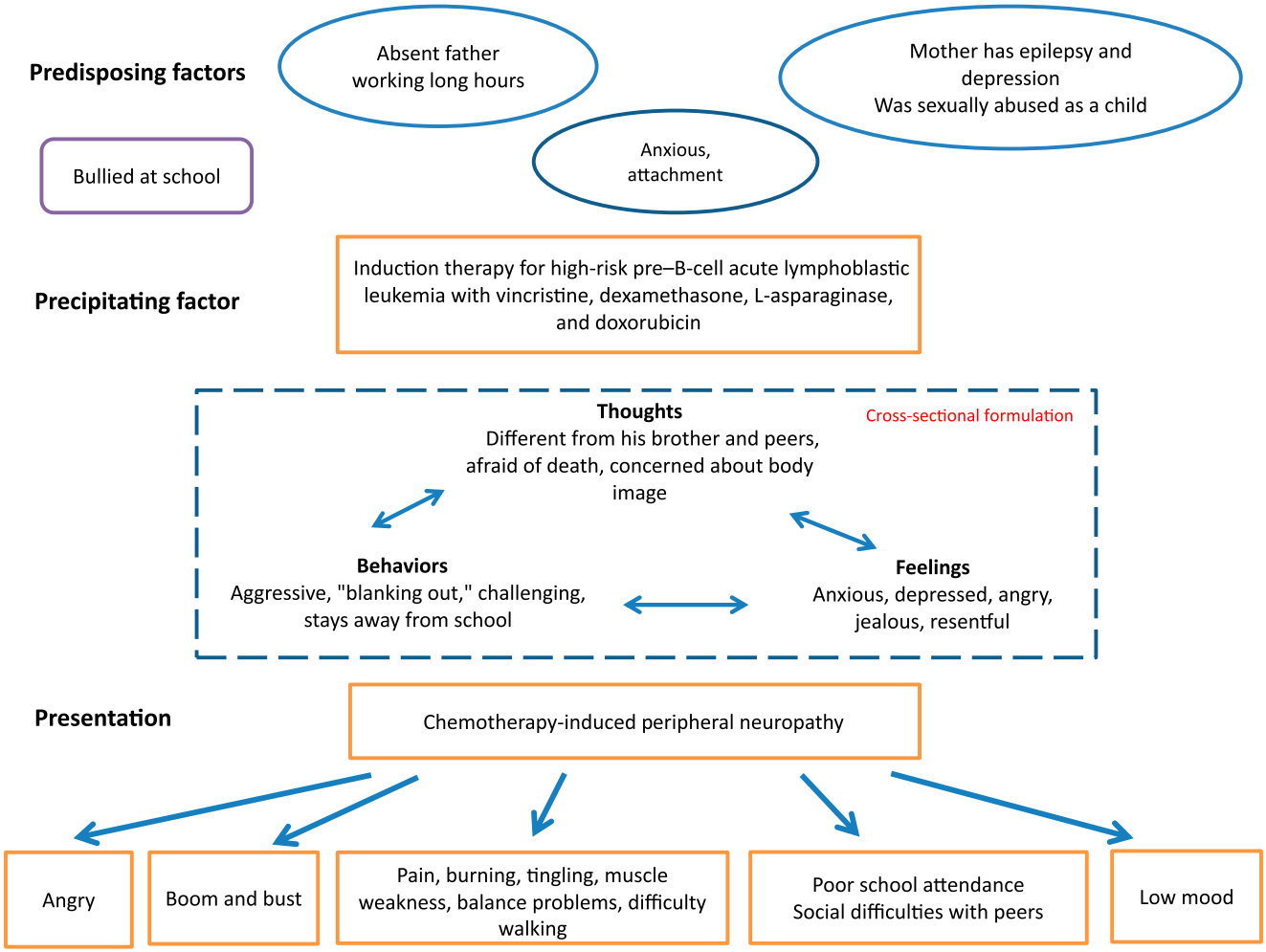

FIGURE 2

Longitudinal formulation for John's chemotherapy-induced peripheral neuropathy (the Case Study in the Supplemental Information discusses this topic in more detail).

peers compared with children and adolescents without pain.[144]

CASE FORMULATION

Case formulation provides the essential link between assessment and management planning. Assessment, formulation, and treatment are in fact dynamically linked with each other, each informing the other over time. Although case formulation has been described in adult CP,[145] limited literature exists in pediatric pain.[115,146]

Case formulation or conceptualization (these 2 terms are used interchangeably) is where theory, research, and young peoples' unique presentations come together. It is an individualized model that attempts to systematically draw together the precipitating, predisposing, perpetuating, and protective biological, psychological, and social factors believed to be idiosyncratically related to a particular young person's clinical presentation.[147,148] An effective case conceptualization should essentially answer the young person's question "why me, and why now?"

At its simplest level (ie, cross-sectional), the case conceptualization might focus on "negative automatic thoughts," which are locked into vicious cycles with dysfunctional emotions, behaviors, and somatic symptoms (Fig 2). A more comprehensive, longitudinal case conceptualization involves 3 steps. First, the clinician learns about the young person's pain problem and behavioral, emotional, and cognitive responses by observing, assessing, and measuring; second, the clinician then moves on to meaningfully organizing this information into patterns and themes; and third, he or she finishes by explaining the patterns and themes by using theory and research. When the case conceptualization is completed, the clinician should have a picture of what he or she believes has led to the young person's pain problem (etiology) and what features are maintaining or perpetuating the

problem (sustaining factors; Fig 2, see Supplemental Information). Understanding the etiology and sustaining factors will then lead to treatment planning, which uses the case conceptualization to decide how to best address, reduce, manage, or resolve the young person's pain and associated disability.

Crucially, the case conceptualization is collaboratively co-constructed with the young patients and their family and not simply presented to them. This approach allows for problems to be normalized and contextualized, and it facilitates empathy. The clinician and family work collaboratively to first describe and then explain the pain and associated issues a young person presents with.

CONCLUSIONS

Pediatric CP can be a difficult problem to conceptualize and treat, but evidence is rapidly accumulating that supports an integrative biopsychosocial approach to assessment, formulation, and management. Interdisciplinary outpatient and intensive inpatient treatment have been shown to improve pain intensity and disability in children with CP,[149,150] and the effects are maintained at the 1-year follow-up.[151] Future research could beneficially explore the association between brain reorganization seen on imaging and the chronicity of pain, with emphasis on how changes on imaging relate to pain behaviors and response to treatment longitudinally.

ABBREVIATIONS

CP: chronic pain
CRPS: chronic regional pain syndrome

REFERENCES

1. Zernikow B, Wager J, Hechler T, et al. Characteristics of highly impaired children with severe chronic pain: a 5-year retrospective study on 2249 pediatric pain patients. *BMC Pediatr*. 2012;12:54
2. Mulvaney S, Lambert EW, Garber J, Walker LS. Trajectories of symptoms and impairment for pediatric patients with functional abdominal pain: a 5-year longitudinal study. *J Am Acad Child Adolesc Psychiatry*. 2006;45(6):737–744
3. 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. *J Abnorm Psychol*. 1993;102(2):248–258
4. Groenewald CB, Essner BS, Wright D, Fesinmeyer MD, Palermo TM. The economic costs of chronic pain among a cohort of treatment-seeking adolescents in the United States. *J Pain*. 2014;15(9):925–933
5. Sleed M, Eccleston C, Beecham J, Knapp M, Jordan A. The economic impact of chronic pain in adolescence: methodological considerations and a preliminary costs-of-illness study. *Pain*. 2005;119(1–3):183–190
6. King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain*. 2011;152(12):2729–2738
7. Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. *PLoS One*. 2015;10(5):e0126982
8. Brun Sundblad GM, Saartok T, Engström LM. Prevalence and co-occurrence of self-rated pain and perceived health in school-children: age and gender differences. *Eur J Pain*. 2007;11(2):171–180
9. Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, et al. Pain in children and adolescents: a common experience. *Pain*. 2000;87(1):51–58
10. Stanford EA, Chambers CT, Craig KD. The role of developmental factors in predicting young children's use of a self-report scale for pain. *Pain*. 2006;120(1–2):16–23
11. McBeth J, Jones K. Epidemiology of chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol*. 2007;21(3):403–425
12. Palermo TM, Riley CA, Mitchell BA. Daily functioning and quality of life in children with sickle cell disease pain: relationship with family and neighborhood socioeconomic distress. *J Pain*. 2008;9(9):833–840
13. Franck LS, Treadwell M, Jacob E, Vichinsky E. Assessment of sickle cell pain in children and young adults using the adolescent pediatric pain tool. *J Pain Symptom Manage*. 2002;23(2):114–120
14. Fortier MA, Chou J, Maurer EL, Kain ZN. Acute to chronic postoperative pain in children: preliminary findings. *J Pediatr Surg*. 2011;46(9):1700–1705
15. Lauridsen MH, Kristensen AD, Hjortdal VE, Jensen TS, Nikolajsen L. Chronic pain in children after cardiac surgery via sternotomy. *Cardiol Young*. 2014;24(5):893–899
16. Nikolajsen L, Brix LD. Chronic pain after surgery in children. *Curr Opin Anaesthesiol*. 2014;27(5):507–512
17. Gilchrist L. Chemotherapy-induced peripheral neuropathy in pediatric cancer patients. *Semin Pediatr Neurol*. 2012;19(1):9–17
18. Gilchrist LS, Tanner L. The pediatric-modified total neuropathy score: a reliable and valid measure of chemotherapy-induced peripheral neuropathy in children with non-CNS cancers. *Support Care Cancer*. 2013;21(3):847–856
19. Moore RJ, Groninger H. Chemotherapy-induced peripheral neuropathy in pediatric cancer patients. *Cureus*. 2013;5(6):e124
20. Schanberg LE, Anthony KK, Gil KM, Maurin EC. Daily pain and symptoms in children with polyarticular arthritis. *Arthritis Rheum*. 2003;48(5):1390–1397
21. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science*. 1965;150(3699):971–979
22. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull*. 2007;133(4):581–624
23. Williams SE, Smith CA, Bruehl SP, Gigante J, Walker LS. Medical evaluation of children with chronic

abdominal pain: impact of diagnosis, physician practice orientation, and maternal trait anxiety on mothers' responses to the evaluation. *Pain*. 2009;146(3):283–292

24. McGrath PJ, Walco GA, Turk DC, et al; PedIMMPACT. Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. *J Pain*. 2008;9(9):771–783
25. Melzack R. From the gate to the neuromatrix. *Pain*. 1999;(suppl 6):S121–S126
26. Byers M, Bonica J. Peripheral pain mechanisms and nociceptor plasticity. In: Fishman S, Ballantyne J, Rathmell JP, Bonica JJ, eds. *Bonica's Management of Pain*, 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins; 2001:26–72
27. Craig AD. Pain mechanisms: labeled lines versus convergence in central processing. *Annu Rev Neurosci*. 2003;26:1–30
28. Terman G, Bonica J. Spinal mechanisms and their modulation. In: Fishman S, Ballantyne J, Rathmell JP, Bonica JJ, eds. *Bonica's Management of Pain*, 3rd ed. Baltimore, MD: Lippincott Williams & Wilkins; 2001:73–152
29. Rainville P. Brain mechanisms of pain affect and pain modulation. *Curr Opin Neurobiol*. 2002;12(2):195–204
30. Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. *Eur J Pain*. 2005;9(4):463–484
31. Casey KL, Svensson P, Morrow TJ, Raz J, Jone C, Minoshima S. Selective opiate modulation of nociceptive processing in the human brain. *J Neurophysiol*. 2000;84(1):525–533
32. Geha PY, Baliki MN, Chialvo DR, Harden RN, Paice JA, Apkarian AV. Brain activity for spontaneous pain of postherpetic neuralgia and its modulation by lidocaine patch therapy. *Pain*. 2007;128(1–2):88–100
33. Rogers R, Wise RG, Painter DJ, Longe SE, Tracey I. An investigation to dissociate the analgesic and anesthetic properties of ketamine using functional magnetic resonance imaging. *Anesthesiology*. 2004;100(2):292–301
34. Wagner KJ, Sprenger T, Kochs EF, Tölle TR, Valet M, Willoch F. Imaging human cerebral pain modulation by dose-dependent opioid analgesia: a positron emission tomography activation study using remifentanil. *Anesthesiology*. 2007;106(3):548–556
35. Wise RG, Rogers R, Painter D, et al. Combining fMRI with a pharmacokinetic model to determine which brain areas activated by painful stimulation are specifically modulated by remifentanil. *Neuroimage*. 2002;16(4):999–1014
36. Wise RG, Williams P, Tracey I. Using fMRI to quantify the time dependence of remifentanil analgesia in the human brain. *Neuropsychopharmacology*. 2004;29(3):626–635
37. Tracey I, Mantyh PW. The cerebral signature for pain perception and its modulation. *Neuron*. 2007;55(3):377–391
38. Tracey I. Nociceptive processing in the human brain. *Curr Opin Neurobiol*. 2005;15(4):478–487
39. Wager TD, Atlas LY, Lindquist MA, Roy M, Woo CW, Kross E. An fMRI-based neurologic signature of physical pain. *N Engl J Med*. 2013;368(15):1388–1397
40. Baliki MN, Chialvo DR, Geha PY, et al. Chronic pain and the emotional brain: specific brain activity associated with spontaneous fluctuations of intensity of chronic back pain. *J Neurosci*. 2006;26(47):12165–12173
41. Apkarian AV, Hashmi JA, Baliki MN. Pain and the brain: specificity and plasticity of the brain in clinical chronic pain. *Pain*. 2011;152(suppl 3):S49–S64
42. Hashmi JA, Baliki MN, Huang L, et al. Shape shifting pain: chronification of back pain shifts brain representation from nociceptive to emotional circuits. *Brain*. 2013;136(pt 9):2751–2768
43. Bushnell MC, Ceko M, Low LA. Cognitive and emotional control of pain and its disruption in chronic pain. *Nat Rev Neurosci*. 2013;14(7):502–511
44. Gore M, Sadosky A, Stacey BR, Tai KS, Leslie D. The burden of chronic low back pain: clinical comorbidities, treatment patterns, and health care costs in usual care settings. *Spine*. 2012;37(11):E668–E677
45. Apkarian AV, Sosa Y, Sonty S, et al. Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. *J Neurosci*. 2004;24(46):10410–10415
46. Dick BD, Rashiq S. Disruption of attention and working memory traces in individuals with chronic pain. *Anesth Analg*. 2007;104(5):1223–1229
47. Flor H, Knost B, Birbaumer N. The role of operant conditioning in chronic pain: an experimental investigation. *Pain*. 2002;95(1–2):111–118
48. Eisenberger NI. The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. *Nat Rev Neurosci*. 2012;13(6):421–434
49. Chapin H, Bagarinao E, Mackey S. Real-time fMRI applied to pain management. *Neurosci Lett*. 2012;520(2):174–181
50. Grachev ID, Fredrickson BE, Apkarian AV. Abnormal brain chemistry in chronic back pain: an in vivo proton magnetic resonance spectroscopy study. *Pain*. 2000;89(1):7–18
51. Wand BM, Parkitny L, O'Connell NE, et al. Cortical changes in chronic low back pain: current state of the art and implications for clinical practice. *Man Ther*. 2011;16(1):15–20
52. Rodriguez-Raecke R, Niemeier A, Ihle K, Ruether W, May A. Brain gray matter decrease in chronic pain is the consequence and not the cause of pain. *J Neurosci*. 2009;29(44):13746–13750
53. Seminowicz DA, Shpaner M, Keaser ML, et al. Cognitive-behavioral therapy increases prefrontal cortex gray matter in patients with chronic pain. *J Pain*. 2013;14(12):1573–1584
54. Shpaner M, Kelly C, Lieberman G, et al. Unlearning chronic pain: a randomized controlled trial to investigate changes in intrinsic brain connectivity following cognitive behavioral therapy. *Neuroimage Clin*. 2014;5:365–376
55. Seminowicz DA, Wideman TH, Naso L, et al. Effective treatment of chronic low back pain in humans reverses

abnormal brain anatomy and function. *J Neurosci*. 2011;31(20):7540–7550

56. Gwilym SE, Filippini N, Douaud G, Carr AJ, Tracey I. Thalamic atrophy associated with painful osteoarthritis of the hip is reversible after arthroplasty: a longitudinal voxel-based morphometric study. *Arthritis Rheum*. 2010;62(10):2930–2940
57. Erpelding N, Simons L, Lebel A, et al. Rapid treatment-induced brain changes in pediatric CRPS. *Brain Struct Funct*. 2016;221(2):1095–1111
58. Becerra L, Sava S, Simons LE, et al. Intrinsic brain networks normalize with treatment in pediatric complex regional pain syndrome. *Neuroimage Clin*. 2014;6:347–369
59. Liossi C, Clinch J, Howard R. Need for early recognition and multidisciplinary management of paediatric complex regional pain syndrome. *BMJ*. 2015;351:h4748
60. Williams G, Howard R. *The pharmacological management of complex regional pain syndrome in pediatric patients*. Paediatric Drugs. 2016;18(4):243–250
61. Fitzgerald M. The development of nociceptive circuits. *Nat Rev Neurosci*. 2005;6(7):507–520
62. Howard RF, Wiener S, Walker SM. Neuropathic pain in children. *Arch Dis Child*. 2014;99(1):84–89
63. Goksan S, Hartley C, Emery F, et al. fMRI reveals neural activity overlap between adult and infant pain. *Elife*. 2015;4:e06356
64. Lebel A, Becerra L, Wallin D, et al. fMRI reveals distinct CNS processing during symptomatic and recovered complex regional pain syndrome in children. *Brain*. 2008;131(pt 7):1854–1879
65. Rubia K. Functional brain imaging across development. *Eur Child Adolesc Psychiatry*. 2013;22(12):719–731
66. Hocking MC, Barnes M, Shaw C, Lochman JE, Madan-Swain A, Saeed S. Executive function and attention regulation as predictors of coping success in youth with functional abdominal pain. *J Pediatr Psychol*. 2011;36(1):64–73
67. Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain*. 2001;93(2):173–183
68. Stinson JN, Petroz GC, Tait G, et al. e-Ouch: usability testing of an electronic chronic pain diary for adolescents with arthritis. *Clin J Pain*. 2006;22(3):295–305
69. Bennett M. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. *Pain*. 2001;92(1–2):147–157
70. von Baeyer CL, Lin V, Seidman LC, Tsao JC, Zeltzer LK. Pain charts (body maps or manikins) in assessment of the location of pediatric pain. *Pain Manag*. 2011;1(1):61–68
71. Varni JW, Thompson KL, Hanson V. The Varni/Thompson Pediatric Pain Questionnaire. I. Chronic musculoskeletal pain in juvenile rheumatoid arthritis. *Pain*. 1987;28(1):27–38
72. Walker LS, Greene JW. The functional disability inventory: measuring a neglected dimension of child health status. *J Pediatr Psychol*. 1991;16(1):39–58
73. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care*. 2001;39(8):800–812
74. Owens JA, Spirito A, McGuinn M, Nobile C. Sleep habits and sleep disturbance in elementary school-aged children. *J Dev Behav Pediatr*. 2000;21(1):27–36
75. Kovacs M. The Children's Depression Inventory (CDI). *Psychopharmacol Bull*. 1985;21(4):995–998
76. Chorpita BF, Yim L, Moffitt C, Umemoto LA, Francis SE. Assessment of symptoms of DSM-IV anxiety and depression in children: a revised child anxiety and depression scale. *Behav Res Ther*. 2000;38(8):835–855
77. Spielberger C. *STAIC Preliminary Manual*. Palo Alto, CA: Consulting Psychologists Press; 1973
78. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol*. 1988;56(6):893–897
79. Spielberger CD. *State-Trait Anger Expression Inventory-2 (STAXI-2). Professional Manual*. Tampa, FL: Psychological Assessment Resources; 1999
80. Brunner TM, Spielberger CD. *State-Trait Anger Expression Inventory-2 Child and Adolescent (STAXI-2 C/A)*. Odessa, FL: Psychological Assessment Resources; 2010
81. O'Connor S, Carney T, House E, Ferguson E, Caldwell F, O'Connor R. Revision of the hospital anxiety and depression scale (HADS) to produce the paediatric index of emotional distress (PI-ED). *PRO Newsletter*. 2010;43:2–4
82. Reid GJ, Gilbert CA, McGrath PJ. The Pain Coping Questionnaire: preliminary validation. *Pain*. 1998;76(1-2):83–96
83. Crombez G, Bijttebier P, Eccleston C, et al. The child version of the pain catastrophizing scale (PCS-C): a preliminary validation. *Pain*. 2003;104(3):639–646
84. Nicholas MK. The pain self-efficacy questionnaire: taking pain into account. *Eur J Pain*. 2007;11(2):153–163
85. Abidin RR. *Parenting Stress Index:(Short Form)*. Charlottesville, VA: Pediatric Psychology Press; 1990
86. 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
87. Spielberger CD, Gorsuch RL, Lushene RE. *State Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press; 1970
88. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361–370
89. Beck AT, Steer RA, Brown RA. *Manual for the Beck Depression Inventory-II*, Second Edition Manual. San Antonio, TX: Psychological Corporation; 1996
90. Eccleston C, Jordan AL, Crombez G. The impact of chronic pain on adolescents: a review of previously used measures. *J Pediatr Psychol*. 2006;31(7):684–697

91. Jordan A, Eccleston C, Crombez G. Parental functioning in the context of adolescent chronic pain: a review of previously used measures. *J Pediatr Psychol*. 2008;33(6):640–659

92. Harrison L, Wilson S, Munafò MR. Exploring the associations between sleep problems and chronic musculoskeletal pain in adolescents: a prospective cohort study. *Pain Res Manag*. 2014;19(5):e139–e145

93. Lipsitz JD, Masia C, Apfel H, et al. Noncardiac chest pain and psychopathology in children and adolescents. *J Psychosom Res*. 2005;59(3):185–188

94. Lipsitz JD, Gur M, Sonnet FM, et al. Psychopathology and disability in children with unexplained chest pain presenting to the pediatric emergency department. *Pediatr Emerg Care*. 2010;26(11):830–836

95. Di Lorenzo C, Youssef NN, Sigurdsson L, Scharff L, Griffiths J, Wald A. Visceral hyperalgesia in children with functional abdominal pain. *J Pediatr*. 2001;139(6):838–843

96. Kashikar-Zuck S, Parkins IS, Graham TB, et al. Anxiety, mood, and behavioral disorders among pediatric patients with juvenile fibromyalgia syndrome. *Clin J Pain*. 2008;24(7):620–626

97. Cruz N, O'Reilly J, Slomine BS, Salorio CF. Emotional and neuropsychological profiles of children with complex regional pain syndrome type-I in an inpatient rehabilitation setting. *Clin J Pain*. 2011;27(1):27–34

98. Knook LM, Konijnenberg AY, van der Hoeven J, et al. Psychiatric disorders in children and adolescents presenting with unexplained chronic pain: what is the prevalence and clinical relevancy? *Eur Child Adolesc Psychiatry*. 2011;20(1):39–48

99. Seshia SS. Chronic daily headache in children and adolescents. *Can J Neurol Sci*. 2004;31(3):319–323

100. Campo JV, Bridge J, Ehmann M, et al. Recurrent abdominal pain, anxiety, and depression in primary care. *Pediatrics*. 2004;113(4):817–824

101. Kashikar-Zuck S, Lynch AM, Slater S, Graham TB, Swain NF, Noll RB. Family factors, emotional functioning, and functional impairment in juvenile fibromyalgia syndrome. *Arthritis Rheum*. 2008;59(10):1392–1398

102. Gauntlett-Gilbert J, Eccleston C. Disability in adolescents with chronic pain: patterns and predictors across different domains of functioning. *Pain*. 2007;131(1–2):132–141

103. Logan DE, Simons LE, Kaczynski KJ. School functioning in adolescents with chronic pain: the role of depressive symptoms in school impairment. *J Pediatr Psychol*. 2009;34(8):882–892

104. Youssef NN, Atienza K, Langseder AL, Strauss RS. Chronic abdominal pain and depressive symptoms: analysis of the National Longitudinal Study of Adolescent Health. *Clin Gastroenterol Hepatol*. 2008;6(3):329–332

105. Dunn KM, Jordan KP, Mancl L, Drangsholt MT, Le Resche L. Trajectories of pain in adolescents: a prospective cohort study. *Pain*. 2011;152(1):66–73

106. Larsson B, Sund AM. One-year incidence, course, and outcome predictors of frequent headaches among early adolescents. *Headache*. 2005;45(6):684–691

107. Stanford EA, Chambers CT, Biesanz JC, Chen E. The frequency, trajectories and predictors of adolescent recurrent pain: a population-based approach. *Pain*. 2008;138(1):11–21

108. American Pain Society. Pediatric chronic pain: a position statement from the American Pain Society. Available at: wwwampainsocorg/advocacy/pediatrichtm.

109. van Tilburg MA, Spence NJ, Whitehead WE, Bangdiwala S, Goldston DB. Chronic pain in adolescents is associated with suicidal thoughts and behaviors. *J Pain*. 2011;12(10):1032–1039

110. Cohen SP, Mao J. Neuropathic pain: mechanisms and their clinical implications. *BMJ*. 2014;348:f7656

111. Roberts RE, Roberts CR, Chen IG. Functioning of adolescents with symptoms of disturbed sleep. *J Youth Adolesc*. 2001;30(1):1–18

112. Kanstrup M, Holmström L, Ringström R, Wicksell RK. Insomnia in paediatric chronic pain and its impact on depression and functional disability. *Eur J Pain*. 2014;18(8):1094–1102

113. Palermo TM, Fonareva I, Janosy NR. Sleep quality and efficiency in adolescents with chronic pain: relationship with activity limitations and health-related quality of life. *Behav Sleep Med*. 2008;6(4):234–250

114. Logan DE, Sieberg CB, Conroy C, Smith K, Odell S, Sethna N. Changes in sleep habits in adolescents during intensive interdisciplinary pediatric pain rehabilitation. *J Youth Adolesc*. 2015;44(2):543–555

115. Rajapakse D, Liossi C, Howard RF. Presentation and management of chronic pain. *Arch Dis Child*. 2014;99(5):474–480

116. Turner JA, Aaron LA. Pain-related catastrophizing: what is it? *Clin J Pain*. 2001;17(1):65–71

117. Sullivan MJ, Thorn B, Haythornthwaite JA, et al. Theoretical perspectives on the relation between catastrophizing and pain. *Clin J Pain*. 2001;17(1):52–64

118. Tran ST, Jastrowski Mano KE, Hainsworth KR, et al. Distinct influences of anxiety and pain catastrophizing on functional outcomes in children and adolescents with chronic pain. *J Pediatr Psychol*. 2015;40(8):744–755

119. Walker LS, Sherman AL, Bruehl S, Garber J, Smith CA. Functional abdominal pain patient subtypes in childhood predict functional gastrointestinal disorders with chronic pain and psychiatric comorbidities in adolescence and adulthood. *Pain*. 2012;153(9):1798–1806

120. Compas BE, Connor-Smith JK, Saltzman H, Thomsen AH, Wadsworth ME. Coping with stress during childhood and adolescence: problems, progress, and potential in theory and research. *Psychol Bull*. 2001;127(1):87–127

121. Skinner EA, Edge K, Altman J, Sherwood H. Searching for the structure of coping: a review and critique of category systems for classifying ways of coping. *Psychol Bull*. 2003;129(2):216–269

122. Rudolph KD, Dennig MD, Weisz JR. Determinants and consequences of children's coping in the medical setting: conceptualization,

review, and critique. *Psychol Bull*. 1995;118(3):328–357

123. Taylor SE, Stanton AL. Coping resources, coping processes, and mental health. *Annu Rev Clin Psychol*. 2007;3:377–401

124. Compas BE. Psychobiological processes of stress and coping: implications for resilience in children and adolescents—comments on the papers of Romeo & McEwen and Fisher et al. *Ann N Y Acad Sci*. 2006;1094:226–234

125. Dufton LM, Dunn MJ, Slosky LS, Compas BE. Self-reported and laboratory-based responses to stress in children with recurrent pain and anxiety. *J Pediatr Psychol*. 2011;36(1):95–105

126. Thomsen AH, Compas BE, Colletti RB, Stanger C, Boyer MC, Konik BS. Parent reports of coping and stress responses in children with recurrent abdominal pain. *J Pediatr Psychol*. 2002;27(3):215–226

127. Shirkey KC, Smith CA, Walker LS. Dispositional versus episode-specific assessment of children's coping with pain. *J Pediatr Psychol*. 2011;36(1):74–83

128. Walker LS, Baber KF, Garber J, Smith CA. A typology of pain coping strategies in pediatric patients with chronic abdominal pain. *Pain*. 2008;137(2):266–275

129. Palermo TM, Chambers CT. Parent and family factors in pediatric chronic pain and disability: an integrative approach. *Pain*. 2005;119(1–3):1–4

130. Fogarty CT. Evaluating and treating families: the McMaster approach. *Prim Care Companion J Clin Psychiatry*. 2009;11(4):176

131. Alderfer MA, Fiese BH, Gold JI, et al Evidence-based assessment in pediatric psychology: family measures. *J Pediatric Psychol*. 2008;33(9):1046–1061; discussion 1062–1064

132. Lewandowski AS, Palermo TM, Stinson J, Handley S, Chambers CT. Systematic review of family functioning in families of children and adolescents with chronic pain. *J Pain*. 2010;11(11):1027–1038

133. Logan DE, Simons LE, Carpino EA. Too sick for school? Parent influences on school functioning among children with chronic pain. *Pain*. 2012;153(2):437–443

134. Liossi C, White P, Croome N, Hatira P. Pain-related bias in the classification of emotionally ambiguous facial expressions in mothers of children with chronic abdominal pain. *Pain*. 2012;153(3):674–681

135. Liossi C, White P, Franck L, Hatira P. Parental pain expectancy as a mediator between child expected and experienced procedure-related pain intensity during painful medical procedures. *Clin J Pain*. 2007;23(5):392–399

136. Wallace DP, McCracken LM, Weiss KE, Harbeck-Weber C. The role of parent psychological flexibility in relation to adolescent chronic pain: further instrument development. *J Pain*. 2015;16(3):235–246

137. Campo JV, Bridge J, Lucas A, et al. Physical and emotional health of mothers of youth with functional abdominal pain. *Arch Pediatr Adolesc Med*. 2007;161(2):131–137

138. Walker LS, Greene JW. Children with recurrent abdominal pain and their parents: more somatic complaints, anxiety, and depression than other patient families? *J Pediatr Psychol*. 1989;14(2):231–243

139. Logan DE, Simons LE, Stein MJ, Chastain L. School impairment in adolescents with chronic pain. *J Pain*. 2008;9(5):407–416

140. Chan E, Piira T, Betts G. The school functioning of children with chronic and recurrent pain. *Pediatric Pain Letter*. 2005;7(2-3):11–16

141. Gorodzinsky AY, Hainsworth KR, Weisman SJ. School functioning and chronic pain: a review of methods and measures. *J Pediatr Psychol*. 2011;36(9):991–1002

142. Sedaghat M, Abedin A, Hejazi E, Hassanabadi H. Motivation, cognitive engagement, and academic achievement. *Procedia Soc Behav Sci*. 2011;15:2406–2410

143. Beauregard M. *Consciousness, Emotional Self-Regulation and the Brain*. Philadelphia, PA: John Benjamins; 2004

144. Forgeron PA, King S, Stinson JN, McGrath PJ, MacDonald AJ, Chambers CT. Social functioning and peer relationships in children and adolescents with chronic pain: a systematic review. *Pain Res Manag*. 2010;15(1):27–41

145. Linton S, Nicholas M. After assessment, then what? Integrating findings for successful case formulation and treatment tailoring.. In: Breivik H, Campbell WI, Nicholas MK, eds. *Clinical Pain Management Second Edition: Practice and Procedures*, 2nd ed. London, UK: Hodder Arnold; 2008:95–106

146. Liossi C, Howard RF. The biopsychosocial assessment of chronic pain. In: Rajapakse D, Howard RF, eds. *Pain Management*. London, UK: Royal College of Paediatrics and Child Health; 2015

147. Nezu AM, Nezu CM, Lombardo ER. *Cognitive-Behavioral Case Formulation and Treatment Design: A Problem-Solving Approach*. New York, NY: Springer Publishing Company; 2004

148. Bruch M. The development of case formulation approaches. In: Bruch M, ed. *Beyond Diagnosis: Case Formulation in Cognitive Behavioural Therapy*, 2nd ed. West Sussex, UK: Willey Blackwell; 2015:1–23

149. Hechler T, Wager J, Zernikow B. Chronic pain treatment in children and adolescents: less is good, more is sometimes better. *BMC Pediatr*. 2014;14:262

150. Hechler T, Blankenburg M, Dobe M, Kosfelder J, Hübner B, Zernikow B. Effectiveness of a multimodal inpatient treatment for pediatric chronic pain: a comparison between children and adolescents. *Eur J Pain*. 2010;14(1):97.e1–97.e9

151. Hirschfeld G, Hechler T, Dobe M, et al. Maintaining lasting improvements: one-year follow-up of children with severe chronic pain undergoing multimodal inpatient treatment. *J Pediatr Psychol*. 2013;38(2):224–236

152. Barkus C, McHugh SB, Sprengel R, Seeburg PH, Rawlins JN, Bannerman DM. Hippocampal NMDA receptors and anxiety: at the interface between cognition and emotion. *Eur J Pharmacol*. 2010;626(1):49–56

153. Phillips RG, LeDoux JE. Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. *Behav Neurosci*. 1992;106(2):274–285

154. Davis M, Whalen PJ. The amygdala: vigilance and emotion. *Mol Psychiatry*. 2001;6(1):13–34

155. Dolan RJ. The human amygdala and orbital prefrontal cortex in behavioural regulation. *Philos Trans R Soc Lond B Biol Sci*. 2007;362(1481):787–799

156. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*. 2001;24:167–202

157. Ochsner KN, Gross JJ. The cognitive control of emotion. *Trends Cogn Sci*. 2005;9(5):242–249

158. Leh SE, Petrides M, Strafella AP. The neural circuitry of executive functions in healthy subjects and Parkinson's disease. *Neuropsychopharmacology*. 2010;35(1):70–85

159. Zaehle T, Bauch EM, Hinrichs H, et al. Nucleus accumbens activity dissociates different forms of salience: evidence from human intracranial recordings. *J Neurosci*. 2013;33(20):8764–8771

160. Bhojwani D, Howard SC, Pui CH. High-risk childhood acute lymphoblastic leukemia. *Clin Lymphoma Myeloma*. 2009;9(suppl 3):S222–S230

161. Balayssac D, Ferrier J, Descoeur J, et al. Chemotherapy-induced peripheral neuropathies: from clinical relevance to preclinical evidence. *Expert Opin Drug Saf*. 2011;10(3):407–417

162. Boland EG, Selvarajah D, Hunter M, et al. Central pain processing in chronic chemotherapy-induced peripheral neuropathy: a functional magnetic resonance imaging study. *PLoS One*. 2014;9(5):e96474

163. Tremblay I, Sullivan MJ. Attachment and pain outcomes in adolescents: the mediating role of pain catastrophizing and anxiety. *J Pain*. 2010;11(2):160–171

164. Nelson EC, Heath AC, Madden PA, et al. Association between self-reported childhood sexual abuse and adverse psychosocial outcomes: results from a twin study. *Arch Gen Psychiatry*. 2002;59(2):139–145

165. Kwako LE, Noll JG, Putnam FW, Trickett PK. Childhood sexual abuse and attachment: an intergenerational perspective. *Clin Child Psychol Psychiatry*. 2010;15(3):407–422

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Pediatric Chronic Pain: Biopsychosocial Assessment and Formulation

Christina Liossi and Richard F. Howard

Pediatrics 2016;138;
DOI: 10.1542/peds.2016-0331 originally published online October 14, 2016;