Classification of pain in children with cerebral palsy

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PUBLICATION DATA
Accepted for publication 30th September 2021.
Published online

ABBREVIATIONS

CPPC	Cerebral Palsy Pain Classification
ICD-11	International Classification of Diseases, 11th Revision

Pain in patients with cerebral palsy (CP) is a major health issue strongly associated with reduced quality of life. In this study, we provide an overview of pain conditions in children with CP using the International Classification of Diseases, 11th Revision (ICD-11), which has been updated with a classification of chronic pain. Common causes of pain in children with CP, including hip displacement, muscle spasms, and procedures, are discussed; less studied pain types including headaches, neuropathic pain, visceral pain, and acute versus chronic pain are also highlighted. The addition of chronic pain to the ICD-11 is an important step forward in optimizing both the registration and assessment of pain conditions. However, a tool designed specifically for the different types of pain in patients with CP is imperative. In this paper, we propose a Cerebral Palsy Pain Classification that is aligned with the underlying mechanisms of pain and the ICD-11 pain classification.

Pain is common in children with cerebral palsy (CP), with a reported prevalence of 27% to 77% depending on the setting, research criteria, time frame, age, CP type, and Gross Motor Function Classification System level.[1] Pain in patients with CP has often been described as underdiagnosed and undertreated, most likely because of the many complex clinical pain problems and communication difficulties that complicate the diagnostic process.[2] A study in northern England showed that only two-thirds of children with CP had a documented discussion about pain in their medical records.[3] However, early recognition of pain is vital because pain in children with CP has wide-ranging consequences. Pain significantly reduces quality of life in children with CP and is connected to mental health.[4,5] Pain is associated with impaired sleep and lower involvement in activities of daily living (e.g. relationships and recreation) even after adjustment for the severity of CP; pain in childhood is a predictor of restricted participation and lower quality of life later in life.[6,7] Because of the complexity of pain in children with CP, this patient group may benefit from a consistent and agreed classification of pain.

The International Association for the Study of Pain introduced a revised definition of pain in 2020 defining pain as 'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage'.[8] The accompanying notes also emphasize that verbal description is only one of several behaviours used to express pain. This addition is important for the inclusion of neonates, young children, and patients with severe developmental and intellectual disabilities. The updated International Classification of Disease, 11th Revision (ICD-11) includes, for the first time, a systematic classification of chronic pain.[9] Pain is classified according to duration as either acute or chronic, where chronic pain is pain that persists or recurs for more than 3 months. Chronic pain is classified either as chronic primary pain, where pain cannot be explained by another condition and may be considered a disease in itself, or chronic secondary pain, where pain is a symptom of an underlying condition (Fig. 1).

Apart from the new ICD-11 classification, pain can also be divided into three different pain types according to the physiological terms of nociceptive, neuropathic, and nociplastic pain. Nociceptive pain arises from actual or

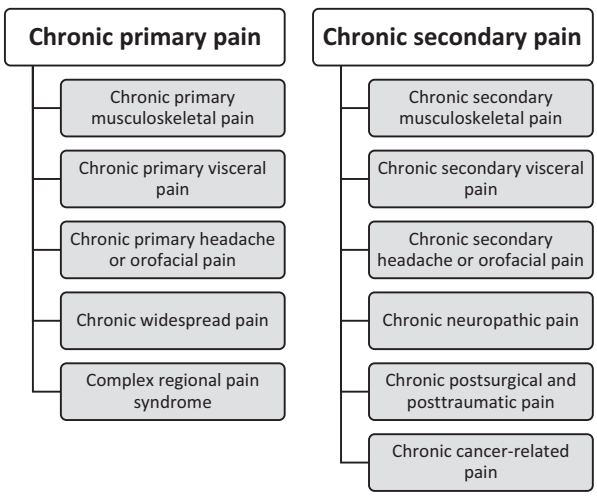

Figure 1: Systematic classification of chronic pain according to the International Classification of Diseases, 11th Revision.

threatened damage to non-neural tissue and is due to the activation of nociceptors. In contrast, neuropathic pain is caused by a lesion or disease of the somatosensory nervous system and nociplastic pain is pain that arises from altered nociception without activation of nociceptors or a disease or lesion of the somatosensory system.[10] Understanding the underlying mechanisms is important for identifying the origin of the pain and choosing the right treatment regimen. However, the ICD-11 classification of pain does not consistently differ between the mechanisms of pain.

The aim of this narrative review was to discuss pain in children with CP in the context of the new ICD-11 classification, highlighting the focus of previous studies. Furthermore, we propose a Cerebral Palsy Pain Classification (CPPC) that is specific for pain in patients with CP based on both the ICD-11 classification of pain and physiological terminology.

METHOD

We developed a search strategy to identify original research papers on pain in children with CP. A literature search was performed in PubMed, Embase, and Scopus on 8th January 2021 and 25th January 2021 using the MeSH terms 'pain' and 'cerebral palsy' and different keywords for the age groups 'child', 'adolescent', 'toddler', and 'pediatric'/'paediatric'.

A total of 2388 unique references were imported after removing 1995 duplicates. Screening was performed by MNV. First, titles and abstracts were screened; studies where pain was either the main theme or a specified outcome were included. Next, 593 full texts were reviewed. Studies with patients older than 18 years (if children were not evaluated separately) or studies with multiple diagnoses (if CP was not evaluated separately), reviews, conference abstracts, studies not written in English, and studies not available online were excluded. Finally, 195 studies were included and categorized based on the primary theme and the cause of pain (Fig. S1, online supporting information).

RESULTS

We identified 39 (20.0%) studies on acute pain, with only one study differentiating between acute and chronic pain. Acute procedural pain from botulinum neurotoxin A injections and acute pain after surgery were the most represented (Table 1).

Chronic secondary pain was reported by 81 (41.5%) of the reviewed studies; 75 of these studies focused on musculoskeletal pain. Most of these published studies were observational studies exploring the effect of surgical treatment on motor function and pain. In comparison, only two studies explored peripheral neuropathic pain and none focused on central neuropathic pain. Furthermore, only one study specifically examined primary chronic pain.

The remaining 74 (37.9%) studies did not specify the cause or type of pain. These studies were primarily about pain prevalence and quality of life. Other studies on non-specified pain included data on sleep, physical activity, sensory function, biomarkers, and parental stress. Details on how pain was classified in the studies included in this review are shown in Tables S1 to S3 (online supporting information).

What this paper adds

- Most studies investigate musculoskeletal pain but overlook other types of pain.
- The Cerebral Palsy Pain Classification encompasses both International Classification of Diseases, 11th Revision and pain physiological classifications.

In the following sections, based on the ICD-11, we review the causes of acute pain and chronic primary and secondary pain in children with CP.

Acute pain

Children with CP often have many health care encounters during their childhood and often undergo interventions such as surgery, botulinum neurotoxin A injections, and physiotherapy that may be painful. Botulinum neurotoxin A injections are used to reduce spasticity and dystonia; up to 35% of injections are reported as painful.[11] Acute nociceptive pain is frequent after surgical procedures and may increase muscle spasms, which can be an additional source of pain.[12] This vicious cycle of pain-induced spasms that further increases pain is discussed under the chronic secondary pain section of this review.

Table 1: Primary themes in the studies about pain in children with cerebral palsy identified in this review

	n (%)
Acute pain	39 (20.0)
Procedural pain	
Pain from botulinum neurotoxin A injections	11 (5.6)
Pain during surgery	3 (1.5)
Other	1 (0.5)
Postsurgical pain	16 (8.2)
Rehabilitative pain	
Pain from physiotherapy	5 (2.6)
Pain from using standing frames	3 (1.5)
Chronic primary pain	1 (0.5)
Complex regional pain syndrome	1 (0.5)
Chronic secondary pain	81 (41.5)
Musculoskeletal pain	
Pain from deformities and misalignment	40 (20.5)
Spasticity and dystonia-related pain	27 (13.8)
Bone pain	2 (1.0)
Other	6 (3.1)
Visceral pain	
Gastrointestinal pain	3 (1.5)
Headache	0 (0)
Neuropathic pain	
Peripheral neuropathic pain	2 (1.0)
Central neuropathic pain	0 (0)
Postsurgical pain	1 (0.5)
Chronic cancer-related pain	0 (0)
Non-specified pain	74 (37.9)
Pain prevalence	15 (8.0)
Quality of life, mental health, and coping	40 (20.5)
Other	19 (9.7)

Overview of 195 studies on pain in children with cerebral palsy categorized based on the primary theme and cause of pain.

Physiotherapy is very important for improving and preventing loss of motor-related functions, such as balance, movement, and posture. However, up to 45% of children with CP report pain during physiotherapy[1] and assisted stretching and range of motion manipulation have been reported as commonly provoking pain.[13] Standing frames are used for postural management; these have been reported to be painful in 14% of children with CP.[14]

According to the studies included in this review, acute pain is most often caused by an intervention; therefore, it is likely to activate nociceptors. However, neuropathic pain (e.g. after surgery), which is discussed later in this review, should also be classified as acute pain in the first 3 months.

Chronic primary pain

Complex regional pain syndrome has been described in children with CP in a few cases after multilevel surgery[15] but is otherwise not mentioned in the studies reviewed here.

Migraine and tension-type headache are classified as primary pain. Headache is common in children with CP, with a reported incidence of 34%.[1] None of the studies included in this review categorized headache as chronic or distinguished between primary and secondary headache.

Pain of nociplastic origin, such as chronic widespread pain (e.g. fibromyalgia), is not mentioned in the existing literature on CP.

Chronic secondary pain

Secondary musculoskeletal pain

Musculoskeletal pain is the most common pain described in children with CP; it is often caused by joint misalignment, increased muscle tone, and osteoporosis.[16] Muscle spasms can be a direct cause of recurring pain. It has been hypothesized that pain from muscle spasms is caused by muscle contractions leading to vascular compression. This causes muscles to consume large amounts of oxygen while working under ischaemic conditions, resulting in the activation of group IV nociceptors.[17] Pain itself may lead to an increase in muscle spasms, creating a vicious cycle. Other common causes of increased muscle spasms are fatigue, overuse, and inflammation.

Spasticity together with muscle weakness and soft tissue changes contribute to secondary painful conditions, such as contractures.[17,18] Furthermore, spasticity and contractures contribute to painful conditions, such as deformities and joint misalignment, especially in weight-bearing joints. The prevalence of hip pain was reported at 7% in a mixed group of children with CP; hip pain increases with age, Gross Motor Function Classification System level, and the degree of hip misalignment, that is, hip dislocation and subluxation.[19] The causes of knee pain can be divided into three groups: patella alta (high riding patella), which is very common;[20] inferior pole fractures; and misalignment of the patella.[21] Crouch gait caused by excessive knee, hip, and dorsal ankle flexion may cause knee pain due to excessive loading of the patellofemoral joint.[22] Foot and ankle deformities have a reported incidence of up to 93% in children with CP and may cause pain due to uneven pressure.[23]

Postural asymmetries are also associated with pain.[24] Back pain is more frequent in patients with scoliosis and increases with age. A register study of children with CP found back pain in 4% without scoliosis and in 16% with severe scoliosis.[25] Scoliosis commonly affects patients with spasticity and its incidence corresponds to the severity of CP. Patients with spasticity predominantly affecting the lower extremities have a much lower incidence of scoliosis (5%) compared with patients with spasticity affecting all four extremities (65%–74%). Back pain is also described in other spinal deformities, such as excessive kyphosis or lordosis. Furthermore, scoliosis can cause pain due to impingement of the ribs against the iliac crest.[26]

Osteoporosis is seen at an early age in patients with CP due to decreased mechanical loading. Osteoporosis can cause bone pain and non-ambulant children are at risk of painful pathological fractures mainly of the lower extremities. Children classified in Gross Motor Function Classification System levels III to V have a 4% incidence of fractures per year; fractures are not only painful but also lead to further immobilization.[27]

Secondary visceral pain

Visceral pain can be subdivided based on the underlying cause (e.g. mechanical, vascular, inflammatory). Abdominal pain is common and has been reported in 26% of children with CP.[1] Another study showed that 92% of children with CP had clinically significant gastrointestinal symptoms.[28] Some were painful conditions, such as abdominal pain, gastro-oesophageal reflux, and constipation. It is likely that a physiological mechanism (and consequently a nociceptive mechanism) causes some of the abdominal pain in children with CP. An increased colon transit time in the rectosigmoid colon is common in children with CP, even in children without constipation problems.[29] A disturbance of the neural modulation of colonic motility may play a role in the development of gastrointestinal disorders, such as constipation and gastro-oesophageal reflux.[28] However, visceral pain is still not fully understood; it is not unlikely that some visceral pain conditions may be underpinned by a neuropathic or nociplastic mechanism.

Secondary headache or orofacial pain

Bruxism is reported in up to 70% of children with CP; it is a risk factor for painful temporomandibular disorders causing symptoms such as secondary headaches and jaw pain.[30,31] Furthermore, pain may arise from trauma to the internal oral mucosa and lower lip caused by oral reflex automatism with spastic tonic bite and interposition of the lower lip.[32]

Neuropathic pain

Neuropathic pain is characterized by ongoing pain, which may be persistent or intermittent with shooting paroxysms of pain and experienced as burning, squeezing, pricking, or

Table 2: Cerebral palsy pain classification

Pain			
Origin	Type	Subtype	Source
Secondary pain	Nociceptive pain	Musculoskeletal pain	Subluxation, dislocation, scoliosis, deformities, spasms, contractures, overuse syndromes, surgery (postsurgical pain)
		Visceral pain	Constipation, gastro-oesophageal reflux
		Other nociceptive pain	Skin ulcers, mucosal ulcers, secondary headache, or orofacial pain
	Neuropathic pain	Peripheral neuropathic pain	Surgical nerve injury (postsurgical pain), nerve compression
		Central neuropathic pain	Early brain injury
Primary pain	–	–	Migraine, tension-type headache, complex regional pain syndrome

Classification of pain for patients with cerebral palsy based on the physiological and International Classification of Diseases, 11th Revision pain classifications.

freezing pain. Patients with neuropathic pain may also experience evoked pain, for example, allodynia where light touch or contact with a cold object can cause pain or hyperalgesia where the response to painful stimuli is heightened. Peripheral neuropathic pain may arise after surgery or injury of the peripheral somatosensory nervous system. In a case series, six children out of 40 developed neuropathic pain after multilevel surgery. It was assumed that pain arose after stretching the nerves on releasing joint contractures.[33] Furthermore, postoperative neuropathic pain has been reported in 5.3% of cases after selective dorsal rhizotomy.[34]

Central neuropathic pain is pain caused by damage or disease in the central somatosensory system. It is well described after acquired brain injury in adults but not in patients with CP even though sensory disturbances are reported. One study found that children with CP have reduced sensitivity to non-painful stimuli but enhanced sensitivity to painful stimuli.[35] Another study found that children and young adults were less sensitive to mechanical and thermal stimuli and more sensitive to all mechanical painful stimuli while 23% had allodynia.[36] Despite injury of the central somatosensory nervous system and the presence of sensory disturbances, to our knowledge no studies examined whether central neuropathic pain develops as a direct consequence of brain injury in individuals with CP.

Chronic postsurgical pain

After undergoing surgery, children with CP are at risk of developing chronic postoperative pain. Back pain and leg pain have been reported in children several years after undergoing selective dorsal rhizotomy.[37] The goals of surgical interventions in patients with CP are often to improve mobility and relieve pain. Few studies have assessed if continued pain after surgery is due to an unsuccessful correction of the source of the pain or the surgery itself; hip pain after unsuccessful surgery has been mentioned in the literature.[38]

DISCUSSION

Categorizing pain in children with CP using the ICD-11 enabled us to identify commonly studied pain types. However, it is apparent that some pain types in children with CP may fit into multiple categories depending on the underlying mechanism. As an example, postsurgical neuropathic pain due to peripheral nerve injury may be classified as both neuropathic pain and postsurgical pain and may be found under both categories since the ICD-11 allows the same diagnosis to be subsumed under more than one category.

A classification system of pain specific to patients with CP is paramount for facilitating new pain research while also being a helpful tool for clinicians. Thus, we propose a CPPC that is aligned with both physiological and ICD-11 classifications, leaving out pain not directly associated with CP (Table 2). The proposed classification has been inspired by the International Spinal Cord Injury Pain Classification and organizes pain in individuals with CP into four tiers.[39] The first tier differentiates between primary and secondary pain in the ICD-11, while the second tier differentiates between the physiological origins of pain. The underlying mechanism is essential for both the general understanding and treatment of pain. The third tier includes pain subtypes and the fourth tier the possible sources of pain; both include elements from the ICD-11. Using an agreed classification in both clinical and research settings increases consistency and the ability to compare studies on pain. When classifying pain, some studies refer to McKearnan et al.'s[40] list of common contributors to pain in children with CP. However, it is important that a classification is translatable to the ICD-11, which should be a criterion standard for coding information about diseases once fully implemented. The inclusion of chronic pain in the ICD-11 is an important step forward. It is designed to be applicable to all painful conditions; however, this makes it less specific for a condition such as CP, which encompasses many different types of pain. The CPPC is a tool that may help those working with patients with CP, while still being translatable to the ICD-11, from the pain researcher trying to classify pain from a physiological point of view to the neuropaediatrician or physiotherapist trying to assess pain in patients with CP. Just as

the introduction of a classifications system in the field of headache greatly facilitated research in that area, we hope the same will apply to pain research in CP.

Categorizing the studies included in this review also highlighted possible pain contributors that may require investigation. Postoperative peripheral neuropathic pain in both children and adults with CP has been sparsely studied. To our knowledge, central neuropathic pain has not been studied despite the presence of sensory disturbances in patients with CP and clear evidence of this type of pain in adults with acquired brain injury.

Despite the high prevalence of gastrointestinal symptoms in children with CP, few studies have examined visceral and/or gastrointestinal pain. The reason could be that it is difficult to locate pain in children with communication problems or may be due to the assumption that pain is mainly of musculoskeletal origin in this patient group. We suggest including a pain dimension as an outcome measure in future studies of the gastrointestinal system in patients with CP. A correlation between pain and gastrointestinal symptoms may compensate for the difficulties in recognizing and localizing abdominal pain.

Although headaches are common in patients with CP, it is uncertain whether they are acute or chronic, primary or secondary. From a treatment perspective, it would be beneficial for clinicians to know if certain types of headaches are associated with certain types of CP, for example, if patients with spasticity often develop tension-type headache or migraine, especially since the diagnosis of migraine is based on the description of multiple attacks, something that might be difficult to verbalize for children with cognitive or verbal impairments. In general, chronic primary pain is sparsely mentioned in the literature on CP, probably with good reason since chronic pain caused by the consequences of CP would be classified as secondary.

Multiple chronic pain assessment tools are available to address pain in children with CP.[41] In young children and patients with communication problems, pain assessment may have to rely on proxy reports. Additionally, assessment of pain severity can be done by health professionals using tools measuring non-verbal behaviour.[42] Musculoskeletal pain is easier to diagnose than neuropathic pain and headaches. While misalignment of the hip or restricted range of motion is measurable, and pain can be provoked manually, the diagnosis of neuropathic pain and headaches relies on subjective descriptions of pain; this is a challenge for patients who cannot verbalize. Therefore, there is a need for new tools to assess these pain types in children and adults with impaired communication.

CONCLUSION

Musculoskeletal pain is widely studied in children with CP, whereas there are only a few studies on visceral pain and headaches, although there is evidence to suggest that these pain types are frequent in both adults and children with CP, with a detrimental effect on their quality of life. Furthermore, central neuropathic pain has not been studied despite its presence in adults with acquired brain injury. Implementation of the ICD-11 classification of chronic pain will facilitate research greatly by improving the assessment and registration of pain. The CPPC is meant as an additional tool to specifically assess pain in patients with CP. Hopefully, the CPPC will be adopted as a useful tool that benefits both the researcher classifying pain and the clinician diagnosing it.

ACKNOWLEDGEMENTS

This review was supported by the Elsass Foundation.

SUPPORTING INFORMATION

The following additional material may be found online:

Figure S1. PRISMA flow diagram of included studies.

Table S1. Studies on acute pain in children with cerebral palsy

Table S2. Studies on chronic secondary pain in children with cerebral palsy

Table S3. Studies on non-specified pain in children with cerebral palsy

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