CLINICAL CARE FRAMEWORK

Chronic Pain in Children with Severe Impairment of the Central Nervous System: A Framework for Assessment and Initial Management

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ABSTRACT

Children with severe impairment of the central nervous system (CNS), often referred to as children with severe neurological impairment (SNI), have a significantly higher incidence of acute and chronic pain compared to children with mild impairment or with typical development. This article is focused on chronic pain sources due to the altered CNS, referred to as neuro-pain in this article. Chronic pain has a significant impact on quality of life and health outcomes of the child and family. It requires a distinctly different approach from acute pain, including goals of treatment. A case example highlights many of the challenges that delay treatment for neuro-pain, including lack of diagnostic tests or criteria, risk for multiple comorbid problems, and the impact of cognitive bias. A proposed screening process and assessment tool are provided, intended to identify children at risk for neuro-pain as a reason for recurrent symptoms who therefore may benefit from a medication trial for neuro-pain. Parents also face many worries throughout this process. Language strategies are provided to assist with needed support.

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INTRODUCTION

Children with severe impairment of the central nervous system (CNS), often indicated as children with severe neurological impairment (SNI), have a significantly higher incidence of pain compared to children with mild impairment or with typical development.[1] This includes both acute pain, which alerts to a cause of tissue injury in need of identification and treatment, and chronic pain often due to the altered nervous system.

A child with SNI and pain without a clear source may be described as irritable or agitated, terms that indicate a problem in need of attention. Irritability is defined as an abnormal response to stimuli or physiological arousal that can be in response to pain, a medication, an emotional situation, an acute illness or medical condition.[2] Pain is a frequent cause of irritability in children with SNI, highest in those with severe to profound intellectual disability and with cerebral palsy classified as Gross Motor Function Classification System (GMFCS) level 4 and 5 or indicated to have limited to no use of extremities.[3-6] Those with the greatest impairment were identified to have recurrent pain that is weekly to daily.[3-6]

The American Academy of Pediatrics (AAP) clinical report on pain in children with SNI provides a comprehensive review of the assessment and management of acute and chronic pain in such children.[1] This article will focus on chronic pain that is due to the altered nervous system. This focus is essential given the high incidence of chronic pain in children with SNI, the lack of diagnostic tests to guide identification, and the significant impact on quality of life and health outcomes of the child and family. Ensuring symptom control has been identified by parents as one of the essential domains of care.[7,8]

Chronic pain, defined as pain that recurs for more than 3 months, requires a distinctly different approach from acute pain, including goals of treatment as noted in

Table 1. Acute versus Chronic Pain

	Acute	Chronic
Cause	Expected with surgery or due to causes of tissue inflammation and injury (i.e. nociceptive pain)	Pain that recurs for more than 3 months; categories include musculoskeletal, visceral, post-surgical, and neuropathic
Duration	Hours to days	> 3 months, persists
Identification	Sources typically identified by diagnostic tests	No routine diagnostic tests or criteria for sources due to the impaired nervous system
Goals	Resolution after treatment of cause and healing of tissue injury	Pain control, not cure

Table 2. Chronic neuro-pain sources

Problem	Features, Comments, and Treatment Options
Central neuropathic pain	Symptoms include pain localized to the GI tract, such as pain triggered by normal distention of the GI tract; this can be suggested by pain associated with tube feedings or intestinal gas, with relief following a bowel movement or flatus Pain features can occur spontaneously and with no trigger, described by adults as "shock-like" and "out of the blue" Due to impairment of the spinothalamic tract and thalamus Treatment: gabapentinoids, tricyclic antidepressants, SNRIs, methadone
Visceral hyperalgesia	Decreased threshold to pain generation in response to a stimulus in the GI tract, including a decrease in the amount of distention that triggers a pain signal Attributable to sensitization of visceral afferents and central sensitization in the CNS Treatment: gabapentinoids, tricyclic antidepressants, clonidine
Chronic post-surgical pain (CPSP)	Defined as pain that lasts more than 2 months post-surgery without other causes of pain such as chronic infection or pain from a chronic condition preceding surgery The mechanisms leading to chronic CPSP can include inflammation, tissue and nerve damage, and alterations in central pain processing Treatment: gabapentinoids, tricyclic antidepressants
Autonomic dysfunction (dysautonomia)	Features include skin flushing, hyperthermia, pain localized to the GI tract, retching, bowel dysmotility, discomfort, agitation, tachycardia, sweating, arching, stiffening Dysautonomia can be a source of discomfort, and pain can trigger the features that occur with dysautonomia Treatment: gabapentinoids, clonidine
Dystonia	Involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both Pain from other sources can trigger and worsen dystonic movement Treatment: baclofen, trihexyphenidyl, gabapentinoids, clonidine
Paroxysmal autonomic instability with dystonia (PAID)	Involves features of both autonomic dysfunction and dystonia Indicates altered function of the CNS areas that regulate autonomic function and movement; such children are also at risk for co-morbid central neuropathic pain Pain from other sources can trigger and worsen the observed features Treatment: see dysautonomia and dystonia
Spasticity	Velocity-dependent increase in muscle tone that results in muscles that are resistant to movement Spasticity is often not painful but can result in musculoskeletal pain over time Treatment: baclofen, alpha2-agonists (clonidine or tizanidine)
Muscle spasms	Sudden involuntary contraction of a muscle or group of muscles; associated features can include arching, stiffening, tremors, and clonus Pain behaviors can indicate pain from muscle spasms and indicate pain from another source as the trigger for muscle spasms Treatment: interventions for spasticity, chronic neuro-pain, and other triggers

GI: gastrointestinal; SNRIs: serotonin norepinephrine reuptake inhibitors

Table 1.[9] Chronic pain sources due to the altered nervous system are reviewed in Table 2. Neuro-pain is used in this article to refer to these sources given the overlap in presenting features of each. A case example highlights the many challenges that delay treatment for neuro-pain, including the lack of diagnostic tests or criteria, risk for multiple comorbid problems, and the impact of cognitive bias.

Figure 1 provides a proposed screening process when symptoms recur in a child with SNI. The neuro-pain risk assessment tool (N-PRAT) is a hypothesis-generated tool developed to screen for a reasonable likelihood of benefit from an empirical trial directed at neuro-pain sources (Figure 2). The case illustrates the need for a screening process and tool. Experts in managing chronic pain in children with SNI, such as pediatric palliative care clinicians, can assist those with limited experience. For others, expertise might be sought when a child has continued symptoms following the first medication trial.

Figure 1

Screening children with SNI for risk of chronic neuro-pain

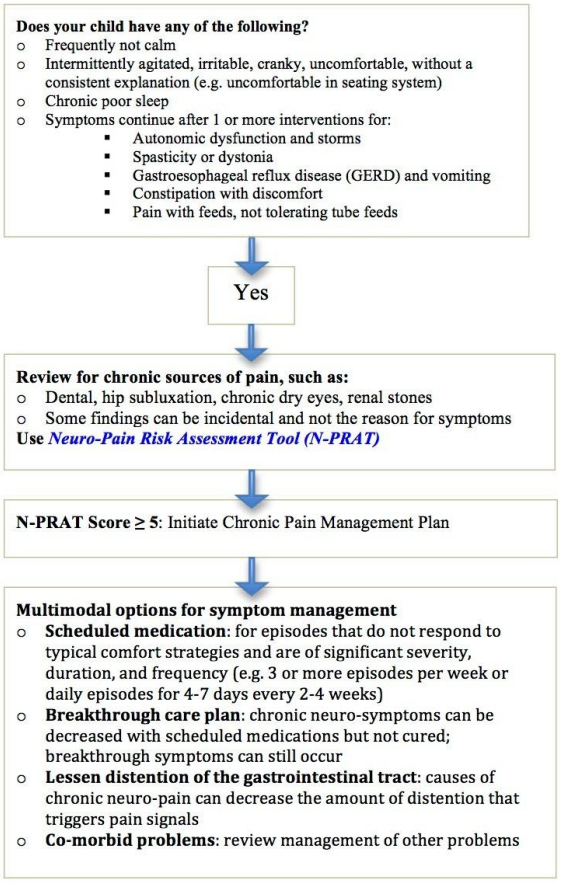

Figure 2. Neuro-Pain Risk Assessment Tool (N-PRAT)

Neuro-Pain Risk Assessment Tool (N-PRAT)	Score: Circle if present
Episodes with pain behaviors from 2 or more of the following categories, recurring for more than 3 months without a consistent source*; episodes may be weekly or cyclical (e.g. daily for 3 to 5 days every 2 to 4 weeks) • *Vocalizations*: crying, moaning • *Facial expression*: grimacing, frowning, eyes wide open • *Unable to console*: difficult to calm, not soothed by parent comfort actions • *Interaction*: withdrawn, seeking comfort • *Physiological*: tachycardia, sweating, pale or flushed skin, tears • *Muscle tone*: intermittent stiffening of extremities, clenching of fists, muscle tensing, tremors, back arching • *Movement*: increased movement, restless, startles easily, pulls away when touched, twisting	1 point for 2 or 3 categories 2 points for 4 or more categories
GMFCS* level 4 and moderate to severe intellectual disability OR	1
GMFCS* level 5 and severe to profound intellectual disability	2
Some episodes occur rapidly and out of the blue with no known trigger, quickly changing from calm to agitated / irritable / in pain	1
Intermittent increase in muscle tone, movement and posture: features continue following 1 or more drugs for spasticity or dystonia	1
Autonomic dysfunction and storms: features remain significant following 1 or more drugs for autonomic dysfunction	1
GI symptoms: Pain behavior episodes noted with tube feeds, intestinal gas, and constipation, with improvement when feeds are held and following a bowel movement; symptoms continue following 1 or more drugs for GERD	1
Chronic poor sleep with symptoms of agitation / discomfort	1
Post-surgical: new or worsening pain behavior episodes for > 2 months following surgery without a clear cause	1
Intractable seizures following 3 or more anti-seizure drugs	1
Planned surgery: prior to surgical interventions for GERD, spasticity, or dystonia to determine if chronic neuro-pain is a trigger; gabapentinoids may decrease need for post-surgical opioids and development of postsurgical pain[28]	1
Total score (highest score = 12)	

Total score ≥ 5: initiate multimodal approach to symptom management (Figure 1)

*__Nociceptive assessment noted in Figure 1 of AAP clinical report__.[1] Consider cognitive bias towards positive tests that may result in recurrent treatment in a symptomatic child with SNI, yet the positive test may represent colonization or an incidental finding and not be the source of symptoms (e.g. positive urine culture with less than 10 white blood cells in urinalysis, positive clostridium difficile with test that does not distinguish carrier from infection, gallstones with no other abnormal findings on labs or ultrasound)

*__GMFCS:__ used here as an indicator of motor function level in children with severe impairment of CNS

CASE

Parents gave informed written consent. This case series was structured as per the case report guidelines.[10]

A 14-year-old boy with Bohring-Opitz syndrome (BOS), a condition caused by mutations in the ASLX1 gene, has multiple features reported with BOS, including profound intellectual disability, hypotonic cerebral palsy (CP) GMFCS level 5, characteristic facial features, seizure disorder, and recurrent emesis and retching over years that is classified as cyclic vomiting syndrome.[11] He also has has a long-standing history of severe sleep disruption that has been assessed by a sleep specialist. Other problems include multiple congenital anomalies, right hip subluxation and progression of scoliosis. Head MRI identified agenesis of the corpus callosum and parenchymal volume loss of the frontal lobe. All feeds, fluids, and medications are given by a gastrostomy feeding tube. There has been no sustained weight gain in 3 years, due to the recurrent emesis and need to hold feeds intermittently. His respiratory status remains stable with occasional use of supplemental oxygen overnight.

Past major surgeries include: bilateral complete cleft lip and palate repair and open gastrostomy tube placement (2005), craniofacial surgery (2005, 2006), tracheotomy (2005), laryngotracheal reconstruction reconstruction and decannulation (2007), adenoidectomy (2011), bilateral orchidopexy (2012), diagnostic laparoscopy, gastrocutaneous fistula closure and placement of new gastrostomy button (2015), lower extremity orthopedic surgery (2018). Fundoplication surgery is being considered.

Diagnostic assessment has been unremarkable and included: abdominal ultrasound (2007, 2017, 2018), gastric emptying (2008, 2010), upper GI endoscopy (2008, 2011), and sinus radiographs (2012, 2015). Interventions for recurrent emesis

have “not made a clear difference” per parent report, including proton pump inhibitors, carafate, various interventions for constipation, and other medication trials including ondansetron, lorazepam, and cyproheptadine. There was limited benefit in sleep with melatonin and lorazepam, followed by improvement with clonidine, initially started at 0.003 mg/kg then increased to 0.006 mg/kg at nighttime.

Emesis occurs daily for 2 to 4 days, with a cycle every 2 to 4 weeks. He is irritable during these events as well as irritable at other times. Irritability can be triggered by intestinal gas and prior to a bowel movement; other irritably can occur “out of the blue” without an identified trigger. Pain behaviors during these events include facial grimacing, tightening of extremities, appearing restless, increased movement, tachycardia, and difficult to soothe. Other associated problems include the long-standing history of severely disrupted sleep. It is unclear if symptoms worsened following any specific surgery. Assessment with the N-PRAT identified a total score of 8. Gabapentin was initiated and titrated to a dose of 40 mg/kg/day. There has been a significant sustained benefit 7 months later, including almost no episodes of emesis, further improvement in sleep, and described as much more comfortable and interactive during the day, “like a new kid”. This improvement included a 24% increase in weight 5 months after starting gabapentin.

Figure 3. Case N-PRAT Score

Neuro-Pain Risk Assessment Tool (N-PRAT)	Score:
Episodes with pain behaviors from 2 or more categories, recurring for more than 3 months without a consistent source; episodes are cyclical, occurring for 2 to 4 days every 2 to 4 weeks	2 points (features from 6 categories: moaning, frowning, restless, movement, tachycardia, difficult to soothe)
GMFCS level 5 and severe to profound intellectual disability	2
Some episodes occur rapidly and out of the blue	1
Intermittent increase in muscle tone, movement and posture	1
Autonomic dysfunction and storms	0
GI symptoms	1
Chronic poor sleep	1
Post-surgical	0 (unclear given surgeries in infancy)
Intractable seizures	0
Planned surgery	0
Total score (highest score = 12)	**8**

CHRONIC PAIN DUE TO THE ALTERED NERVOUS SYSTEM

Chronic pain categories identified by the International Association for the Study of Pain (IASP) include musculoskeletal, neuropathic, visceral, and post-surgical pain, categories that are relevant to children with SNI.[9] Other sources in children with SNI include autonomic dysfunction, spasticity, and dystonia as both sources of intermittent pain and with features that are triggered by the other causes of chronic pain.[1]

This article uses the term neuro-pain to indicate chronic pain sources due to the altered nervous system yet without diagnostic tests to identify or to distinguish one source from another. Children with SNI

are at risk for more than 1 of the causes noted in Table 2. The term neuro-pain is recommended over neuro-irritability when episodes are recurrent and include pain behaviors. With recurrent episodes, word choice can impact how the problem is approached. A child might be described as "this is what he does" when neuro-irritability is used versus a problem that may benefit from further assessment and interventions when neuro-pain is used.[12]

Table 3 provides language strategies that anticipate parental worry when discussing neuro-pain. Parents experience many worries throughout this process. Parents can benefit from time to reflect on this complex information, as well as a process that supports shared decision making.

PRESENTING FEATURES OF NEURO-PAIN

Identifying neuro-pain requires knowledge of pain behaviors, which are the observable features expressed by a nonverbal child with SNI when in pain, with examples noted in the N-PRAT.[1] Behavioral pain assessment tools for such children are reviewed in the AAP clinical report.[1] The revised Face, Legs, Activity, Cry, Consolability scale and the Individualized Numeric Rating Scale can be individualized with a child's specific behaviors, useful for new providers unfamiliar with the child.[13,14] These tools were validated in the acute care and post-surgical settings. The pain behaviors noted in these and other tools can assist parents and providers in identifying an individual child's specific features.

Pain assessment tools can assist with rating the worst and typical pain episodes. Chronic pain requires broader considerations beyond rating, including the frequency and duration of episodes along with the impact on sleep and engagement in activities. This holistic approach aids in determining benefit when a scheduled medication is initiated. Some children will have cyclical episodes, such as daily episodes for 3 to 7 days every

2 to 4 weeks, as noted in this case example and in other case reports.[15]

Children with SNI and chronic neuro-pain can present with the other features noted in Table 2. These include GI symptoms (i.e. pain localized to the GI tract, emesis, and feeding intolerance), recurrent muscle spasms, tensing and movement, intermittent autonomic storms, and pain that persists following surgery.[1,16] Such children can have irritability and pain that recurs without a clear source, or keeps returning following interventions for gastroesophageal reflux disease (GERD), constipation, spasticity, dystonia, and autonomic dysfunction. Figure 1 incorporates this information into the proposed screening process to identify children with SNI in need of further assessment. The case had many of the features noted in “Does your child have any of the following?” from Figure 1, with a subsequent score of 8 with the N-PRAT, following recurrent assessment and a variety of interventions for constipation, GERD, cyclic vomiting, and sleep.

THE IMPACT OF COGNITIVE BIAS

Cognitive bias results in ways of thinking that influence decision making and judgment.17 Anchoring bias, a tendency to rely heavily on one piece of information, and availability heuristic, the tendency to overestimate the likelihood of explanations that are more readily available in one's memory, are examples that can interfere with the consideration of neuro-pain in children with SNI. A focus on spasticity as the primary reason for recurrent muscle spasms is one example; cognitive bias awareness can then increase consideration of chronic neuro-pain sources as another reason for recurrent spasms. Other examples include remaining focused on GERD, cyclic vomiting, and constipation as the reasons for recurrent GI symptoms, and dystonia with intermittent dystonic movement as the cause of associated pain during these episodes.

Attributing an etiology of neuro-pain behaviors to a positive bacterial culture that may be due to colonization is a form of cognitive bias. Examples include a positive tracheal culture, a positive urine culture in someone with clean intermittent catheterization for neurogenic bladder with less than 10 white blood cells per high-power field in the urinalysis, and a positive clostridium difficile test that does not distinguish carrier from infection.18-20 A decision to treat a positive test is a result of the patient being symptomatic, with the understandable anchoring bias that the recurrent symptoms are due to the positive

test. Yet symptoms may be due to underlying neuro-pain, a category of problems without diagnostic tests. Other examples of positive tests in children with SNI that in retrospect were incidental include persistent symptoms following cholecystectomy and following anti-inflammatory treatment for nonspecific colitis identified by colonoscopy.1,21 In these cases, symptoms improved after medication use for neuro-pain.

Awareness of cognitive bias is not about being right or wrong; instead, awareness of the impact of cognitive bias can loop us back to other considerations, given the many inherent challenges in children with SNI and risk for multiple comorbid problems. These examples highlight the benefit of considering neuro-pain sources when symptoms continue to recur after treatment for infectious sources that might represent colonization, and considering a medication trial prior to an invasive diagnostic test or surgery. Treatment can then determine how much neuro-pain is contributing to recurrent symptoms that may be attributed to these other problems. Transparent discussions and support will help parents throughout this complex process.

TREATMENT WHEN SYMPTOMS ARE RECURRENT

Figure 1 outlines a proposed process for children with SNI and recurrent symptoms. The N-PRAT screens for risk of neuro-pain and therefore guides a decision to start an empirical medication trial. The GMFCS is used with the N-PRAT to identify those who have the greatest impairment in motor function. Identifying children with SNI who are GMFCS level 4 or 5, along with severe to profound intellectual disability, assists with identifying individuals who have the highest risk for chronic pain. Some children will not meet the criteria for CP due to having a neurodegenerative disease or injury of the CNS beyond the age cut-off used for CP.

The N-PRAT was applied retrospectively to the last 22 children with SNI and recurrent symptoms assessed by this author and viewed as benefitting from gabapentin, some with greater benefit following a second medication. All were on treatment for other problems, including GERD, spasticity, and seizures. The total score with the N-PRAT was 5 or greater in each child, greater than 6 in most. This tool addresses the lack of diagnostic tests or criteria for neuro-pain sources in children with SNI, which contribute to treatment delay. The

criteria used to diagnose central neuropathic pain in adults is not valid for children with SNI given a need for input from the patient.[22] The N-PRAT is intended as a screening tool to prompt the steps outlined in Figure 1. A score of 5 or greater identifies those who have a greater potential for benefit than risk with a medication trial for neuro-pain. This tool is needed and promising, but is also in need of prospective study to determine its usefulness, including its validity, interrater reliability, and the sensitivity of the identified cutoff score of 5.

A gabapentinoid is recommended as a first line medication trial, based on evidence and safety.[1] The goal of a scheduled medication is to decrease the frequency, severity, and duration of episodes, along with improvement in other associated problems, such as sleep. Parents can be asked if it is more important to avoid sedation by using a slower titration in the medication dose or to improve comfort with a faster titration even if it means some initial sedation. The AAP clinical report provides dosing guidelines to ensure an adequate trial.[1] Other considerations in chronic neuro-pain management include:

- Developing breakthrough care plans
- Minimizing GI tract distention as a trigger for symptoms
- Managing other comorbid problems, such as spasticity

Distention of the GI tract can trigger symptoms given that causes of chronic neuro-pain can decrease the amount of distention needed to trigger pain signals.[23,24] Parents can be instructed to use a suppository or enema during a persistent pain episode to determine if distention of the colon prior to a bowel movement is contributing to symptom generation. This can be part of the breakthrough care plan if the intervention results in a bowel movement followed by a significant decrease in the acute symptoms. Overestimation of calories can also contribute to symptoms. Children with SNI at high risk for calorie overestimation include those with limited to no movement of extremities, with intermittent hypothermia, or with declining health resulting in less activity. These circumstances can decrease estimated metabolic expenditure by 30-50% for non-ambulatory children with cerebral palsy.[23]

BREAKTHROUGH SYMPTOMS AND CARE PLANS

Following a medication trial for neuro-pain, intermittent symptoms may decrease in frequency and intensity yet still occur, given that symptoms generated by these sources can be modified but not eliminated. At other times, persistent breakthrough symptoms

can be from a new nociceptive pain source. Medications for neuro-pain will not eliminate the generation of pain signals from a new cause of nociceptive pain.

Breakthrough care plans can be developed to manage breakthrough symptoms due to chronic neuro-pain sources. The AAP clinical report provides details about developing a breakthrough care plan, including examples.[1] Care plans can be updated as experience determines which interventions are useful for each child. Interventions to consider include non-pharmacologic (repositioning, swaddling, vibration, rocking) and pharmacologic (ibuprofen, acetaminophen, clonidine, opioid, and benzodiazepine).[1]

Experience will also guide when to evaluate for a new nociceptive source. This might include a time when symptoms persist following breakthrough interventions that typically help, when new features are observed, or when something seems worrisome to the parent. Likewise, as tests are repeated and are normal, parents and clinicians might feel more comfortable not repeating tests. The breakthrough care plan can also be adjusted and a new medication trial considered. This process can be distressing, given the worry about a new pain source and the risk that symptoms due to neuro-pain can persist following the first medication trial.

SEDATION THAT PERSISTS FOLLOWING A MEDICATION TRIAL

Increased sleeping can initially mean the drug is working if a medication for neuro-pain results in improved comfort (Table 3). Sedation in the first 1-2 weeks may be a marker of pain control given that chronic pain is exhausting and alters sleep.

The sedating effects of other medications can increase when pain control is achieved. Medications for spasticity or dystonia are important examples when 2 or more drugs are being used for ongoing muscle spasms or dystonic movement that might also be triggered by chronic neuro-pain. The sedating effect from medications such as benzodiazepines, baclofen, and trihexiphenidyl can increase, if a medication for neuro-pain manages a primary trigger of these features. It may be of greater benefit to wean the dose of such medications, rather than decrease the dose of the medication for neuro-pain if pain control is achieved.

Parents benefit from frequent support throughout this process, as they worry about the balance between comfort and sedation. It can be helpful to identify, validate, and

spend time supporting these worries, while offering options to how the problem might be best managed. This process can take several months in a child with improved comfort and persistent sedation who is on multiple medications that can contribute to sedation. A slow and methodical process can minimize a beneficial neuro-pain medication being decreased or discontinued too soon, with frequent check-ins for parental support. This can take 2-3 months when medications such as benzodiazepines need to be weaned slowly so as to avoid withdrawal symptoms, which can involve decreasing by 10% of the original dose every 7 days when a benzodiazepine has been used for an extended time.

BEFORE ADDING A SECOND OR THIRD MEDICATION

When symptoms persist, 2 medications for neuropathic pain with different mechanisms of action can provide greater benefit compared to either one used solely.[1] To lessen polypharmacy, the following should be considered:

- Maximize dose of medication being used for neuro-pain
- Review and manage GI tract distention triggers
- Review event frequency and effectiveness of breakthrough care plan
- Review management of other comorbid problems (e.g. spasticity, dystonia, sleep)

A decision to add a 2nd medication can make sense in a child with 3 or more prolonged pain episodes occurring on average each week and when there is inconsistent benefit from the breakthrough care plan. The first medication should be continued when adding another.[1] In contrast, it can make sense not to add a 3rd medication when episodes are less frequent and routinely improve within 1 to 2 hours after initiating the breakthrough care plan, the length of time for the onset of action of as needed medications and for the nervous system to “quiet” down.

The goal is symptom free, yet this goal is not possible for some if not many children with SNI. We can strive to maximize symptom control with a balance to minimize side effect risk from multiple medications. This process requires a team with expertise and availability given the complex decision-making and inherent worries, as well as expertise in the use of 2nd and 3rd line medications.[1]

COMMUNICATION WITH FAMILIES

Parents face many worries throughout this process. Table 3 covers some of these

worries, with language suggestions provided. There is further information covered in an information sheet for parents at the Courageous Parents Network.[25] General worries that do not have a definitive answer still benefit from validation, by providing recognition of the importance of the worry, as noted in Table 3.

CONCLUSIONS

Chronic pain in children with SNI is a significant and challenging problem. There is a need for better screening and defined criteria to guide initiation of an empirical medication trial for neuro-pain. The proposed screening process and N-PRAT provide guidance given the lack of diagnostic tests to confirm neuro-pain as a source. The strength of this tool is its ease of use that allows application at point of care. Limitations include the need to validate the usefulness of this tool and the sensitivity of the identified cutoff score of 5 or greater. This case also highlights the impact of cognitive bias when the focus remains on commonly recognized problems, such as spasticity and GERD. Criteria for the identification and management of chronic neuro-pain can improve comfort in this vulnerable group of children.

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Tables & Figures

Table 1. Acute versus Chronic Pain

	Acute	Chronic
Cause	Expected with surgery or due to causes of tissue inflammation and injury (i.e. nociceptive pain)	Pain that recurs for more than 3 months; categories include musculoskeletal, visceral, post-surgical, and neuropathic
Duration	Hours to days	> 3 months, persists
Identification	Sources typically identified by diagnostic tests	No routine diagnostic tests or criteria for sources due to the impaired nervous system
Goals	Resolution after treatment of cause and healing of tissue injury	Pain control, not cure

Table 2. Chronic neuro-pain sources

Problem	Features, Comments, and Treatment Options
Central neuropathic pain	Symptoms include pain localized to the GI tract, such as pain triggered by normal distention of the GI tract; this can be suggested by pain associated with tube feedings or intestinal gas, with relief following a bowel movement or flatus Pain features can occur spontaneously and with no trigger, described by adults as "shock-like" and "out of the blue" Due to impairment of the spinothalamic tract and thalamus Treatment: gabapentinoids, tricyclic antidepressants, SNRIs, methadone
Visceral hyperalgesia	Decreased threshold to pain generation in response to a stimulus in the GI tract, including a decrease in the amount of distention that triggers a pain signal Attributable to sensitization of visceral afferents and central sensitization in the CNS Treatment: gabapentinoids, tricyclic antidepressants, clonidine
Chronic post-surgical pain (CPSP)	Defined as pain that lasts more than 2 months post-surgery without other causes of pain such as chronic infection or pain from a chronic condition preceding surgery The mechanisms leading to chronic CPSP can include inflammation, tissue and nerve damage, and alterations in central pain processing Treatment: gabapentinoids, tricyclic antidepressants
Autonomic dysfunction (dysautonomia)	Features include skin flushing, hyperthermia, pain localized to the GI tract, retching, bowel dysmotility, discomfort, agitation, tachycardia, sweating, arching, stiffening Dysautonomia can be a source of discomfort, and pain can trigger the features that occur with dysautonomia Treatment: gabapentinoids, clonidine
Dystonia	Involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both Pain from other sources can trigger and worsen dystonic movement Treatment: baclofen, trihexyphenidyl, gabapentinoids, clonidine
Paroxysmal autonomic instability with dystonia (PAID)	Involves features of both autonomic dysfunction and dystonia Indicates altered function of the CNS areas that regulate autonomic function and movement; such children are also at risk for co-morbid central neuropathic pain Pain from other sources can trigger and worsen the observed features Treatment: see dysautonomia and dystonia
Spasticity	Velocity-dependent increase in muscle tone that results in muscles that are resistant to movement Spasticity is often not painful but can result in musculoskeletal pain over time Treatment: baclofen, alpha2-agonists (clonidine or tizanidine)
Muscle spasms	Sudden involuntary contraction of a muscle or group of muscles; associated features can include arching, stiffening, tremors, and clonus Pain behaviors can indicate pain from muscle spasms and indicate pain from another source as the trigger for muscle spasms Treatment: interventions for spasticity, chronic neuro-pain, and other triggers

GI: gastrointestinal; SNRIs: serotonin norepinephrine reuptake inhibitors

Figure 1

Screening children with SNI for risk of chronic neuro-pain

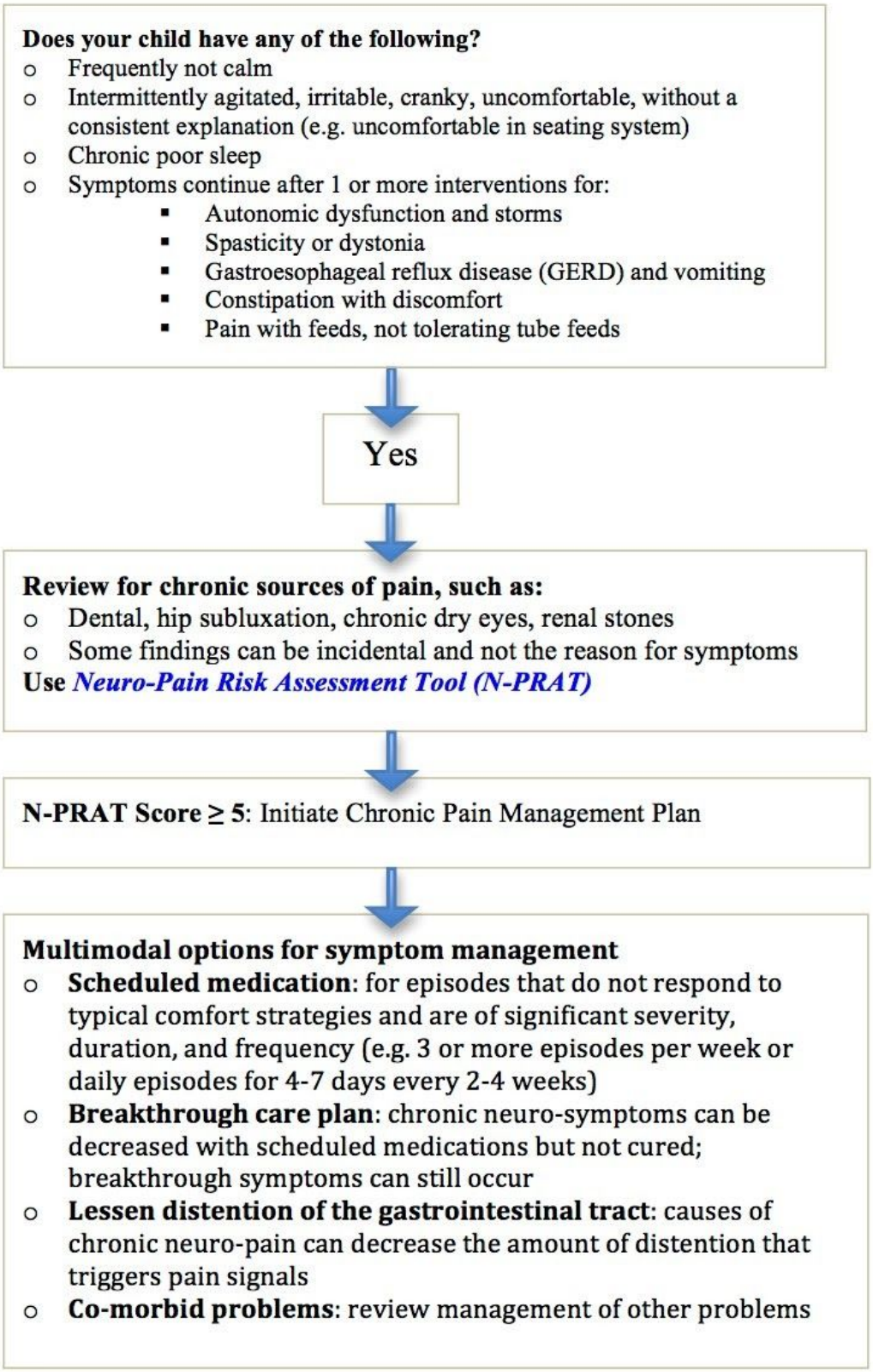

Figure 2. Neuro-Pain Risk Assessment Tool (N-PRAT)

Neuro-Pain Risk Assessment Tool (N-PRAT)	Score: Circle if present
Episodes with pain behaviors from 2 or more of the following categories, recurring for more than 3 months without a consistent source*; episodes may be weekly or cyclical (e.g. daily for 3 to 5 days every 2 to 4 weeks) • *Vocalizations*: crying, moaning • *Facial expression*: grimacing, frowning, eyes wide open • *Unable to console*: difficult to calm, not soothed by parent comfort actions • *Interaction*: withdrawn, seeking comfort • *Physiological*: tachycardia, sweating, pale or flushed skin, tears • *Muscle tone*: intermittent stiffening of extremities, clenching of fists, muscle tensing, tremors, back arching • *Movement:* increased movement, restless, startles easily, pulls away when touched, twisting	1 point for 2 or 3 categories 2 points for 4 or more categories
GMFCS* level 4 and moderate to severe intellectual disability OR	1
GMFCS* level 5 and severe to profound intellectual disability	2
Some episodes occur rapidly and out of the blue with no known trigger, quickly changing from calm to agitated / irritable / in pain	1
Intermittent increase in muscle tone, movement and posture: features continue following 1 or more drugs for spasticity or dystonia	1
Autonomic dysfunction and storms: features remain significant following 1 or more drugs for autonomic dysfunction	1
GI symptoms: Pain behavior episodes noted with tube feeds, intestinal gas, and constipation, with improvement when feeds are held and following a bowel movement; symptoms continue following 1 or more drugs for GERD	1
Chronic poor sleep with symptoms of agitation / discomfort	1
Post-surgical: new or worsening pain behavior episodes for > 2 months following surgery without a clear cause	1
Intractable seizures following 3 or more anti-seizure drugs	1
Planned surgery: prior to surgical interventions for GERD, spasticity, or dystonia to determine if chronic neuro-pain is a trigger; gabapentinoids may decrease need for post-surgical opioids and development of postsurgical pain[28]	1
Total score (highest score = 12)	

Total score ≥ 5: initiate multimodal approach to symptom management (Figure 1)

***Nociceptive assessment noted in Figure 1 of AAP clinical report**.[1] Consider cognitive bias towards positive tests that may result in recurrent treatment in a symptomatic child with SNI, yet the positive test may represent colonization or an incidental finding and not be the source of symptoms (e.g. positive urine culture with less than 10 white blood cells in urinalysis, positive clostridium difficile with test that does not distinguish carrier from infection, gallstones with no other abnormal findings on labs or ultrasound)

***GMFCS:** used here as an indicator of motor function level in children with severe impairment of CNS

Figure 3. Case N-PRAT Score

Neuro-Pain Risk Assessment Tool (N-PRAT)	Score:
Episodes with pain behaviors from 2 or more categories, recurring for more than 3 months without a consistent source; episodes are cyclical, occurring for 2 to 4 days every 2 to 4 weeks	2 points (features from 6 categories: moaning, frowning, restless, movement, tachycardia, difficult to soothe)
GMFCS level 5 and severe to profound intellectual disability	2
Some episodes occur rapidly and out of the blue	1
Intermittent increase in muscle tone, movement and posture	1
Autonomic dysfunction and storms	0
GI symptoms	1
Chronic poor sleep	1
Post-surgical	0 (unclear given surgeries in infancy)
Intractable seizures	0
Planned surgery	0
Total score (highest score = 12)	**8**

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