PReS Latin America Basic Rheumatology Course
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Complex regional pain syndrome, and related entities: **Pain Amplification Syndromes**

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La Costa
Todo en un solo lugar

Pain is famously defined by Margo McCaffery (1968) as "whatever the experiencing person says it is, existing whenever he says it does" (McCaffery & Pasero, 1999, p. 17).

Evaluation of musculoskeletal pain

History and physical examination

- Character of the pain
- Other symptoms
- Family history
- Family, social, emotional and educational environment

Laboratory and imaging

Pain assessment

- Physiological measures
- Behavioral measures
- Self-report measure

History of musculoskeletal pain

What is the character of the pain?
Is the pain sharp, aching, deep, boring, etc?
How long has the pain been present?
Which body parts are painful? Does the pain radiate, migrate, or spread?
Is the pain getting better, worse, or staying the same?
What makes the pain better? What makes the pain worse?
Is there diurnal variation in the severity of the pain?
Is the pain present at night and, if so, does it wake the child?
Does the pain interfere with function, and, if so, which one?
Is the painful area tender to touch or clothing?
Is the painful area either cold or hot to the touch?
Does the painful part look abnormal or swollen?
What is the child's or parent's assessment of the pain severity?

History of musculoskeletal pain

Are there other symptoms?

Fever?

Rash?

Change in gastrointestinal function?

Weight loss?

Upper or lower respiratory tract symptoms?

Muscle weakness?

Sleep disturbance?

Depression?

Anxiety?

History of musculoskeletal pain

Family and social history

Ankylosing spondylitis, reactive arthritis, or inflammatory bowel disease?

Back pain, heel pain, or acute iritis?

Psoriasis?

Fibromyalgia or other chronic pain condition?

Is there an identifiable stressor in the family, school, or peer group?

Are there significant or recent life changes?

Where is the child sleeping?

What activities does the child participate in?

How do the parents describe the child's personality?

Key observations

Does the child look well or ill?
Is the child's affect commensurate with the level of reported pain?
Does the child have an air of *la belle indifference* about him or her?
Is there any joint swelling, muscle weakness or atrophy?
Is there any tenderness to palpation and, if so, is it over joints, entheses, or muscles?
Is there any body area of allodynia, and, if so, is the area constant or does it vary over time?
Is there any color, temperature, or perspiration change?
Are there any inconsistencies in the examination?
Is there any neurological dysfunction?
Are there abnormal child-parent interactions, such as enmeshment, hostility, or berating?
Is there evidence of concurrent conversion symptoms?
In children with back pain, are signs of nonorganic back pain present?

Pain Assessment

PHYSIOLOGICAL MEASURES

Heart rate, blood pressure, palmar sweating, transcutaneous oxygen tension, and cutaneous blood flow.

Most of these tests have little or no data to support their reliability, validity, sensitivity, specificity, or practicality

BEHAVIORAL MEASURES

Physicians routinely interpret the child's behavior as an indicator of the severity of pain

A number of different scales of pain behavior have been developed. These include various assessments of crying or other verbal responses, facial expressions, and limb movements: CHEOPS, Pain Behavior Observation Method, FLACC scale, and others

Pain Assessment

SELF-REPORT MEASURES

Unidimensional Pain Measures

The most frequently used simple unidimensional pain scale is the visual analog scale (VAS).

Multidimensional Pain Measures

These are questionnaires that collect information about a number of domains relevant to pain, including pain severity; psychological well-being, such as levels of anxiety and depression; coping strategies; and self-efficacy. The best known of these is the Varni/Thompson Pediatric Pain Questionnaire.

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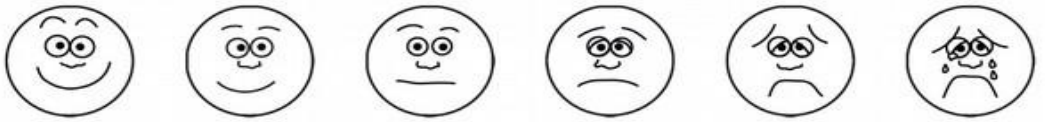
Translations of Wong-Baker FACES™ Pain Rating Scale



	0	2	4	6	8	10
English	No Hurt	Hurts Little Bit	Hurts Little More	Hurts Even More	Hurts Whole Lot	Hurts Worst
Spanish	No Duele	Duele Un Poco	Duele Un Poco Más	Duele Mucho	Duele Mucho Más	Duele El Máximo
French	Pas Mal	Un Petit Peu Mal	Un Peu Plus Mal	Encore Plus Mal	Très Mal	Très Très Mal
Italian	Nessun Dolore	Dolore Lieve	Dolore Moderato	Dolore Forte	Dolore Molto Forte	Il Più Forte Dolore Immaginabile
Portuguese	Não Doi	Doi Um Pouco	Doi Um Pouco Mais	Doi Muito	Doi Muito Mais	Doi O Máximo
Bosnian	Ne Boli	Boli Samo Malo	Boli Malo Više	Boli Još Više	Boli Puno	Boli Najviše
Vietnamese	Không Dau	Hôi Dau	Dau Hôn Chút	Dau Nhiêu Hón	Dau Thât Nhiêu	Dau Qúa Dô
Chinese	無痛	微痛	較痛	更痛	很痛	劇痛
Greek	Δεν Πονaϊ	Πονaϊ Λιγο	Πονaϊ Λιγο Πιο Πολν	Πονaϊ Πολν	Πονaϊ Πιο Πολν	Πονaϊ Παρα Πολν
Romania	No Doare	Doare Puţin	Doare Un Pic Mai Mult	Doare Şi Mai Mult	Doare Foarte Tare	Doare Cel Mai Mult
Mongolian	Зовиургүй байна	Бага зэрэг өвдөж байна	Өвчин нэмэгдэж байна	Их өвдөж байна	Маш их өвдөж байна	Тэсэхийн аргагүй өвдөж байна
Japanese	痛みはない	わずかに痛い	少し痛い	かなり痛い	ひどく痛い	耐えられないほど痛い
Bahasa Malaysia	Tidak Sakit	Sangat Sedikit Sakit	Sedikit Sakit	Sakit	Sangat Sakit	Teramat Sakit

Definition of these conditions

I use *pain amplification syndromes or amplified musculoskeletal pain* in these talks because:

- it is descriptive
- does not presume an etiology
- differentiates these children from adults with chronic pain
- does not "label" the child with a disease

When reading a particular study, it is important to know what criteria were used to classify children with various forms of amplified musculoskeletal pain

Classification

Complex Regional Pain Syndrome, Type I *(reflex sympathetic dystrophy [RSD], Sudeck's atrophy, reflex neurovascular dystrophy [RND], or algoneurodystrophy)*

Criteria 2-4 must be satisfied.

1. The presence of an initiating noxious event, or a cause of immobilization
2. Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event
3. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain
4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degrees of pain and dysfunction

Classification

Complex Regional Pain Syndrome, Type II *(Causalgia)*

All three criteria must be satisfied.

1. The presence of continuing pain, allodynia, or hyperalgesia after a nerve injury, not necessarily limited to the distribution of the injured nerve
2. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain
3. This diagnosis is excluded by the existence of conditions that would otherwise account for the degrees of pain and dysfunction

Classification

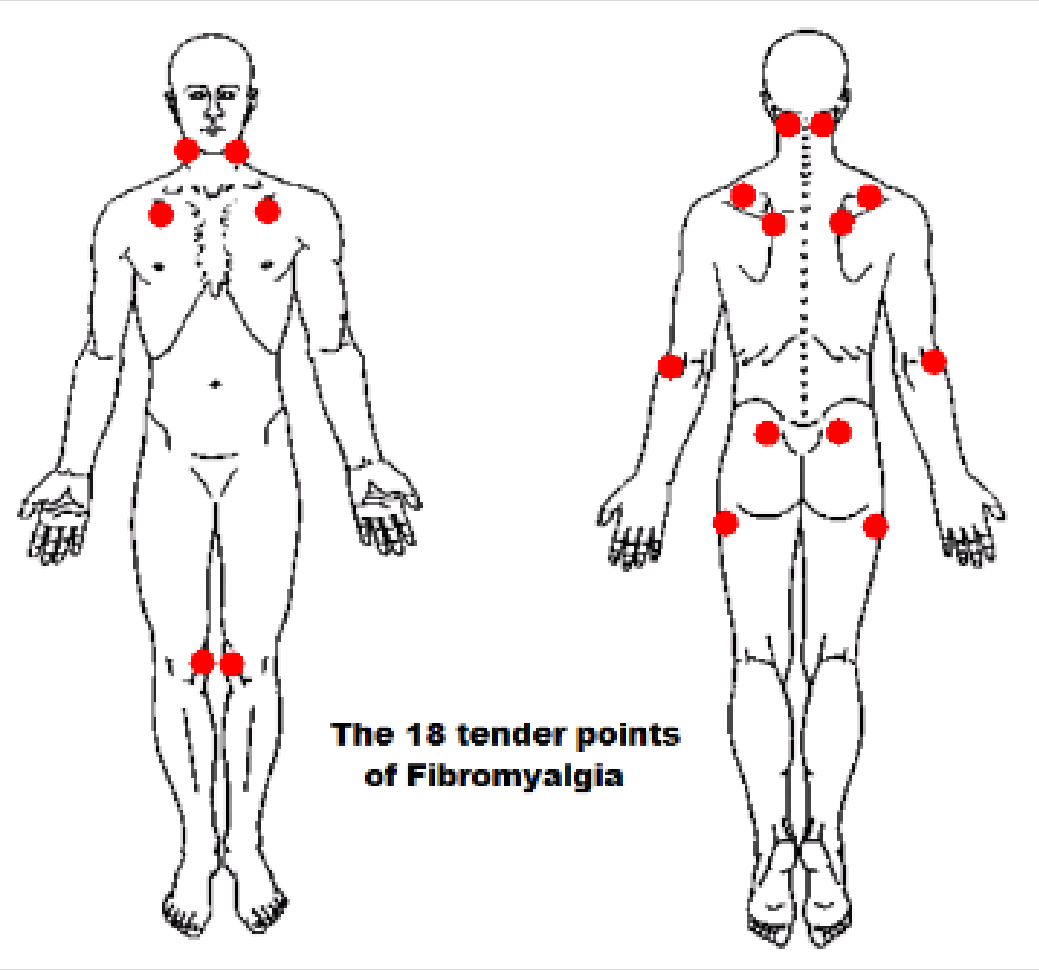
Fibromyalgia (ACR, 1990)

Both criteria must be satisfied.

1. Widespread pain (bilateral, and above and below the waist and axial pain) present for at least 3 months
2. Pain (not tenderness) on digital palpation with 4 kg of pressure on 11 of the following 18 sites:

   a. Occiput: at insertion of suboccipital muscle. b. Low cervical: at anterior aspect of the intertransverse spaces of C5-C7. c. Trapezius: at the midpoint of the upper border. d. Second rib: just lateral to the second costochondral junction at the upper rib border. e. Scapula: the medial border just above the spine of the scapula. f. Lateral epicondyle: 2 cm distal to the epicondyle. g. Gluteal: in the upper outer quadrant of the buttocks. h. Greater trochanter: 1 cm posterior to the trochanteric prominence. i. Knees: at the medial fat pad 1 cm proximal to the joint mortise

Fibromyalgia trigger points



Classification

Yunus and Masi Criteria for Childhood Fibromyalgia

All 4 major and 3 minor, OR the first 3 major, 4 painful sites, and 5 minor need to be satisfied.

Major:

1. Generalized musculoskeletal aching at 3 or more sites for 3 or more months
2. Absence of underlying condition or cause
3. Normal laboratory tests
4. Five or more typical tender points (1990 ACR criteria)

Minor:

1. Chronic anxiety or tension. 2. Fatigue. 3. Poor sleep. 4. Chronic headaches.
   5. Irritable bowel syndrome. 6. Subjective soft tissue swelling.
   7. Numbness. 8. Pain modulation by physical activities.
   9. Pain modulation by weather factors.
   10. Pain modulation by anxiety or stress

Classification

Diffuse Idiopathic Pain

Both criteria must be satisfied.

1. Generalized musculoskeletal aching at 3 or more sites for 3 or more months
2. Exclusion of disease that could reasonably explain the symptoms.

Localized Idiopathic Pain

All 3 criteria must be satisfied.

1. Pain localized to one limb persisting
   a. 1 week with medically directed treatment OR
   b. 1 month without medically directed treatment
2. Absence of prior trauma that could reasonably explain the symptoms
3. Exclusion of diseases that could reasonably explain the symptoms

Epidemiology

Incidence and prevalence

Musculoskeletal pain is common: back pain 20%, limb pain 16%
Fibromyalgia 2 to 6%
About 10% of new patients in PR clinics have some sort of amplified musculoskeletal pain

Age of onset

Mean age is generally at 12 or 13 years old

Gender

Ratio is about 4:1 (F:M)

Geographical and Racial distribution

All reports are from developed countries

Etiology and Pathogenesis

Causes are unknown

In adults, several hypothesis: abnormal muscle anatomy and physiology, altered sleep pattern, abnormal serotonin metabolism, hypothalamic-pituitary-adrenal axis hypofunction, decreased cerebral blood flow, trauma, and psychological distress, but there is no convincing evidence that any of these factors is of primary importance.

Different findings in bone scan of children and adults with CRPSI
Causally related to injury, illness, or psychological distress, either singly or in combination
Interdependency or enmeshment is common

Etiology and Pathogenesis

NERVE PLASTICITY (describing the ability of the brain to change easily) or CENTRAL SENSITIZATION

Changes that occur in the brain in response to repeated nerve stimulation or after repeated experiences with pain.

Following repeated stimulation, levels of neurotransmitters and brain electrical signals change as neurons develop a "memory' for responding to those signals. Frequent stimulation results in a stronger brain memory, so that the brain will respond more rapidly and effectively when experiencing the same stimulation in the future.

Thus, the brain is activated or sensitized by previous or repeated stimuli to become more excitable.

Etiology and Pathogenesis

CLINICAL EFFECTS OF CENTRAL SENSITIZATION

- Hyperalgesia
- Allodynia
- Pain summation
- Radiation of pain beyond the dermatomal distribution

Clinical Manifestations

Amplified Musculoskeletal Pain

Conversion symptoms are common

Numbness is frequently reported, but they also can manifest paralysis, nonepileptic episodes (pseudoseizures), muscle shaking or rigidity, blindness, or a bizarre (histrionic) gait

Eating disorders can be present, and a high index of suspicion for these need to be maintained.

La belle indifference can be present, even when reporting severe pain and dysfunction

A few children will demonstrate marked pain behaviors such as crying or screaming.

These children seems to be mature for their age, are accomplished in school and extracurricular activities, and are described by their parents as perfectionistic, empathetic, and pleasers.

Clinical Manifestations

Localized Amplified Musculoskeletal Pain

Minor trauma that might not be clearly recalled is common

The pain and consequent disability increase over time

Autonomic signs (edema, cyanosis, coolness, increased perspiration) may be persistent or transient or may not occur

Allodynia can be marked (“the breeze of someone walking by hurts”) and can lead to significant impairment.

Any body part can be involved, and the child may have several areas of pain, but the lower extremity is more commonly involved than the upper, and peripheral body parts are more commonly involved than central areas. Occasionally, only one small area is involved, such as a finger, the nose, or a tooth

Clinical Manifestations

Diffuse Amplified Musculoskeletal Pain

Onset is usually more gradual and can be vague in location and character

Absence of autonomic signs, but affected children complain of poor sleep and depression more often than do those with localized pain

Report a multiplicity of symptoms is common

The pain is often centrally located, involving the back, chest, abdomen, head, and extremities

A significant number of children with diffuse amplified musculoskeletal pain who start out with very localized pain or even clear cut complex regional pain syndrome that then spreads and may involve the entire body

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Clinical Manifestations

Physical Exam

There is no findings suggesting an underlying disease, neurological examination is normal, and allodynia is present.
Careful sensory testing is required.
Allodynia is present if pain is reported when lightly touching the skin, the border of the allodynia can vary dramatically.
Signs of autonomic dysfunction, especially coolness and cyanosis, may only be present after exercising the limb or may become apparent if the limb is held in a dependent position for a few minutes.
The distribution of painful points is outlined in the previous slide.
Control points, such as the forehead, shin, and thumbnail, will define how widespread the pain is.

Differential Diagnosis

Diagnosis of exclusion

No laboratory or radiographical examination is diagnostic

A number of other painful conditions need to be excluded *(Fabry disase, Neoplasia, erythromelalgia, pernio, spinal cord tumors, Raynaud, hypermobility, restless legs syndrome, CRMO, progressive diaphyseal dysplasia, peripheral neuropathy, transient migratory osteoporosis, vitamin D deficiency, thyroid disease)*

Keep an eye for seronegative enthesopathy arthropathy syndrome, in children with back pain

The most common misdiagnoses for children who actually have an amplified pain syndrome are trauma, mechanical pain, or arthritis.

General Assessment

There are two major independent variables to consider when assessing pain:

1. The quality and quantity of the pain complaint itself, and
2. The amount of dysfunction as a consequence of the pain.

The report of pain is always valid because, by definition, pain is subjective. Therefore, the most useful measurement of pain is the self-report on a verbal or visual analog scale.

The quality of Pain can be assessed using various instruments such as the McGill Pain Questionnaire or Pediatric Pain Questionnaire.

General Assessment

The amount of reported pain does not directly correlate with the degree of incapacity, which vary from almost none to being bedridden

With treatment, function usually returns before the pain diminishes

Functional measurements vary depending on the location of the pain and the presence of coexisting conditions

Children with amplified musculoskeletal pain suffer more than children with other musculoskeletal conditions do, which may indicate the degree to which the disorder is a manifestation of psychological distress. Psychological dysfunction is almost universally present by the time these children are identified

Even though these syndromes are not psychological in cause, the psychological toll on the child and family is often severe.

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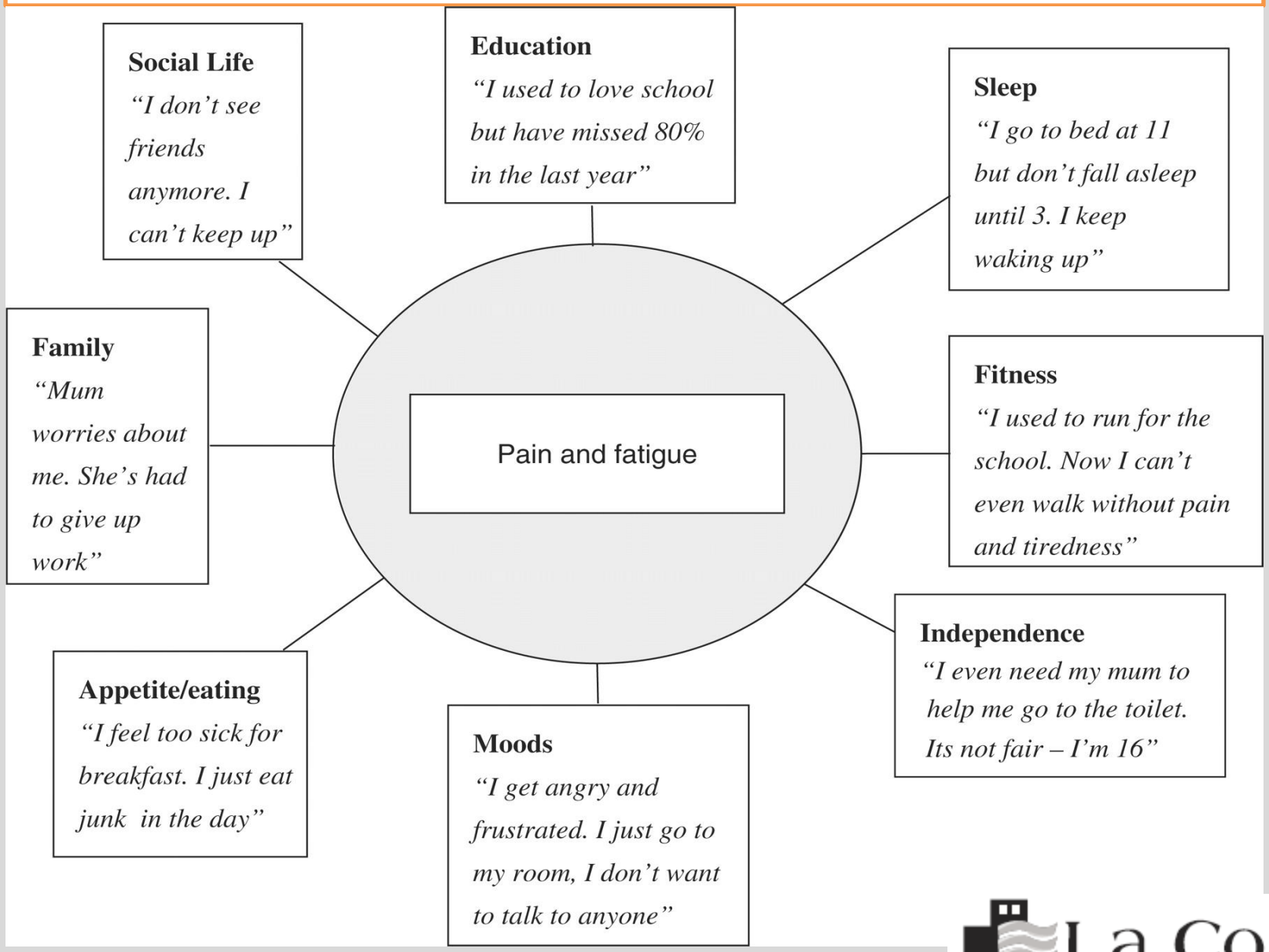

Jacqui Clinch, and Christopher Eccleston Rheumatology 2009;48:466-474

Treatment Goals

1. **Restoration of function**
2. **Relief of pain**

- ***Physical and occupational therapy with desensitivization maneuvers***
- ***Psychological evaluation and cognitive behavioral evaluation***
- ***Cheerleading***
- ***Adjuvant therapy***

Treatment

PHYSICAL AND OCCUPATIONAL THERAPY

Aggressive physical and occupational therapy aimed at reversing immobility and increasing function

One-on-one therapist, encouraging both speed and quality of movement.

Exercises are focused on normal function and aerobic training, such as walking times, rope jumping, climbing stairs, dressing, and other activities of daily living

Allodynia is treated with desensitization maneuvers, deep muscle massage using towel and lotion rubs, vibration, and wearing normal clothing and footwear.

Treatment

COUNSELING

Psychological evaluation to determine co-morbid situations (i.e. mood, anxiety and sleep disorders) and formal psychotherapy to treat these conditions

Cognitive Behavioral Therapy (CBT): relaxation training, setting and working toward behavioral goals (typically including systematic increases in exercise and other activities), behavioral activation, guidance in activity pacing, problem-solving training, and cognitive restructuring (Thorn, 2004; Turner & Romano, 2001).

CBT typically includes between-session activities to practice and apply new skills (e.g., completion of thought records, relaxation practice, work toward behavioral goals).

Treatment

COUNSELING

Goals of Cognitive Behavioral Therapy (CBT):

- Reduce pain and psychological distress
- Improve physical and role function *(by helping individuals decrease maladaptive behaviors, increase adaptive behaviors, identify and correct maladaptive thoughts and beliefs)*
- Increase self-efficacy for pain management

Treatment

CHEERLEADING

It is the role of the PR to monitor, set realistic goals and reassure these children and their families that they will get through this

ADJUVANT THERAPY

Low-dose tricyclic antidepressants
NSAIDs
Tramadol
Muscle relaxants (cyclobenzaprine)
Pregabalin

Treatment

WHAT DOES NOT SEEMS TO WORK

- Glucocorticoids
- Anticonvulsants
- Opioids
- Epidural infusions
- Lidocaine infusions
- Nerve and ganglion blocks
- Spinal cord stimulators
- Pain pumps
- Ketamine coma

Course and Prognosis

Some children have amplified pain that persists for years, and yet there are children with self-limited involvement who are never evaluated in a tertiary center

Many children have spontaneous remission of illness

Around 90% of children diagnosed with fibromyalgia in a pediatric rheumatology center still had significant pain 15 to 60 months (mean, 33 months) later

The frequency of relapses is rarely reported but occurs in all forms of amplified musculoskeletal pain.

The clinical manifestation of the second episode may be different from the first, even changing between localized and diffuse disease

Thank you!

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