How painful is juvenile chronic arthritis?

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Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage and it is one of the major symptoms in arthritis. Pain is also the sensory modality that alerts patients so that it leads to protective responses. Pain also informs the patient that there is a potential noxious threat, which brings him or her to the doctor for diagnosis and treatment of his illness (or ailment).

Unfortunately, a warning signal like acute pain can turn into chronic pain and in this stage pain itself can be the most dominant symptom and threat for the quality of life of the patient. In the pathogenesis of inflammatory pain, receptors sensitive for noxious stimuli generated as a consequence of inflammation, have a role. These receptors, called nociceptors, activate predominantly unmyelinated, small diameter sensory nerves, mediating nociceptive information to higher order neurons in the dorsal horn of the spinal medulla. On spinal as well as supraspinal level, the nociceptive signal is modulated by regulating pathways (fig 1). Besides these regulating pathways there are many substances that are able to stimulate different nociceptive fibres (table 1).

Children express pain in a different way than adults do. This is often interpreted as if children feel less or even no pain as in the case of neonates. The idea that newborns and children differ fundamentally from adults in the perception of pain, has led to approaches that fundamentally from adults in the perception of pain, has led to approaches that

Differences in pain perception explain why there are so many discrepancies in the literature with respect to pain in children with juvenile chronic arthritis. Some investigations report that children with juvenile chronic arthritis experience substantially less pain or even no pain in comparison to adults with rheumatoid arthritis. However, we and others have found that children with juvenile chronic arthritis do express pain. By using algometry, we found an enhanced sensitivity in children with juvenile chronic arthritis to noxious stimulation in comparison to healthy age related controls. When juvenile chronic arthritis patients had actively inflamed joints, the pain threshold was reduced by 31%. There was a significant inverse correlation between

indices of disease activity and the pain threshold. We studied the relationship between pain threshold and pain expression as measured with visual analogue scales in a group of 57 children with juvenile chronic arthritis. By correlating three articular disease activity indices (active joint count, swollen joint count, and Ritchie index), visual analogue scales, and the functional child health assessment questionnaire with the mean pain threshold, we found that all the above mentioned items correlated negatively with the pain threshold. The latter may be interpreted that the pain threshold is related to disease activity and pain experience. No correlation was found between the mean pain threshold and the C reactive protein.

Huskisson and Hart found a similar correlation between the Ritchie index and pain threshold in adults with rheumatoid arthritis. In contrast, Walco et al found no correlation between the pain threshold and the visual analogue scales in children with juvenile chronic arthritis. This difference can be partly explained by the choice of pressure sites and/or by patient selection. We found a significant inverse correlation between the pain threshold and pain experience measured with visual analogue scales, which could explain 25% of the variance. However, the pain threshold and the visual analogue scales measure different aspects of pain. The pain threshold as measured by the algometer might be easier to express and may be closely connected to the discharge of nociceptive afferents. In juvenile chronic arthritis the pain threshold is probably decreased as a result of the existing tissue damage in the inflamed joints. In comparison, the pain score measured with visual analogue scales is more influenced by the emotional experience associated with the disease.

An interesting phenomenon is that in juvenile chronic arthritis patients we measured a lower pain threshold of the involved joint as well as of the non-inflamed joints. In children with juvenile chronic arthritis in remission, we also found a lower pain threshold on all sites of measurement, although the effect was less pronounced than in children with active disease. In other words, the change in the pain threshold persists even after the input of the injured site has subsided. This shows that sensory induced changes and the impact they have on the central memory can be long lasting. The neurons on which these sensory induced changes can have such a long lasting impact are dorsal
Table 1 Stimulating and sensitising substances for primary afferent nociceptive fibres

<table>
<thead>
<tr>
<th>Stimulating substances</th>
<th>Sensitising substances</th>
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<tbody>
<tr>
<td>bradykinin, histamine, serotonin, and prostaglandins</td>
<td>Substance P, tachykinins, and many inflammatory mediators (interleukin-1, interleukin-6, tumour necrosis factor-α)</td>
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Figure 1 Neuronal events when inflammation in a joint is present. TST = tractus spinothalamicus; SDR = spinal dorsal horn; II, IIIa, IIIb, IV = myelinated afferents type II and IIIa, IIIb, IV = thinly or unmyelinated nociceptive afferents type IIIb and IV.

Diminished diffuse inhibitory control

Increased in neuropeptide synthesis

Increased release of neuropeptide

Sensitised afferents

Motoric reflexes

Sympathetic reflexes

Inflammation. Silent, nociceptive fibres, unreceptive to non-noxious stimuli, become excited by non-noxious stimuli: for example 5-hydroxytryptamine, prostaglandins, bradykinin, adenosine, serotonin, noradrenaline, leukotrienes, tachykinins, and many inflammatory mediators (interleukin-1, interleukin-6, tumour necrosis factor-α).

The other type of afferent mediated inhibition of nociception is known as 'counterirritation'. Small diameter (III and IV) afferents at some distance of the inflamed joint are stimulated and this results in inhibition of both small and large diameter input to the convergent wide dynamic range nerves.
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ereceptor nerves. Somatosensory nerves activate inhibitory
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Figure 2 Non-nociceptive stimuli applied to sites on the
 same segment as the inflamed joint stimulate somatosensory afferent nerves. Somatosensory nerves activate inhibitory

a treatment based on counterirritation is heat/cold therapy. The effect of both types of afferent mediated inhibition has still to be evaluated. It is known that the placebo effect of these treatments may contribute to the effect.

Another way to control pain is to influence the
central sensitisation. In children there is a growing
interest in cognitive behavioural approaches, although its place in the treatment of chronic pain is still unknown. In juvenile chronic arthritis relaxation and cognitive behavioural management of pain sensitisation have proved to be more effective. Although much more research has to be done, it is questionable whether patients with a longstanding pain behaviour will benefit only from cognitive behavioural approaches. In addition, it may be worthwhile to consider to treat the patient with a therapy directed at the interference with central as well as peripheral sensitisation at the same time.

Moreover, it has to be emphasised that a proper and individual balance of movement versus rest is very important. Too much exercise may exacerbate symptoms and increase destruction of the joint, while movement is important for functional restoration. The documentation of peripheral and central sensitisation could help the doctor/physical therapist to dose the exercise. When the spread of sensitisation is high (low pain thresholds), mild non-painful forms of treatment appear to be the most appropriate approach. More demanding forms of treatment can be asked of the patient when a lower level of sensitisation is present. Optimal treatment should be based on a multidimensional bio-psychosocial approach in a multidisciplinary team in order to ensure integration of the treatment goals into the child’s daily routine.

In summary there is still much debate about the role of pain in children with juvenile chronic arthritis. We have shown that pain plays an important part in the symptomatology of this condition. Better knowledge of the neurophysiology of chronic pains leads to new therapeutic regimens. Antinociceptive intervention in juvenile chronic arthritis not only serves to diminish pain, but may become increasingly important to modulate the degree of inflammation.


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