

# Can physical activity modulate pain perception during ontogenesis?

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**A** Study Design  
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## abstract

The aim of the paper is to emphasise the significance of physical activity as an element directly or indirectly modulating the perception of pain during ontogenesis.

Pain is a distinctive sensory sensation and also a subjective criterion of health or disease. In contrast to other modalities (taste, smell, touch), it triggers solely negative emotions and sensations. Pain is a highly individualised sensory phenomenon, involving the physical, cognitive and emotional spheres of human life. Different reactions to pain during ontogeny most often result from the loss of communication skills, a systematic decrease in the functions of all systems and organs, in particular the nervous system, and limited physical activity. Motivation for physical activity translates into motivation to improve the quality of life. From the ontogenetic perspective pain perception cannot be limited to nociception, because the perception of pain is subjective and depends on the community in which we live, our religion, individual life philosophy, as well as intellectual interests.

**Key words:** physical activity, ontogenesis, pain, nociception.

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## INTRODUCTION

Pain is a distinctive sensory sensation defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [1]. The primary function of pain is to protect and inform about a possible danger. Pain is also a subjective criterion of health or disease. In contrast to other modalities (taste, smell, touch) it triggers solely negative emotions and sensations [2].

Pain perception results from the activation of the nociceptive system, which receives stimuli (in the process of transduction) through the endings of slowly-conducting nerve fibres (nociceptors) and transmits the stimuli turned into action potentials from the periphery to the posterior horns of the spinal cord and further to the brain (Fig. 1). The mechanism also involves modulation (activation, inhibition, summation of the stimuli), which takes place already in the first synapse in the spinal cord, and perception, which adds a subjective aspect to the oncoming information, allowing for the pain to be perceived and experienced [3]. It is this aspect that differentiates nociception from pain as it takes into consideration the circumstances in which pain arises and accounts for a wide range of factors to be included in the process of pain perception: not only psychological and social but also religious and spiritual ones.

Certainly important, but not always measurable so far, is the role of genetic factors in the reception and central processing of nociceptive stimuli. These factors undoubtedly affect, directly or indirectly, the differences in the perception of pain and in the observed in everyday life or clinical management inter-subject variability.

An issue that is less frequently discussed in the literature with regard to pain perception and modulation is the role of physical activity analysed from the ontogenetic perspective. It has been acknowledged that the prevalence of chronic pain increases with age [4], while acute pain occurs significantly less frequently in elderly adults [5]. This is probably a direct or indirect consequence of structural and functional ageing processes in the nervous system, which are manifested for instance in decreased nerve fibre density in individuals aged over 60 years [6] and decreased nociceptive information input through A delta fibres in relation to C-fibres [7]. Other studies [8] have indicated that sensory innervation decreases with age, with a greater loss of unmyelinated fibres. Also worth mentioning when discussing age-related changes are molecular processes determining the coding of nociceptive stimuli and their further processing, especially with regard to channel and receptor expression in the cell membrane and the quantitative and qualitative changes in neurotransmitter release. It is currently known that due to its cognitive, emotional and social aspects, physical activity may modulate these processes, and its influence may extend beyond creating neural connections, building neural networks and synthesis and metabolism of neurotransmitters [9]. Physical activity may, in fact, compensate for changes in neurotransmitter synthesis and metabolism, such as decreased levels of beta-endorphins and GABA in the lateral thalamus, lower concentration of catecholamines [10] or the density of opioid and serotonin receptors in the limbic system [11].

The aim of the paper is to emphasise the significance of physical activity as an element directly or indirectly modulating the perception of pain during ontogenesis.

## ONTOGENY OF PAIN

PubMed search with the keywords “ontogenesis” and “pain” yields 39 publications, 17 of which appeared before 2000. The first paper in this field was published in 1954. A much higher number of references to pain in the subsequent stages of ontogenesis, amounting to thousands of records, appears after typing: “pain-foetus”, “pain-neonates/infants”, “pain-child”, “pain-middle-aged”, “pain-adult” or “pain-old”. Some of these publications were used in preparing Figures 1 and 2, which combines the most important phenomena connected with nociception, pain and physical activity on a time axis.

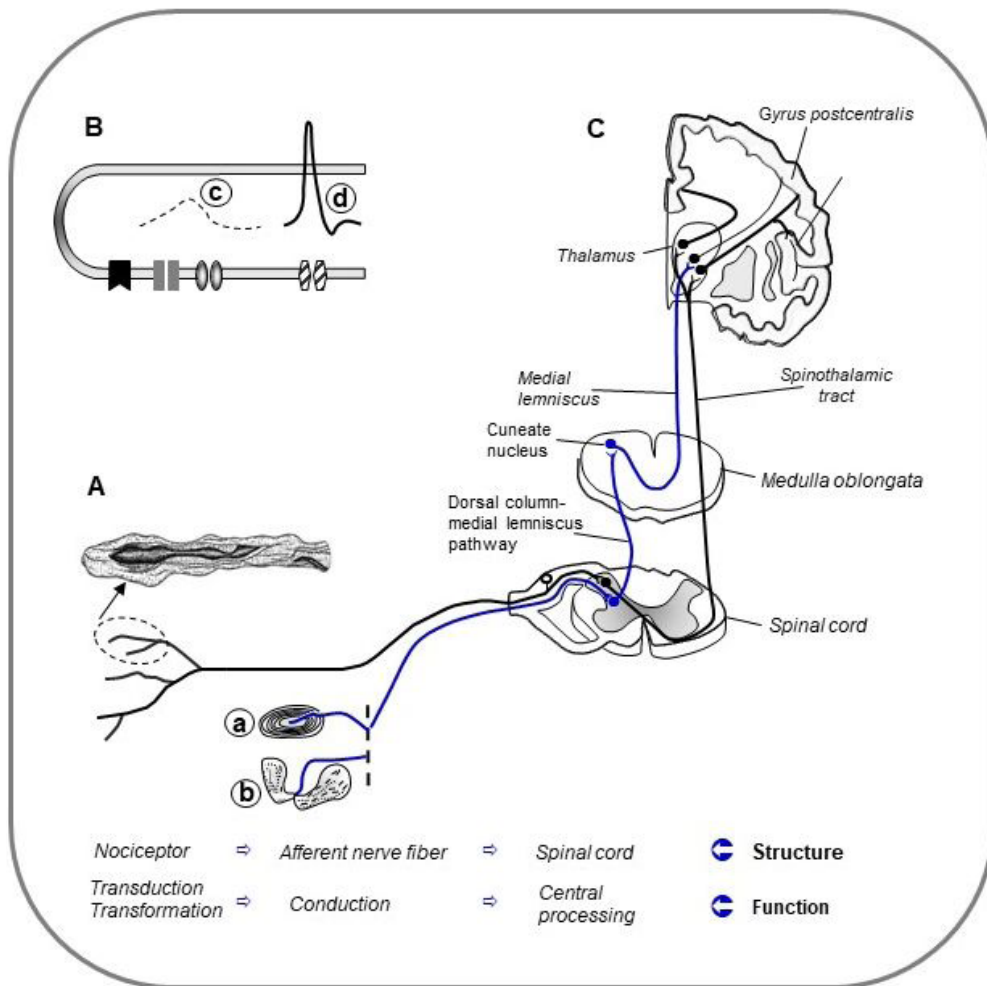


Fig. 2. Diagram showing the reception, conduction and central processing of nociceptive stimuli. (A) Nociceptors, unlike other sensors placed in the body (e.g. marked as a, b - respectively Vater-Pacini or Ruffini corpuscles) take the form of so-called free endings of slowly-conductin afferent fibers responding to strong stimuli harmful to the tissue. (B) There are a number of receptors and ion channels for various inflammatory factors localised at the sensory ending. Nociceptors, like other sensors, generate sensory potentials after the reception of a stimulus (c) and then build action potentials (d) enabling the transmission of impulses to the central nervous system. (C) Nociceptive information encoded in the form of the frequency of action potentials is transmitted by the afferent fibers to the dorsal horns of the spinal cord, where after switching to the second neuron (synapse) reaches the contralateral site (black line) to the brainstem, thalamus and cerebral cortex. The remaining non-nociceptive sensory input information, e.g. from a and b, is carried out on the ipsilateral side (blue line).

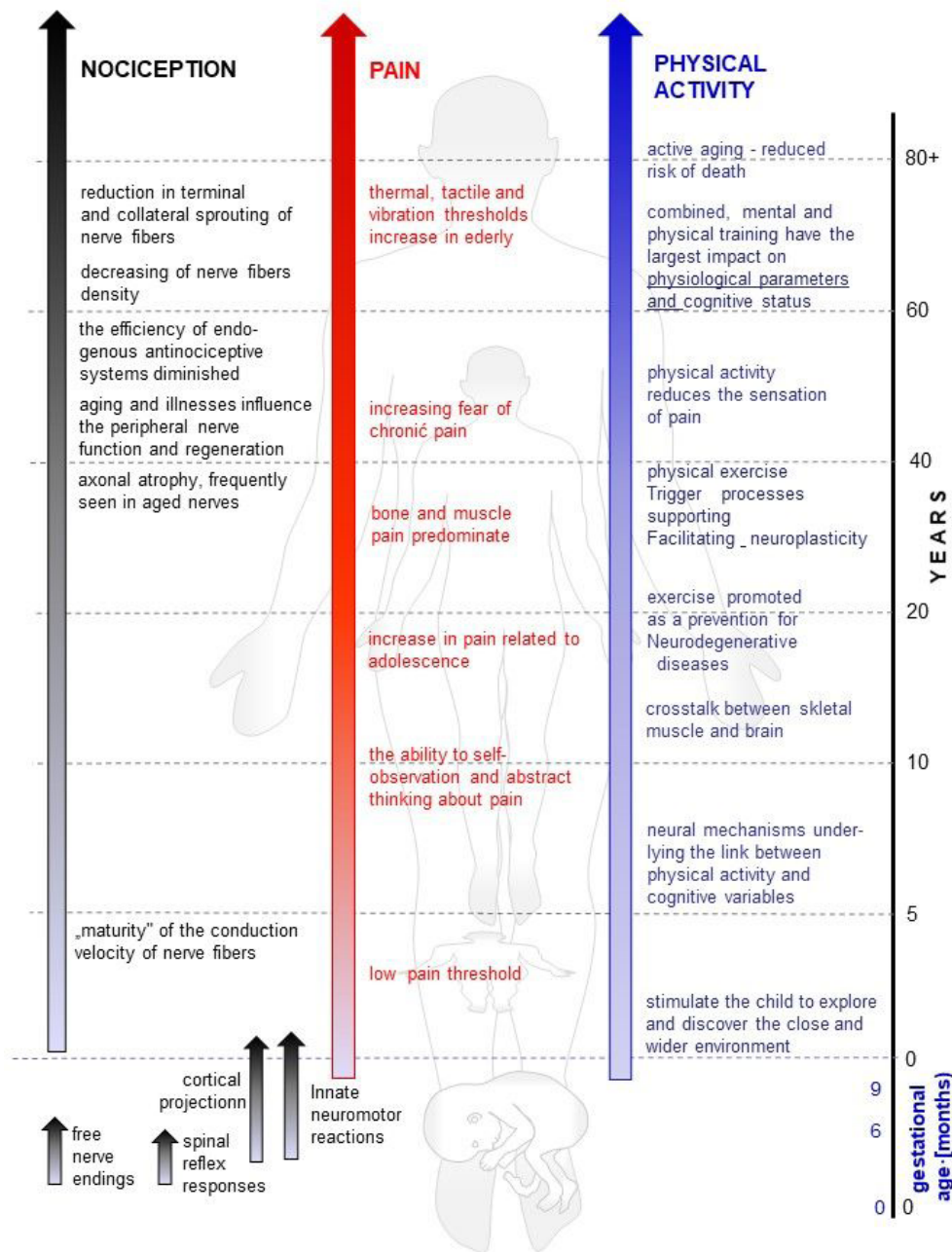


Fig. 2. The most important phenomena connected with nociception, pain and physical activity on a time axis

In the context of neuroanatomical criteria, it can be stated that pain can be felt already by a 26-week-old foetus [12]. Previously, Fitzgerald et al. [13] showed that preterm infants born before the 30th week had very low thresholds for mechanical stimuli (less than 1 g). The thresholds were equivalent to those in normal term babies only around 37.5 weeks of postconceptional age, although these were still below adult levels. The same study also indicated that preterm infants probably differentiate between painful and non-painful stimuli. Nevertheless, there is a difference between nociception and feeling pain, and suffering. The latter requires not only a fully developed somatosensory cortex and descending and ascending pathways to the spinal control system but also synaptic connections and the age-related subjective aspect to be considered [14].

The central and peripheral nervous systems of a new-born are not fully developed. Due to the yet undeveloped nervous system and an imperfect pain control system, infants of less than 12 months have a limited ability to inhibit the effects of nociceptive stimulation, which results in lower pain thresholds [15]. It can be assumed that pain experienced in this period is not without relevance for pain perception later in life [16].

Childhood, understood as the time span between 1 and 12 years of age, is characterised by numerous small pain incidents which result from high motor activity in this period of life, mostly related to a child's need to satisfy curiosity. The incidents are also an aspect of uncontrolled competition in sports and, less frequently, the effect of necessary medical procedures, such as vaccinations, bone marrow cell harvesting or injections [17]. Chronic pain in this age group occurs mostly in children suffering from chronic arthritis, muscular dystrophy, scoliosis or the effects of accidents. It is assumed that the process of full nervous system development continues until the age of five, which is confirmed, for example, by the fact that at this age nerve fibre conduction reaches its "mature" velocity [18]. Untreated pain has an adverse effect on the function of the immune and nervous systems and on health attitudes and behaviours. It also significantly affects sensitivity to pain [19].

A number of studies have indicated that the country of origin and the environment play an important role in shaping pain behaviours in adults. Children's behaviours, in turn, reflect the behaviours of their parents [20, 21]. It has been observed that some parental behaviours and attitudes, such as pacifying, criticism and empathy, may exacerbate the child's suffering, while cheerfulness, humour or encouraging the child to use problem-solving strategies help to alleviate it [22].

The period of life between 12 and 25 years of age, called adolescence and young adulthood, involves an increased risk of headaches, abdominal, bone and muscular pains [23]. Such symptoms occur more frequently in girls and interpreted as menstrual pains, are often ignored. In turn, adolescent boys who experience acute pain prefer calm behaviour associated with the image of a "tough guy", a real man [24]. A well-known cause of pain at this stage of life is too intense or improperly conducted training, which puts excessive stress on the osteoarticular and muscular systems [25]. The influence of pain resulting from injuries and sports competition in adolescence on the experience of pain in later life remains to be investigated [26, 27].

A significant increase in the prevalence of pain has been observed in adults between 25 and 50 years of age. On average, over 30% of adults report a headache at least once a month, more than 50% complain of muscle and joint pains occurring at least once a year, and more than 80% of women report severe menstrual pain during the year [28]. It is also known that despite the fact that adults experience severe pain of known or alleged aetiology, they do not seek professional help and try to cope with this problem on their own [29]. Due to limited data, it is also difficult to assess the effectiveness of alternative methods of pain management used by adults, in particular physiotherapy or occupational therapy.

Old age is defined as > 65 years of age. However, considering the ontogenetic aspect of pain, this can be extended to 75 years of age [30]. The reason for this is that this age group is characterised by high prevalence of several, often chronic diseases, such as osteoarthritis (about 80% of people over 75), hypertension (60-70%) and ischemic heart disease (about 30% of elderly

people) [31]. The incidence of acute pain decreases noticeably with age, whereas the number of people reporting chronic pain increases. The increase in pain in this age group is caused by multiple factors, such as reduced mobility, limited social life or a lack of it, discouragement and/or depression [32]. The belief that elderly people feel less pain and that it is an intrinsic part of ageing and disease may make these individuals more likely to avoid complaining about pain [33]. However, in his study, Harkins [34] did not observe age-related changes in the pain threshold and pain tolerance among the elderly.

Pain assessment and evaluation are subjective and, in adults and elderly people in particular, modulated by physiological factors, directly or indirectly related to tissue damage, and psychogenic factors, treated as non-receptor-mediated pain. The two aspects are inseparable. Pain perception may also be intensified by overprotective behaviour of a partner or close relatives [35]. This and other studies suggest that caution should be taken in interpreting study results, and that it is necessary to carefully select research groups in every stage of ontogenesis.

On the other hand, objective techniques of investigating pain show that the process of ageing involves a number of physiological changes in the body affecting all organs and systems, including the nervous system. Significant differences have been found in threshold values for noxious stimuli depending on the duration of stimulation [36], which could suggest age-related modulation of the transduction process. Other authors have shown that thresholds for tactile, vibration and thermal stimuli increase with age; the same applies to the distance values in two-point discrimination tests [8]. It has also been indicated that the thermal pain threshold increases with age [7], but no such differences have been found for electrical stimuli [37, 38]. It is possible that these processes are affected by a number of factors, such as demyelination of nerve fibres associated with a decreased expression of myelin proteins, axonal atrophy caused by reduced axonal transport in nerve fibres, and their weaker regeneration, leading to a reduction in the number of distal branches. Another issue is the reduced endogenous pain inhibition in the elderly. A more intense response to pain in elderly subjects has also been confirmed electrophysiologically in experiments on laboratory animals [39].

## **PAIN AND PHYSICAL ACTIVITY**

Recent years have seen first publications indicating that physical activity is beneficial, especially for the elderly. Physical activity has been found to stimulate the formation of capillary blood vessels in the brain, an ability previously attributed to skeletal and cardiac muscles [40]. Moreover, several experiments on animals have shown that physical effort leads to the synthesis and metabolism of neurotransmitters: serotonin, dopamine and noradrenaline [9]. Training also increases the intensity of gene expression, especially in terms of different protein synthesis and hormone secretion, which is also subject to variation during ontogenesis. Furthermore, studies on animal models have shown that physical exercise not only aids the creation of new nerve cells but also stimulates growth factors favourable for creating cell connections and building neural networks [41]. During physical activity skeletal muscles, being like an endocrine organ, secrete myokines, whose expression affects the metabolism and tissue interaction and has an anti-inflammatory effect [42]. Physical effort changes the biochemistry of numerous organs, especially muscles, as well as the nervous system. It also modifies the metabolome at the cellular and tissue levels and affects the epigenome and finally the

proteome, which is the entire set of proteins in an organism [43]. Recently described processes at the cellular level and a crosstalk between the elements of individual signalling cascades show that the direct or indirect consequences of physical exercise go far beyond the area of muscles and the force which they generate [42]. The impact of physical effort on the body is also visible with regard to the cognitive aspect and the sense of well-being, including better quality of sleep [44].

Therefore, it can be assumed that the dynamics of ageing mostly affect inactive individuals. It has been recognised that lack of physical activity doubles the risk of developing disabilities or dysfunctions [45], while regular physical activity is an integral component of maintaining good health and functional independence of the elderly. Physical fitness and weakened vital functions are treated as potentially useful markers for assessing health risks in elderly people as they can supplement traditional diagnostic methods [46].

Therefore, the multidimensional aetiology of pain can explain the positive effect of regular physical activity reflected in less disturbing pain and/or pain tolerance [47, 48]. Physically active individuals find it easier to accept increased effort and are able to increase exercise intensity, which translates into subjective effect of pain reduction [49]. Another, often underestimated aspect of physical activity is that it activates the transmission of sensory information associated with the movement and inflow of internal (interaction with the ground through cutaneous receptors, vibrations, muscle tension and joint motion – proprioception, balance, etc.) and external (sight, hearing) signals. Yet another important aspect of physical activity modulating pain perception is the sense of belonging to a group, social contacts and change of the environment. After all, pain is a subjective feeling based on knowledge, something of a software program that we acquire and develop throughout our lives. According to the WHO [50], social support, seen as social ties that determine people's life satisfaction and subjective well-being, is an important marker of active ageing. Loneliness is far less damaging than being socially isolated. Belonging to a group provides individuals with great emotional support and is the main factor motivating them to exercise [51].

Studying physical activity among adults over 65 has been one of the main priorities of global public health in terms of developing effective active ageing programmes [52]. Daily physical activity is particularly important for active ageing as it reduces all-cause mortality and prevents the development of chronic diseases. Moreover, it lowers the risk of accidents among the elderly and helps to maintain age-appropriate physical and cognitive condition [53–55]. However, research has shown that as many as 23% of adults around the world are not active enough and the rates of inactivity increase with age. Around 70% of people over 75 years of age do not engage in moderate-intensity activity of at least two and a half hours a week. In their study on elderly people, Patti et al. [56] have shown that taking systematic exercise for 13 weeks improved cardiovascular capacity, increased joint mobility, strengthened core stability, significantly improved proprioceptive sensitivity and balance skills, and reduced pain perception. Similarly, studies by Haughton et al. [51] and Eyler et al. [57] have pointed to reduced intensity of pain in people who take exercise regularly during recreation or amateur and competitive sports.

Highly active and fit people are significantly less likely to report musculoskeletal pain. Numerous authors point out that pain in the upper and lower limbs does

not depend solely on physical loads [58, 59]. According to Feldman et al. [60], a significantly higher risk of pain in the upper limbs occurs in white-collar workers in comparison with blue-collar workers. In the case of lower joint pain, the main risk factor is overweight [61, 62].

The available studies on the elderly encourage the use of programmes which include strengthening as well as flexibility and endurance-improving exercises in order to increase physical activity, which translates into pain reduction [63–65]. In the last 10 years, much attention has been paid to digital technology and its influence on improving and treating pain among older adults [66]. It has been found that older adults show readiness to use digital technologies (such as the Internet or iPhone) to reduce or eliminate pain [67].

## CONCLUSIONS

Similarly to younger adults, elderly people can adapt to changing internal and external conditions due to the plasticity of the nervous system. Current research findings do not exclude the possibility of the formation of new neurons in brain structures and new interneuronal synapses. Physical activity supports these processes.

Pain is a highly individualised sensory phenomenon, involving the physical, cognitive and emotional spheres of human life. There is no clear evidence that the intensity of pain changes with age, and its control mechanisms are also unclear. It can be speculated that with age there is a consensus between the declining number of afferent nerves and slightly less efficient endogenous inhibition of this nociceptive input.

Different reactions to pain during ontogeny most often result from the loss of communication skills, the systematic weakening of the functions of all systems and organs, in particular the nervous system, and limited physical activity. The impact of physical activity goes beyond activating the sensory and motor systems – it also involves an important social aspect. Motivation for physical activity translates into motivation to improve the quality of life. However, there is no fixed point in time when one should begin taking physical activity in order to experience its benefits.

Furthermore, from the ontogenetic perspective pain perception cannot be limited to nociception, i.e. age-related changes in the “hardware”. This is because the perception of pain depends on the community in which we live, our religion, individual life philosophy, intellectual interests as well as the level of understanding of biological and clinical aspects of pain. Cognitive, emotional and social aspects of pain certainly have both direct and indirect impact on pain perception in the course of ontogeny [68].

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