

Perspective

Pediatric Complex Regional Pain Syndrome - A Multifaceted Phenomenon

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The accepted approach in medicine today is a biopsychosocial approach. A commonly used biopsychosocial model of disability that has been endorsed by the World Health Organization is the International Classification of Functioning, Disability and Health (ICF). The ICF, includes five components – body function and structures (the actual anatomy and physiology/psychology of the human body), activity (the execution of a task or action by an individual), participation (involvement in a life situation), personal factors (e.g., race, gender, age, educational level, coping styles), and environmental factors (factors that are not within the person's control). When it comes to children, the environmental factor includes the family as the main factor [11]. Accordingly, the ICF conceptualizes a person's level of functioning as a dynamic interaction between her or his health conditions, personal, and environmental factors.

Complex Regional Pain Syndrome (CRPS) is recognized in children and youth similar to the adult population. CRPS describes a state of severe pain disproportionate to the trauma or stimulation that preceded the onset of the pain and is accompanied by a wide variety of autonomic, trophic and motor changes. The pathophysiological mechanism of CRPS is still unclear, but several concepts have been proposed to explain its complex symptoms: (i) facilitated neurogenic inflammation; (ii) pathological sympatho-afferent coupling; and (iii) neuroplastic changes within the central nervous system [6]. The clinical

symptoms and findings of a brain functional imaging studies point to brain neuroplastic changes as the main factor in the development and maintenance of the syndrome [10]. Diagnosis of CRPS is mainly based on clinical signs and is made using the Budapest criteria [3]. However, the severe continuous pain is the prominent characteristic of the syndrome and is at the center of the definition (Castillo-Guzmán et al., 2015).

Nociception refers to the central nervous system and peripheral nervous system processing of noxious stimuli, such as tissue injury, which activate nociceptors and their pathways. Pain is the subjective experience one feels as a result of the activation of these pathways [5]. However, the intensity of the pain stems not only from nociception but also from other factors including different psychosocial factors. Thus amplified pain is found to be affected by genetic polymorphism, family factors, stressful events, learning disorders, social difficulties and other biopsychosocial factors [8].

Due to the unbearable pain, the child refrains from using the limb. In children, usually the lower limb is involved [7]. More specifically, the child stops stepping and fixes the lower limb in a certain position. The limb's fixation causes local changes such as muscle weakness, swelling and discoloration due to venous stasis. At the same time as the visible clinical changes appear, there is also a hidden process of reorganization in the brain with

changes in the activity of various neural networks. For example, a recent study showed that prolonged (two weeks) dominant arm immobilization strengthened functional connectivity between disused M1 and the Cingulate-Opercular Network (CON) [9]. The changes in communication and activity in motor and CON networks cause further changes in motor, cognitive and behavioral-emotional activity. It is likely that these changes preserve and accelerate the characteristics of the syndrome - pain, motor, autonomic and even tropical changes. These results suggest complex connectivity to internal organs (e.g., adrenal medulla) and that M1 is punctuated by a system for whole-body action planning, the somato-cognitive action network [2].

Despite the aforementioned imaging evidence many questions still remain to be answered. For example, the primary motor area of the somato-cognitive action network probably functions differently in children with CRPS. However, are the involved neural networks in children with CRPS are different and sensitive before the development of CRPS or maybe brain changes occurred following the limb's disuse? In addition, are changes in the understanding of CRPS mechanism and the new insights from imaging studies likely to contribute to the treatment/intervention of these children?.

The biopsychosocial approach through the lens of ICF is particularly relevant in patients with CRPS. Considering CRPS mechanisms it is very important that rehabilitation of children with CRPS will be in a multidisciplinary framework and include reference to motor function, with a requirement and gradual but constant progress towards maximum activity and participation. At the same time, the sensitive and special child who developed the syndrome and his/her parents, who are a very significant factor in the child's environment in general and in the recovery process in particular, must be considered. Understanding the mechanism of the phenomenon points also to the importance of psychoeducation and explaining to both children and parents (corresponding to the child's age) that brain changes contribute to the various characteristics of the syndrome, that "it's all in the head", but literally!

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