Opinion

The Time has come turn on the Cutaneous Nerve System to manage Pain

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Introduction

Pain remains one the main reasons why people seek medical care. Most of the nociception leading to pain is typically generated in either the musculoskeletal system or the viscera. As the brain receives nociceptive information it will create an awareness of a noxious stimuli and respond accordingly [1]. The interconnection within the functioning of the brain, the immune system, and the health of the skin has been identified within the functioning of the brain, the immune system, and the health of the skin. Cutaneous sensory stimuli are transduced in the periphery by specialized organs or free nerve endings [2]. Primary afferent sensory neurons are long cells, often traversing distances of over 1m in humans. Nociceptive and tactile stimulation can have profound neuroendocrine effects. Nociceptive information enters the central nervous system in an organized segmentally related fashion and can produce both peripheral and central sensitization. This is a state of hyperexcitability of nerve fibers, which react to stimuli weaker than the normal threshold, spreading to adjacent nerve fibers, producing prolonged repetitive electrical discharges from a single stimulus.

The skin is a highly complex organ, responsible for sensation, protection against the environment (contaminants, foreign proteins, infection) and, therefore, is linked to the immune and sensory systems. The skin, hypodermis, and superficial fascia are innervated by the cutaneous branches of an individual spinal nerve [3]. Epithelium cells are arranged in such a manner that they form a cohesive sheet. This function makes it perfect as the outside layer of the body’s surface and as the lining of the digestive system. It originates from the ectoderm and endoderm. It consists of many layers and contains cells (such as lamellar cells, terminal Schwann cells, keratinocytes or Merkel cell) and nerves including free nerve endings (FNE). Although the most abundant cells of the epidermis are keratinocytes, there are also nonepithelial immune cells present in the epidermis, such as Langerhans cells and dendritic epidermal T cells [4]. Keratinocytes play an active role in the immune process. In response to skin damage or microbial intrusion, keratinocytes function as sentinels [5]. They are capable of initiating and amplifying a specific immune reaction through the activation of Langerhans cells that migrate to the lymph nodes [6]. The afferent sensory nerves are responsible for cutaneous perception of pressure, temperature, touch, and pain. Until recently, intra-epidermal FNE were considered exclusive cutaneous nociceptors, thermoreceptors, and proprioceptors [7]. This supported the idea that intra-epidermal nerve fibers were “free,” and thus not associated with other cell types. The intra-epidermal FNE has traditionally been seen as the transducers of cutaneous noxious stimuli. However, there is a growing understanding how the keratinocyte actually contributes to cutaneous nociception. Talagas et al [8,9] identified that the keratinocytes can initiate nociceptive responses.

Talagas et al. showed that FNE are located by keratinocytes. It appears that the keratinocyte cytoplasm is wrapped around the total length of the FNE, almost creating a tunnel for the FNE. It was concluded that the keratinocytes must play a role stimulating
the FNE and therefore the transduction of nociceptive sensory information [8,9]. Findings demonstrate a clear relationship between the keratinocytes and nervous system. This was supported by the findings of Evdokimov et al [10]. They identified that patients with fibromyalgia have a higher interleukin 10 gene expression and this might result in cutaneous nociception. Gouin et al [11] identified that during cutaneous neurogenic inflammation the neuropeptides are released from sensory nerve endings and this will have an effect on the functioning of the keratinocyte.

It has been reported that there is a relationship between psychiatric conditions, such as depression and anxiety, and cutaneous hypersensitivity. The interaction between keratinocytes and nerve endings modulates pain and plays a role in the management of cutaneous hypersensitivity. The pathway by which this might occur is by the Keratinocytes maintaining homeostasis by activating endogenous glucocorticoids [12,13]. Cutaneous innervation innervation or immune components have been the focus of many medical treatments. Promising preliminary results have been obtained from a neuro-immunoendocrine approach with a focus on the cutaneous system. It has been identified that neuropeptides such as NGF, hormonal (vitamin D), anti-cytokine and capsaicin to attack the skin’s sensory neurons [4,14-20].

The identification of keratinocytes as primary transducers of harmful stimuli is a paradigm shift in the field of cutaneous sensory transduction. By using the same afferent pathways, the FNE will send information to the spinal cord based on dermatomal relationships. In the cord non-noxious stimulation could aid in reducing a local central hyperexcitability. With other words stimulating the skin and nerve endings modulates pain and plays a role in the management of cutaneous hypersensitivity. The pathway by which this might occur is by the Keratinocytes maintaining homeostasis by activating endogenous glucocorticoids by activating endogenous glucocorticoids [12,13]. Cutaneous innervation innervation or immune components have been the focus of many medical treatments. Promising preliminary results have been obtained from a neuro-immunoendocrine approach with a focus on the cutaneous system. It has been identified that neuropeptides such as NGF, hormonal (vitamin D), anti-cytokine and capsaicin to attack the skin’s sensory neurons [4,14-20].

The identification of keratinocytes as primary transducers of harmful stimuli is a paradigm shift in the field of cutaneous sensory transduction. By using the same afferent pathways, the FNE will send information to the spinal cord based on dermatomal relationships. In the cord non-noxious stimulation could aid in reducing a local central hyperexcitability. With other words stimulating the skin causing physical ionization through the receptors seems to be a direct, fast and effective way to down regulate the nervous system as a whole will result in decreased pain and improved ROM. It is time we shift focus and turn on the cutaneous nerve system to manage pain.

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