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Brief Review

The axon reflex

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ABSTRACT

This brief review focuses on historical development of the knowledge about the axon reflex and on investigations in which this reflex used to link pathophysiologic processes to symptoms of the disease state through the organization of neuronal networks. Unlike spinal reflexes, there is neither an integration center nor any synapse in the arc of the axon reflex. Receptor and effector of axon reflex are at the peripheral ends of an afferent neuron. To set the basic knowledge and major achievements we first provide a brief account of the understanding of the spinal cord in conventional reflexes. Next, recent work on specifically axon reflex and its involvement in processes such as pain, itch, bronchial asthma and dermal circulation is reviewed. © **Neuroanatomy. 2008; 7: 17–19.**

Key words [history] [axon reflex]

Introduction

We wish to begin with a citation from Sir Charles Sherrington (1857-1952), in his renowned book, he wrote that reflexes are "… the unit reactions in nervous integration" [1]. Sherrington's school made important contributions on spinal reflexes based mainly on careful observation and palpation. Development of experimental tools and techniques enabled to analyse specific spinal reflex pathways both with respect to timing as well as sensory modality [2].

In scientific meaning, the word 'reflex' was first used as an adjective in the 17th century by Rene Descartes (1596-1650). According to Descartes who was a dualist the actions of body are reflex actions, but actions of mind are meaningful, conscious, and voluntary. Jean Astruc (1684-1766) was the first to use the term reflex as a noun. In fact, the first complete scientific description of a reflex was given by John Augustus Unzer (1727-1799), a professor worked in Halle, and by Prochaska (1742-1820), professor of anatomy and ophthalmology in Prague. The term of conditioned reflex which is one of the most important contributions to reflex studies was described by Ivan Petrovitch Pavlov (1849-1936) [3].

In 1873, in the laboratory of Kovalevskiy, a student named Sokovnin, discovered a new type of reflex and coined the term 'peripheral' or 'local reflex'. Sokovnin and Rozhanskiy for the first time described special type of reaction, named axon-reflex in 1889 [4]. Seventeen years later, the term of axon reflex was introduced by Langley [5] to explain observations he made on pilomotor responses evoked by stimulation of the cat sympathetic chain at various points along its length. The term is now rarely, if ever, used in this context, and most will associate the phrase with Sir Thomas Lewis's explanation of the flare component of the triple response. This response, consisting sequentially of the red line, flare, and wheal, can readily be produced by scratching the skin with a blunted point. According to Lewis, the flare was due to dilatation of neighbouring arterioles, this in turn having been triggered by a local nervous system. Although Lewis is usually credited with being the first to propose the axon reflex as the explanation for this response [6], Bruce [7] preceded him in suggesting that local vascular changes would be a consequence of axon reflexes involving sensory nevre fibres.

A classic reflex arc

A reflex is an involuntary, immediate, automatic and stereotyped response to a specific sensory stimulation. Each reflex has an arc. There is a sensory receptor at the starting point of reflex arc, an effector at the final point and an integration center between them. An afferent pathway connects the sensory receptor to the integration center. An efferent pathway connects the integration center to the effector. There is one or more synapses in a reflex arc. It is an interesting tradition that the connection between the motor neuron and the effector is not included when counting the number of synapses in a reflex arc.

Sensory receptors and neurons

Sensory neurons which transmit impulses toward the central nervous system from sensory receptors are pseudounipolar neurons. They have a single process that emerges from the cell soma and divides into two processes running in opposite directions: to the periphery and to the central nervous system. Central process is known as central branch, axonal branch, central axon and axon. Peripheral process is also known as peripheral branch, dendritic branch, peripheral axon, and dendrit.

Sensory receptors may be either specialized endings of sensory neurons or separate specialized cells at the ends of the neurons. When a sensory receptor is stimulated it initiates a signal that is carried to the central nervous system by processes of sensory neurons.

A different reflex: the axon reflex

It is a reflex resulting from a stimulus applied to one branch of a nerve, which sets up an impulse that moves centrally to the point of division of the nerve, where it is reflected down the other branch to the effector organ [8]. Blood vessels, sweating glands and mast cells are most important effectors of axon reflex in the skin. Transmitting a signal from one end of a nerve to another end is a type of antidromic transmission [9].

The reflex arc of axon reflex has neither an integration center nor any synapse (Figure 1). The periferic ends of sensory neurons are not only receptor, they have also secretory functions like as ends of motor fibers with respect to articles about axon reflex. In capsaicine sensitive pain receptors this was named sensocrine function [10].

Physiopathology involving the axon reflexes

According to the literature, axon reflexes are important in a lot of physiological and physiopathological processes from regulation of skin blood flow and sweating to inflammation and pain, from itch to asthma bronchiale and allergic rhinitis [11–26]. It is difficult to define the mechanism of acupuncture. Axon reflex mechanism has been added to the mechanisms responsible for the effects of acupuncture [27, 28]. The effect of axon reflex to skin blood vessels is monitored measuring the skin blood flow by laser doppler. Sudomotor tests like as transepidermal water loss (TEWL) and quantative sudomotor axon reflex test (QSART) are useful for monitoring the effects of axon reflexes on sweat glands. Measurements of effects of axon reflexes are important for neuropathies like as pre-diabetic and diabetic neuropaty [29–32]. According to some investigators, there are axon reflexes in central nervous system, gastrointestinal systeme, urinary system [5,33–36].

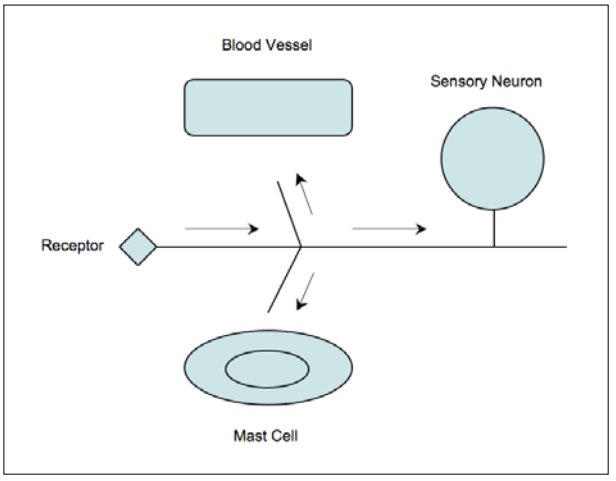

Figure 1. The arc of axon reflex by A. Ninan Bruce [7].

Inflammation

Inflammation which is known as a response to tissue damage whether resulting from infection, ischemia, physical injury, exposure to toxins, or other types of trauma is characterized by pain and swelling and redness and local heat. Inflammation alters the chemistry of damaged region by changing the vascular permeability and secretory functions of cells. Chemicals releasing and exiting from damaged and dead cells are also important for environment. Ultimately excitability of the sensory receptors increase or reduce. The increase of excitability and responsiveness of a receptor by this way is known peripheral sensitization. The reason of this sensitization is a reduction in threshold of excitability because of the chemical and physical alterations in region. Inflammation has a role in almost every pathological process. We may suppose inflammatory region as a soup and denominate "inflammatory soup" and nerve fibers to spoons. Axon reflex makes an important contribution to inflammatory soup. We may also use the name "pain soup" if we approach the question from the point of pain. Some chemicals of these soups are provided by axon reflexes.

Asthma

Asthma is a chronic inflammatory disease of the airways. Bronchial asthma attacks are characterized by narrowing of bronchioles due to smooth muscle spasm, and inflammation. For many years, asthma has been classified as a "neural" disease, with an imbalance between constrictor and dilator nerves being responsible for the symptomatology. Although, nowadays, asthma is recognized as an inflammatory disorder of the airways, neural mechanisms remain very important; axon reflexes, in particular, have received a lot of attention in recent years [37]. Release of sensory neuropeptides such as substance P, neurokinin A, and calcitonin gene-related peptide are potent inducers of airway smooth muscle contraction, bronchial oedema, extravasation of plasma, mucus hypersecretion, and possibly inflammatory cell infiltration and secretion by axon reflex mechaism [11]. It is reported that peripheral endings sensory neuron contributes to bronchial inflammation by exciting parasympathetic ganglia neurons in addition to classic axon reflex mechanism [15]. Axon reflex mechanism is also important for physiopathology of allergic rhinitis and sinusitis [24,25].

Pain

Pain was defined by IASP as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such

damage [38]. From migraine and inflammatory pain to complex regional pain syndrome and neuropathic pain, inflammation is one of the basic components of pain for many kind of pain [21–23,39,40]. Axon reflexes is not associated only with some pain types also some critique mechanism like as allodynia, hyperalgesia and sensitization. It is proposed that axon reflexes are responsible from some effects of acupuncture which is a complementary technique for analgesia [27–29].

Itch

According to Hafenreffer; itch is an unpleasant cutaneous sensation which evokes the desire to scratch [41]. Inflammation and axon reflexes are also important for itch sensation like as nociception. Capsaicine is a useful agent which depletes the chemicals of nerve endings by axon reflex mechanism therapy is effective for itch and pain [10].

Conclusion

In conclusion, although there are a lot of data for the existence of axon reflex mechanisms in human physiology and physiopathology we need more direct evidences about functionality of them. Hopefully, the near future will bring some solutions with the introduction of very potent agonist ve antagonists of chemicals which are secreted from sensory nerve endings for the treatment of inflammatory diseases. The axon reflex may be a promising area of research suggesting that this reflex might confer an interface that, in part, could mediate the inflammatory responses. Furthermore, work on axon reflex offers attractive avenues for the understanding of and future research on pain mechanisms and disease states such as asthma.

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