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Effects triggered in the periphery by acupuncture

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ABSTRACT

The clinical effects following acupuncture stimulation can be attributed to peripheral and central effects. Histological studies have revealed that many acupuncture points have dense innervation, and are often located in direct relation to skeletal muscles, connective tissue, as well as to cells with neuro-immune-modulatory role [66], suggesting that these tissue may contribute both to the peripheral and central effects.

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1. Nervous system

1.1. Sensory receptors

Acupuncture stimulation is associated with the activation of different sensory receptors, i.e., the terminal of the spinal dorsal root ganglion neuron or trigeminal sensory neuron, in the skin and deeper tissues. Their properties and the corresponding sensation they give rise to, that may be activated during acupuncture and moxibustion, include five major modalities [51,85,86,105,106].

1.2. Mechanoreceptors; cutaneous and subcutaneous

Five major types of mechanoreceptors have been identified in skin. Two of these are of the encapsulated type and are located in the superficial layers of the skin: Meissnerís corpuscle and the Merkel disk receptor. The other two receptors, the Pacinian corpuscle and the Ruffini ending, also encapsulated, are found in the subcutaneous and deeper tissue layers (including between layers of muscle and on interosseous membranes). The fifth major type of mechanoreceptor is the bare nerve ending responding to stroking of the hairy skin.

1.3. Mechanoreceptors; tendon, joints and skeletal muscle

Four different types of mechanoreceptor are found in skeletal muscles, tendons and joint structures. Their main task is to give rise to the sense of movement and position of oneís own limbs and body (proprioception), and sense of speed and direction of limb movement, and also to enable maintainance of an upright position (postural information) and manipulation of objects. One of these receptors is the ergo-receptor. Ergo-receptors are activated by hard pressure during muscle contraction [56] and also probably by acupuncture, when the sensation of *de qi* is evoked. It has therefore been suggested that the physiological counterpart to acupuncture is exercise [5]. However, the ergo-receptors can also respond to metabolic stimuli of released H^+, lactate, or K^+ ions, i.e., acting as 'metabolic chemoreceptor' and by a release of neurotransmitters [49,108].

1.4. Nociceptors

Nociceptors are the receptors that selectively respond to nociceptive stimulation of peripheral tissue, as mentioned earlier, leading to perceived pain under certain circumstances. Pain is sometimes perceived in the absence of this activity but could then be due to sensitization processes in higher brain structures.

The polymodal nociceptors are the most common class of nociceptor. During intense acupuncture stimulation, acupressure (painful) or strong massage, mechanical nociceptors may be activated resulting in slight increase of pain sensations but also in an increased activity in endogenous pain inhibiting systems.

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During acupuncture stimulation a sensation of itch may be perceived. It has been suggested that pruritus/itch receptors [105,69] are part of a larger set of nociceptors where activation of the whole group elicits pain while activation of the itch-selective subset elicits exclusively itch. However, itch or pruritus is not just triggered in the peripheral tissue but also more centrally suggesting that there exist multiple neural pathways for itch induction [77].

1.5. Acupuncture and mechanoreceptors

Acupuncture may activate all types of mechanoreceptor in superficial cutaneous and in deep muscular tissue. It has been reported that most acupuncture points contain abundant free nerve endings, encapsulated cutaneous receptors (Merkel, Meissner, Ruffini, and Pacinian corpuscles), sarcous sensory receptors (muscle spindles and tendon organs) as well as ergo-receptors, and their afferent fibres. Acupuncture sites can be classified into three types: muscle-spindle-rich acupuncture sites, cutaneous-receptor-rich acupuncture sites, and tendon-organ-rich acupuncture sites. In acupuncture practice, manipulation is often performed on the inserted needles to enhance needling sensation and therapeutic responses. Different modes of stimulation technique used (for example superficial versus deep needling depth, light or no stimulation versus rotation and thrusting) will also probably determine which type of receptor is activated. Gentle and repetitive manipulation of the inserted needle would be expected to produce mechanical pressure and tissue distortion that activate mechanoreceptors. Also, manual stimulation may result in distant effects which has been attributed to shear force- and stress-induced tissue displacements. All types of manual technique tested have yielded greater distant effects on sarcous stretch receptors than cutaneous mechanoreceptors; twist/rotation has the greatest distant effects on the cutaneous superficial and deep receptors as well as sarcous stretch receptors compared to other techniques. In addition, the sensitivity status of the peripheral terminals, i.e. intact or sensitized as in a pain condition, will be influenced by the receptor's peripheral milieu such as the presence of lactate, K^+, nitric oxide (NO) ions, chemokines, cytokines, myokines, and a number of other factors. Therefore, the same stimulation technique may produce very different sensations ranging from being barely detectable to being painful.

1.6. Afferent nerve fibres

All somatosensory information from the limbs and trunk is transmitted through individual peripheral afferent nerve fibres of spinal dorsal root ganglion neurons, each of which responds to the modality-specific type of stimulation associated with the morphological and molecular specialization of its peripheral receptors [51]. Somatosensory information from cranial structures is transmitted by the trigeminal sensory neurons in the brain stem, which are functionally and morphologically homologous to spinal dorsal root ganglion neurons, and transmitted further to higher levels in the brain via second order neurons. The principal functions of dorsal ganglion neurons and the trigeminal nerve are transduction of the stimulus and transmission of encoded stimulus information to the higher levels of the CNS. Recent studies also indicate that somatosensory stimulation may be transmitted to the nucleus tractus solitarius without bypassing the dorsal root ganglion.

Mechanoreceptors and proprioceptors are commonly innervated by large-diameter myelinated afferents axons, whereas thermal receptors and nociceptors have small myelinated or unmyelinated axons.. Gentle, dynamic touch is encoded by a distinct tactile type receptor and transmitted in un-myelinated afferent nerves found exclusively in hairy skin, C tactile (CT) afferents. CT afferents increase firing when the skin is stroked at a speed of approximately 30 mm/s with gentle contact at a typical skin temperature [85,71,78,2].

The presence of somatic afferent and efferent fibres innervating skin, connective tissues, and skeletal muscles has been reported at acupuncture points. Many of the acupuncture sites investigated had relatively dense neural components, particularly nerves fibres, with a ratio of nearly 1.4:1 compared to non-acupuncture points. Also, the ratio of myelinated to un-myelinated fibres was found to be nearly 4-fold higher in the acupuncture point Zu-San-Li (ST36) than surrounding areas. Sarcous sensory receptors (muscle spindles and tendon organs) and their afferent fibres have been reported to be concentrated at acupuncture points located on thick muscles such as the tibials anterior and rectus femoris muscles [66].

Another important neural component of most acupuncture sites, and indeed many somatic areas, is the dense and fine autonomic nerve fibres, found in close proximity to the sensory receptors and afferents. Most autonomic nerves are norepinephrine (NE) containing sympathetic fibres but also cholinergic (ACh) parasympathetic efferent nerves may be found. Interaction between somatic and autonomic neural components may serve to modulate local and afferent signals in points where acupuncture stimulation is applied.

Interaction between activity in the sensory afferents and autonomic efferent nerve fibres may also take place in the dorsal root ganglions and at segmental level in the spinal cord as well as in more central parts of the CNS.

1.7. Electrical stimulation of afferent nerves

As stated above, the difference in the conduction velocities of different nerves may be attributed to internal resistance to current flow along the axon. This is also the reason why electrical nerve stimulation using either surface electrodes as in transcutaneous electrical nerve stimulation (TENS), or with thin needles connected to an electrical stimulator as in electro-acupuncture (EA), with low intensity, activates afferent nerves with large diameter more easily than the thinner ones [8]. When using higher stimulation intensities, thinner sensory afferents are activated by the stimulus.

Due to the fact that EA results in the electrical activation of many different afferent nerves it is therefore not to be regarded as equivalent to manual acupuncture [80]. It is generally accepted that manual acupuncture sets up activity in superficial and deep Aβ and Aδ fibres but that most of the clinical effects including pain alleviation and autonomic modulation may be attributed to the activation of deep Aβ, Aδ and C fibres [5].

1.8. The de qi sensation

A large body of empirical and experimental evidence suggest that during acupuncture stimulation the so called needling sensation, *de qi*, should be strived for.

Although the perception of needling sensation may vary between individuals and with manual techniques, this distinct sensation is generally characterized by soreness, numbness, heaviness, distension, and aching in the deep tissues surrounding the inserted needle [47]. The *de qi* sensation is also often accompanied by an increased blood flow and a feeling of warmth at the acupuncture point. Simultaneously with the patients' sensation of *de qi*, the acupuncturist often perceives an increased resistance to further movement/manipulation of the inserted needle. Thus, the needling sensation is not a single, but a compound sensation that is generated from the activation of various sensory receptors and their afferent fibres in acupuncture sites. It has been demonstrated that numbness, heaviness, and distension during needling are closely associated with the activation of myelinated Aβ and Aδ afferents in deep tissues of acupuncture points, whereas aching and sore-