Editorial Article

Neural Control of Skin Water Content: The Eccrine Sudoriferous Gland

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Abstract

The skin, the largest organ of the body is composed of several layers and cellular structures, distinctively controlled by modulatory signals arising from the central, peripheral and autonomous nervous systems (CNS, PNS, ANS). Most of its functions depend significantly upon water content levels of its constitutive layers. The sudoriferous gland has been traditionally associated to sweating and its primary form of cooling in body temperature control in humans. However, there is increasing evidence suggesting that a key role in water content modulation and thus in skin moisture is also played by the sudoriferous gland. Dysfunctions of skin moisture under lie several debilitating dry skin problems such as xerosis, atopic dermatitis, psoriasis, and rosacea. Each sweat gland receives several nerve fibers that branch out into bands of axons surrounding the individual tubules of the secretory coil. The latter are surrounded by contractile myoepithelial cells that function as a facilitator of secretory product excretion. Evidence from animal studies suggests that efferent signals from the preoptic hypothalamus travel to the pons (tegmentum), the medullary raphe regions, and the inter mediolateral cell column of the spinal cord for the control of eccrine sudoriferous glands. This editorial aims at summarizing some of the main findings in neural control mechanisms of normal skin functions – specifically those associated with eccrine sudoriferous gland activity.

Eccrine Sudoriferous Gland

Functional anatomy of the skin: The skin is the largest organ (~2m^2) of our body and the first line of defense against external factors. It prevents excessive water content losses and, as such, serves as a lipid-rich structure involved in regulating body temperature. The mammalian skin is composed of four layers – namely the epidermis, basement membrane, dermis and subcutaneous or hypodermis. None of the epidermis sub layers (stratumcorneum or SC, granolosum or SG, spinosum, basal) contains blood vessels per se although the deepest layers are 'nourished', so to speak, by diffusion from blood capillaries extending to the upper layers of the dermis. [1]. The dermis provides strength and elasticity to the skin through an extracellular matrix composed of collagen fibrils, micro fibrils, and elastic fibers, embedded in hyaluronan and proteoglycans [1]. It harbors blood vessels, mechanoreceptors, thermoreceptors and nociceptors that provide the sense of touch, pressure and heat as well as biological fluids released from sudoriferous and sebaceous glands.

General knowledge about neural control of skin functions, water-content and skin health: The sensory roles at-

tributed to skin functions are rather well-described in most text-books. Cutaneous nerves and sensory elements of the Peripheral Nervous System (PNS) respond to stimuli from the circulation and to emotions ("internal trigger factors") as well as from peripheral receptors (i.e., mechanoreceptors, nociceptors, thermoreceptors, chemo receptors) by sending directly or indirectly to the CNS, inputs involved in sensations (hot/cold, pressure/touch, pain, vibration, chemicals, etc.), vasocontraction, vasodilatation, body temperature regulation, barrier function, secretion, growth, differentiation, cell nutrition, nerve growth, inflammatory and immune responses, apoptosis, proliferation, and wound healing [1]. The inner milieu of our body consists of about 70% water (gender- and age-based differences ranging from 55-75%) whereas surrounding ambient air carries less than 1% water [2]. Consequently, skin water content tends to decrease more or less rapidly through sweating and evaporation and, without normal mechanisms for steady replenishment of skin water content levels, xerosis and other dry skin problems are bound to be experienced. Two main mechanisms affect water content at the cellular level – 1) water transport from inner layers towards the epidermis and, 2) water transport and evaporation from epidermal layers towards the external environment.

Water transport from inner layers to the epidermis: Skin hydration levels are regulated by water transport from inner layers, including from blood vessels, that seek bringing in water towards the dermis and, hence, to the epidermis. In other words, water travels from the deeper skin layers towards outmost skin layers to hydrate cells of the SC –where it is eventually being lost to evaporation. Increasing skin water content is thus achievable through enhanced activity of Aquapor in channels, supported by water-binding molecules such as glycerol, expressed on vascular endothelial cells where it facilitates water exchange and transport between blood and dermis [3]. In other words, body water levels as well as blood volumes, circulating flow levels and regional distribution can significantly affect skin water content levels [4]. Indirectly, neural control of water transport may be achieved through neuro endocrine responses (hypothalamic-pituitary-adrenal axis) that regulate vasodilation and vasoconstriction (i.e., arteriovenous anastomoses [5]). This said, the latter are also controlled by CNS structures such as the raphe nucleus, medulla oblongata, preoptic area, hypothalamus, pons and periaqueductal gray matter [6-9].

Water transport and evaporation from epidermal layers to the exterior: Although, water content levels vary accordingly to skin layer (70% in SG but 15-30% in SC), reducing water transport towards the outmost layers and increasing water-binding capabilities while reducing evaporation constitute another key mechanism of skin water content regulation [1,10]. A novel role of sudoriferous glands in skin water content has recently been un-

raveled to achieve that. First of all, human sweat glands are generally divided into two types, the apocrine gland and the eccrine gland. The latter is the primary structure of the skin responsible for thermoregulatory sweating in humans – it is found over the entire body surface [1]. Their density is an important factor of thermoregulation [11]. Structurally, it consists of a bulbous secretory coil (dermis) leading to a duct (epidermis and skin surface) measuring approximately 2–5 mm in length. Spinal neuronssend their axons to sympathetic ganglia where synapses onto postganglionic non-myelinated C fibers are found en route to sweat gland innervations [1]. Direct recordings of postganglionic skin sympathetic nerve activity, possible in humans, enabled finding that a large fraction of the sympathetic activity during heat stress is essentially sudomotor in nature through acetylcholine release that binds to muscarinic receptors [12,13]. This said, sweating can also occur via exogenous administration of α- or β-adrenergic agonists. Immunochemistry studies have also identified a number of possible peptides involved in neuro modulation of sudomotor activity although their specific role(s) remain(s) unclear (e.g., vasoactive intestinal polypeptide, calcitonin gene-related peptide) [14].

Concluding remarks: Endogenous mechanisms and external devices designed to avoid excess water evaporation losses may help optimizing the effects of sudoriferous gland secretion on water skin content. Sebum is one way to protect against friction and impervious loss of moisture. Specialized socks (coton) may also help fulfilling similar functions. All in all, increasing evidence suggests that key roles are played by acetylcholine, muscarinic receptors, some neuropeptides and cutaneous nerves in sudoriferous gland secretion and hence, indirectly, in skin water content through enhanced evaporation given that the latter is controlled. As such, these relatively new control mechanisms may become new targets for the development of innovative CNS and/or PNS products against various types of dry skin problems. In the meantime, science-based, innovative skin care products could be used for temporary stimulation of lipid-rich epidermal layers and stimulation of endogenous water transport mechanisms [15,16].

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