Acupuncture Stimulation Analyzed from Multiple Aspects of Western Medical Science

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(Received: November 10, 2015; Accepted: February 16,2016).

ABSTRACT:

Skin is the biggest and most important organ of us. It has a large surface area and it is easily accessible. While we touch skin, piezoelectric stimulation starts, fundamental property of biological tissues, pressure electrification. And after this stimulation, ferroelectric and pyroelectric effect occur. While we insert the acupuncture needle into skin, we have created a conscious trauma and damage. After this, inflammatory phase, proliferation and tissue formation phase and tissue remodeling phase start. With embriological perspective, at that moment, we give stimulus ectodermal and mesodermal layer of the skin also. We stimulate these embriologic layers and cells not only into skin but also whole body. Because, while we start stimulation with a cell, cell stimulates other cells and cells stimulate body. Also we stimulate neuropeptides, neuro transmitters, neurohormones and receptores. The skin is the largest immunologically active receptore organ in the body. And we see, periferic local stres response (brain-skin) works same as hypatalamo-pituter-adrenal axis. So, what we have done? We only insert the acupuncture needle into skinconsciously.

Keywords: Traditional Chinese Medicine; Skin; Piezoelectric; Pyroelectric; Ferroelectric; Mesodermal Layer; Epigenetic Mechanisms; Energy.

Introduction

Each Yin organ (liver, heart, spleen, lung and kidney) is also linked to a group of tissues and connected to the exterior via a sense organ (mouth, nose, ear, eye). Pathology in organic function can be observed in the sense organ or manifested in the tissues [1]. Furthermore, this sense organ could be used for treatment if you give suitable stimulus. For instance, music therapy. With plasticity of the brain, engages in producing music indulging an array of cognitive functions and the product, the music, in turn permits restoration and alters brain functions [2]. From the physiological perspective, music is provoking the mechano-sensory hair cells in the ear to transduce the sound-induced mechanical vibrations into neural impulses, which are interpreted by the brain, evoking emotional effects. Current research about music has establisheda role, for these effects in the regulation of the hypothalamic–pituitary axis, the sympathetic nervous system and the immune system, all of which have key functions in the regulation of cancer risk and progression [3]. As you have seen, music of the body starts, just like Yin and Yang. What about smell. Impairment of the olfactory system influences interoception (interoceptor is a specialized sensory nerve receptor that receives and responds to stimuli originating from within the body) [4]. Some fragrances and strong odors have been characterized as putative triggers that may exacerbate disease symptoms [5]. Adult neurogenesis, is a lifelong process that, occurs in two main neurogenic niches of the brain,namely in the subventricular zone (SVZ) of the lateral ventricles and in the subgranularzone of the dentate gyrus in the hippocampus [6]. New neurons are added in discrete regions of the adult brain, the olfactory bulb and the dentate gyrus of the hippocampus. The olfactory bulb must be one of the most plastic regions of the nervous system, even more so than the dentate gyrus [7]. If you want, you could reach to the brain from the eyes and could start to treat with hypnosis. For instance, hypno analgesia has proved to be very effective in the treatment of pain, which includes chronic oncological pain, HIV neuropathic pain, pain during extraction of molars, pain associated to physical trauma, pain in surgical procedures, pain associated to temporomandibular joint disorder, phantom limb, fibromyalgia, pain in amyotrophic lateralsclerosis, acute pain in children, lumbago, and pain in child birth, amongst others [8]. And now, we werelearned from the the study conclusions, that adult taste and smell disorders seen after heart, neurological, respiratory and liver problems [9].

Yin and Yang energy circulation. And what we said before writing this article, each Yin organ is also linked to a group of tissues and connected to the exterior via a sense organ [1]. What happened, nearly almost you didn’t touch

the body, but did affect. How? You give stimulus. If you give suitable stimulus to your body anyway, your body perform its miracle. So, Yin and Yang. Nature is inert, and can not dance till Shiva wills it.(Shiva, is a marvelously unified and dynamic composition expressing the rhythm and harmony of life. He symbolizes the cosmic cycles of creation and destruction, as well as the daily rhythm of birth and death. The dance is a pictorial allegory of the five principle manifestations of eternal energy — creation, destruction, preservation, salvation, and illusion.) He rises from his rapture, and dancing sends through inert matter pulsing waves of awakening sound, and no matter also dances, appearing as a glory round about him. The dance of Shiva is the dancing universe; the ceaseless flow of energy going through an infinite variety of patterns that melt into one another. For the modern physicists, then, Shiva's dance is the dance of subatomic matter [10]. Human skin is a well engineered organ that protects organism against enviromental factors and regulates heat and water loss from the body. It has a large surface area and it is easily accessible. Therefore, it offers an ideal application site to deliver for both local and systemic actions [11]. Acupressor [12] and manuel therapies [13] were both decrease the pain, treat the ilness. Treatment-dependent changes in functional connectivity with brain are also observe [13].

So, what are we doing with acupuncture? We give stimulus consciously. And the rythm of the body starts. At this time, we touch whole body and internal organs with known specific acupuncture points. And also exactly, we damaged the skin. How? First of all, we touch skin and sunk the needle into skin. The skin is composed of tree layers: the epidermis, the dermis and the subdermis. The epidermis is continually renewing, stratified, squamous epithelium that keratinizes and gives rise to adnexal structures. Keratinocytes which constitute the majority of cells in the epidermis are organised into four layers, namely stratum basale, stratum spinosum, stratum granulosum and stratum korneum. The other cells that reside within the epidermis include melanocytes, Langerhans cells, Merkel cells [14] and gamma delta ($\gamma\partial$) T-cells [15]. The dermis is composed of two distinct compartment. It consists mostly of fibrous connective tissue and ground substance. Fibroblasts,dendritic and non dendritic monocytes (macrophages, XIIIa expresseddermal dentrosites), mast cellsare regular residents of the dermis. Dermis has also nerves, blood and lymph vessels, muscle and epithelial structure of adnexa. The skin is the largest immunologically active receptore organ in the body [14].

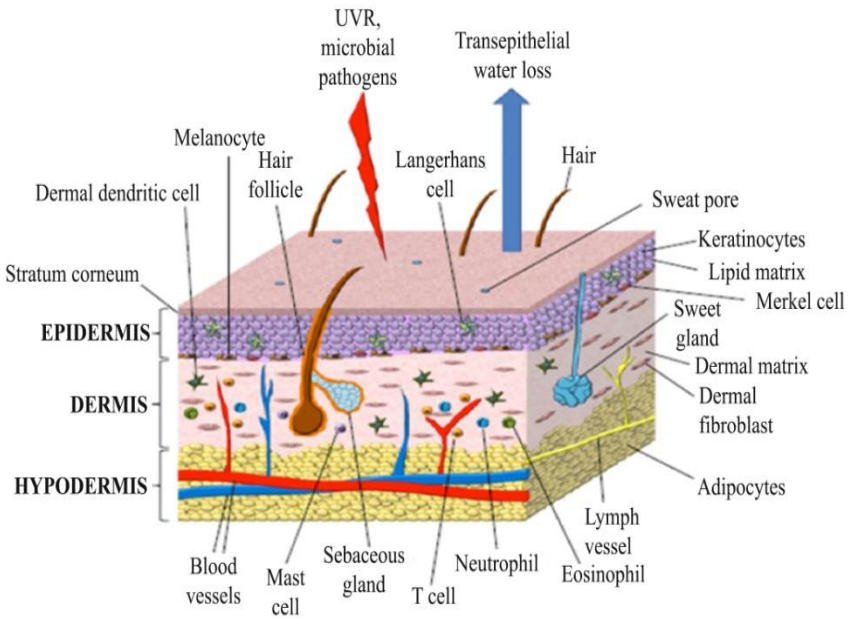

Fig 1: The structure of the skin

When sunk the needle into skin

We have created a conscious trauma and damage. What will do the body? Firstly, what will do the skin? There are three recognized phases that characterize the cutaneous repair process: the inflammatory, proliferative, and remodeling phase.

Inflammatory phase

After an acute injury, inflammation begins injury area. Disruption of blood vessels leads to local release of blood cells and blood-borne elements resulting in clot formation. Migration to the site of injury of a number of key cells, such as keratinocytes, fibroblasts, endothelial cells (E and P selectins) andmonocytes, is aided by their receptors for various components of the thrombus.Platelets comes to injured area, and startintrinsic and extrinsic coagulation pathways.Platelets, also release a number of chemotactic factors(thrombin and fibrillar collagen, adenosine diphosphate,fibrinogen, fibronectin, thrombospondin, and von Willibrand factor VIII, platelet-derived growth factor (PDGF), transforming growth factor ß1 ($TGF_{ß1}$), platelet factor 4, connective tissueactivating peptide ($CTAP_{III}$), beta-thromboglobulin, and neutrophil-activating peptide 2), that attract other platelets, leukocytes, and fibroblasts to the siteof injury.This phase continues as leukocytes, specifically

neutrophils, CD_{11}/CD_{18} complex, PDGF-like molecule, connective tissue growth factor and macrophages, enter the scene [16].

Proliferation and tissue formation phase

Mainly aim was reconstructionof the damaged epidermis and basement membrane, and angiogenesis. Fibroblasts, keratinocytes, monocytes, and macrophages are the key cells. This physiologic processes includes; Fibrin-fibronectin environment, PDGF, integrin subunits $a_{3,}$ $a_{5,}$ gelsolin, $TGF_{ß1}$, matrix integrins $a_5ß_1$, $a_vß_3$,$a_vß_6$, $a_6ß_6$, $a_2ß_1$, integrin, hyaluronan and hyaluran-mediated motility receptor, CD_{44}, tenascin, Arg-Gly-Asp-Ser tetrapeptide, type I, III, IV, VI collagen, elastin, glycosaminoglycans, proteoglycans, basic fibroblast growth factor-2, vascular endothelial growth factor, keratinocyte growth factor, transforming growth factor α(TGFα), flt-1(vascularendothelial growth factor receptor), neuropilin 1, heparin, prostacyclin, antithrombin III,protein C,plasminogen activator, secreted protein acidic and rich in cysteine (SPARC), thrombospondin, collagenase, stromalysin, gelatinase, vitronectin, keratins 6, 16, and 17, p38-MAPK/SAPKpathway(Mitogen-activated protein kinase/Stress-activated protein kinase), tissue-type plaminogen activator, urokinase-type plaminogen activator, matrix metalloproteinases(MMPs) enzyme family, collagenase-1 (MMP_1), stromelysin-2 (MMP_{10}), gelatinase (MMP_9), epilysin (MMP_{28})[16],β-catenin[17].

Tissue remodeling phase

Fibronectin and associated components, hyaluronic acidand proteoglycans, collagen, and myofibroblasts takes part of the remodelling process. PDGF, integrin subunits $a_{3,}$ $a_{2,}$ a_5, TGF-ß, fibronectin, extracelluler matrix macromolecules, tenascin, thrombospondin, dermatan sulfate, SPARC, collagen types I, II, III, IV, V, VI, VII, VIII, vitronectin, glycosaminoglycan, hyaluronic acid, CD_{44}, heparan sulfate, chondroitin-4-sulfate, dermatan sulfate, matrix-degrading metalloproteinases (MMP), fibroblast collagenase, MMP_1, gelatinase B (MMP_9), stromelysin 1 (MMP_3), 2 (MMP_{10}), matrilysin (MMP_7), epilysin (MMP_{28}), a_2-macroglobulin act their roles in tissue remodelling process [16].

Well, skin regenerates itself, but this is not the whole problems. While you damage skin epidermis, as well as repairment, innate immunity system starts another way. Innate immune cells include multiple immune response; such as releasing antimicrobial agents; inflammatory mediators induction, including cytokines, chemokines, neuropeptides, and eicosanoids; and type of adaptive immune response influencing[16].Skin innate barier contein epidermis and subcutan lipidsare composed of ceramides, free fatty acids andcholesterol [18]. This barier is natural and continuous.

Complement components

One of the first innate defense mechanism is the alternativepathway of complement[16].EGFR (epidermal growth factor receptor) in regulating the expression of complement components and complement activation in human epidermis and keratinocytes [19].Seven members of EGFR-ligands have been identified so far and thirteen members of human metalloproteases are involved in ectodomain shedding ofthe EGFR-ligand members. And transactivation of EGFR by G-protein coupled receptors (GPCRs), cytokine receptors, receptor tyrosine kinases, and integrins[20].

Antimicrobial peptides

Cutaneous innate immunity the production of antimicrobialpeptides (AMPs) is a primary system for protection against exterior factors. Many AMPs can be found on the skin, and these include molecules that were discovered for their antimicrobial properties, and other peptides and proteins first known for activity as chemokines, enzymes, enzyme inhibitors and neuropeptides. Cathelicidins (LL-37), ß-defensins (BD_1, BD_2, BD_3), adrenomedullin, members of the calcitonin-related peptide superfamily, α-MSH (Melanocyte stimulating hormone), and secretory leukocyte proteaseinhibitor (SLPI), are among previously identified peptides with antimicrobial activities discovered later in the skin. Complement components C_3 and factor B, eicosanoids, cyclooxygenase product PGE_2, leukotrienes B_4, the proinflammatory12-lipoxygenase product 12(s)-hydroxyeicosatetraenoic acid (12(S)HETE), and 15-HETE, and anti-inflammatory and immunosuppressive metabolite of the 15-lipoxygenase pathway take important roles in skin innate immun system [16].

Also, vitamin D_3 is an important regulator of cutaneous immunity. In particular, vitamin D_3 exerts pluripotent effects on adaptive immune functions such as T cell activation and maturation of dendritic cells. In addition, vitamin D_3 has been suggested to increase innate immunity in skin and to enable efficient antimicrobial defense at epithelial surfaces[21].Whole of things only skin nature compound. If we look after skin’s cell, we will understand so clearly our mentioned affect.

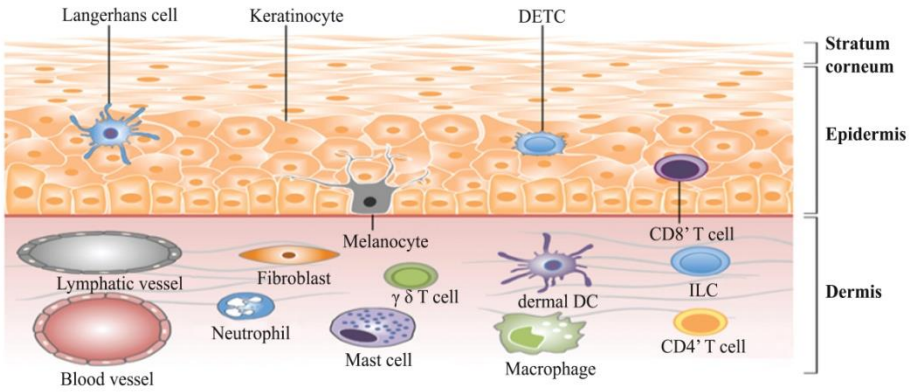

Fig. 2:Skin innate barrier cells

Keratinocytes

Keratinocytes are capable of producing/secreting a large number of cytokines that may affect neighboring cells (Paracrine pattern), modulate their own functional status (Autocrine pattern), and, in situations of massive release,reach the circulation and affect the function of cells at distant sites (Endocrine pattern). Some of these factors [e.g., IL_1,IL_1 receptor antagonist, IL_6, IL_7, IL_8 and other chemokines, IL_{10}, IL_{12}, IL_{15}, IL_{18}, IFN-inducing factor), TNFα, GM-CSF(Granulocyte-macrophage colony-stimulating factor), M-CSF (macrophage colony-stimulating factor), are important mediators of the inflammatory and/or immune response, whereas others (e.g., TGFα and -ß, PDGF, basic fibroblast growth factor, keratinocyte growth factor, nerve growth factor, vascular endothelial cell growth factor) regulate the growth of different epithelial and/or mesenchymal cells. Keratinocytes can synthesize complement and related receptors, including the C_{3b} receptor (CR_1, CD_{35}), the Epstein-Barr virus receptor CR_2 (C_{3d} receptor, CD_{21}), the C_{5a} receptor (CD_{88}), the membrane cofactor protein (CD_{46}), the decay-accelerating factor (CD_{55}), and complement protectin (CD_{59}). CD_{59} may protect keratinocytes from attack by complement. Its engagement by CD_2 stimulates the secretion of proinflammatory cytokines from keratinocytes.

Membrane cofactor (CD_{46}) is reported to be a receptor for M protein of group A streptococci. Its ligation induces proinflammatory cytokines in keratinocytes such as ILα, IL_6, and GM-CSF. Cross-linking of CD_{23} (FceRII), induced by IFN (Interferon) or IL_4 on cultured keratinocytes, results in the secretion of TNFα, IL_6, IL_{10}, and nitric oxygen via inducible NOS (Nitric oxide synthase). CD_{40} is very weakly expressed by keratinocytes under steady-stateconditions. It is upregulated by IFN. Engagement of CD_{40} induces enhanced keratinocyte, intercellular adhesion molecule ($ICAM_1$) and B-cell lymphoma-extra large(Bcl-x) expression, the release of IL_8, and the arrest of

the cell cycle followed by keratinocytedifferentiation.In addition to their role in maintaining and securing the structural properties of the epidermis, keratinocyte-bound adhesion molecules may also subserve immune functions. A particular role was suspected for theLFA_1 (Integrin) ligand, $ICAM_1$ because it is expressed in keratinocytes in a large variety of inflammatory skin conditions.When this adhesion molecule was overexpressed under the control of a K_{14} promoter, however, no phenotype wasfound, even under inflammatory conditions. Gluing together keratinocytes is also not the sole function of E-cadherin.Homotypic interactions with LCs anchor these cells in the epidermis, and heterotypic binding to a integrin $\alpha E_{\beta 7}$helps to immobilize murine dendritic epidermal T cells (DETCs) as well as CD_8+ T lymphocytes in this tissue.Cytokine action on keratinocytes not only leads to a modulation of the inflammatory and/or immune response but canalso result in a change of their proliferation and differentiation program [16].

Antigen-presenting cells: Langerhans cells and dermal dentritic cells

A robust innate reaction is also the major trigger of an adaptive response initiated by dendritic antigen-presenting cells in the epidermis [Langerhans cells (LCs)]and dermis [dermal dendritic cells (DDCs)]. When appropriately stimulated and loaded with antigenic peptides, these cells can leave the skin and migrate to regional lymphoid tissues where they induce lymphocyte activation and expansion at a clonal level.In human epidermis,markers fulfilling these criteria include, CD1a antigens, that is, major histocompatibility antigen (MHC) class I-related restriction elements also found on cortical thymocytes; MHC class II-encoded human leukocyteantigen (HLA)-DR/DQ/DP antigens; Birbeck granule-associated antigen defined by the monoclonal antibodies (MAb) Lag and Langersin ($DCGM_4$); and CD_{39}, recently identified as light chaine ATPase [16].

Merkell cells

Merkel cells(MCs) havegarnered attention for their distinct morphology and putative sensory function. The identification of MCs insubepidermal embryonic mesenchyme initially led to the hypothesis that they arise frommigrating neural crest progenitors.MCsincluding dense core granules and the expression of chromogranin A, B, synaptophysin, neuroactive polypeptides/hormones such as vasoactive intestinal peptide, calcitonin gene-related peptide, neuroendocrine protein B2, prepro-orexin, orexin receptors, serotonin and somatostatin. Endocrine functions, peripheral nerve development roles, cutaneous immune system functionstheir mission have. In addition, all MCs express Sox_2, a transcription factor expressed in adult stem cellsthat plays a crucial role in tissue regeneration in various organs [22].

But in embryological period Sox_2, also show specific expression profiles in the foregut endoderm [23]. Sox_2 was expressed specifically the esophagus and stomach [24]. As we tought; Epithelialmesenchymal interaction is initiated by Sox_2 expression in the gut tube. May be this kind of interactions, embryologic and cell basement pattern perspectives could lead us to understand acupuncture effects on to internal organs.

Skin Neuropeptides

The skin is a rich source of neuropeptides including neurotransmittersand neurohormones. Epidermis release Vitamin D, PTHrP (Parathormone releasing peptide), androgen, T_3, L-DOPA, catecholamines,acetylcholine, serotonin, glutamate, aspartate, prolactin, corticotropin-releasing hormone (CRH), proopiomelanocortin (POMC), urocortin, α,β, γmelanocyte-stimulating hormones (MSH), adrenocorticotropic hormone (ACTH), β-endorphin, enkephalin, TRH. And the dermis and its appendices release, Vitamin D, PTHrP, estrogen, androgen, L-DOPA, serotonin, glutamate, aspartate, CRH, urocortin, α, β, γMSH, ACTH, β-endorphin, enkephalin, growth hormone (GH), histamine, catecholamines,acetylcholine[25].

You see nearly every cell in these three phase. What did we do, wesunk the acupuncture needle there. We give stimulus and damage. And also, wesee skin neuropeptides. Now, if a person ask, how acupuncture works? We can explain easily with every perspective. For instance, if you take care, you see the POMC. This neuropeptides takes part of pain pathways, and we always trying to explaine pain-brain interaction. Now we can do this, periferic local stres response (Brain-skin) works same as hypatalamo-pituter-adrenal axis. Also, in obesity, ürocortine is the most powerfull anorexigenic agent, and we can stimulate it, while we insert the needle into skin. Our most important organ is skin, and may be we do not distinguish enough I suppose. And acupuncture is a also neurotransmitter sign.

Embryology

In embryological perspective, shortly after gastrulation, ectoderm further subdivides into neuroectoderm and presumptive epidermis. Dermis and hypodermis derived from mesodermal layer. The embryonic tissue that forms the dermis depends on the specific body site. Dermal mesenchyme of the face and anterior scalp is derived from neural crest ectoderm. The limb and ventral body wall mesenchyme is derived fromthe lateral plate mesoderm. The dorsal body wall mesenchyme derives from the dermomyotomes of the embryonic somite [16].What is this, this shows us our acupuncture points is not show the same effects, because our body parts carry spesific action. Anterior body part is not same posterior body part. Because, fibroblasts encode positional identities retained from embryonic development. While we insert the needle

into skin, with embriological perspective, needle stimulate ectoderm and mesoderm.

And our body, whole organs content endodermal, mesodermal and ectodermal parts. Interaction between mesenchyme and epithelium are classical examples of inductive interactions. These are instrumental for the development of lung, kidney, liver, tooth, and most glandular organs such as the mammary, salivary and pancreatic glands [26]. Also, when administered stimulus, epidermis that ectodermal origin' was activated. Especially, signals goes to every cells. For instance keratinocytes that originates from ectoderm, melanocytes that originates from neural crista, langerhans cells that originates from mesoderm [16].

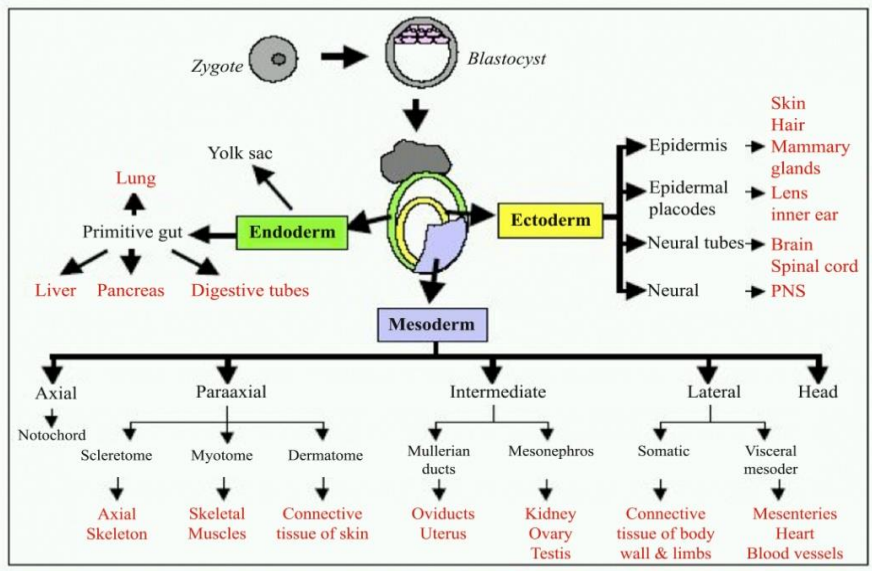

Fig. 3: Embryonic developmental stage and differentiation

What did we do? We insert the needle into skin. And we stimulate ectodermal and mesodermal layer. And we damaged skin, cells come this area for regenaration, and also we give stimulus whole ectodermal and mesodermal embrionic mentioned organs. Is it enough, no. Also, some group of polypeptide growth factors includes FGFwhich stimulate cell proliferation is mainly restricted to cells from mesodermal and neuroectodermal origin, including endothelial cells [27]. Now, still we are trying to explaine acupuncture effect mechanism with the light of the science. And we give only stimulus into body.

Epigenetics is defined as heritable information other than the DNA sequence itself. The concept implies that the regulation of gene expression is a highly complex process in which epigenetics plays a major role that ranges from fine-tuning to permanent gene activation/deactivation [28]. Epigenetic

mechanisms change gene activity or expression by altering chromatin organization, without modifying the genetic code of the DNA [29]. As the fundamental links between metabolic adaptation, epigenetic alteration and cell dedifferentiation during epithelial to mesenchymal transitions(EMT). Especially specific chromatin modifiers or a unique histone mark, or sets of marks associated with EMT [30].

Further more, nature of EMT is closely associated with reversible epigenetic regulatory mechanisms, which refers to a series of stable but reversible modifications, not directly affecting the DNA primary sequence, but rather relies on dynamic transcriptional programming effects. Such heritable regulations in the pattern of gene expression are mediated by the DNA methylation of CpG dinucleotides and several post-transcriptional covalent modifications of the NH_2 terminal ofhistone proteins, including acetylation, methylation, biotinylation, and phosphorylation. Since most enzymes responsible for adding or removing epigenetic modifications require substrates or cofactors that are intermediate metabolites of cells and capable of diffusing through nuclear pores, such as acetyl-CoA, nicotinamide adenine dinucleotide(NAD^+), S-Adenosyl-L-methionine(SAM), α keto glutarate (α-KG), and flavine adenine di nucleotid (FAD), it is not difficult to imagine that the fluctuation of the levels of metabolites could modulate the activities of chromatin modifying enzymes, influence chromatin dynamics, and therefore deliver metabolic information to nuclear transcription. Recent evidence has confirmed that the availability of the necessary metabolites affects epigenetic modifications, providing a direct link between nutritional changes, metabolic output, and gene expression [30].

Non-B DNA conformations interact with a wide variety of DNA processing proteins in cells. The complex interplay between DNA structure and repair can affect each other in both positive and negative ways, demonstrating the “Yin and Yang” of DNA repair mechanisms in DNA structure-induced genetic instability [31].Noncoding RNAs, as key post-transcriptional regulators with the ability to modify the expression of a multitude of mRNA targets and the corresponding proteins [32].

What is happening with acupuncture? For instance, while sunk the needle into Zusanli (ST-36) acupoints, cerebral regional homogeneity (ReHo) significantly increased, in left brainstem, the right cerebellum posterior lobe, right parahippocampal gyrus, right fusiform gyrus, left angular gyrus, temporal lobe and the left frontal lobe; and a significantly decreased ReHo in the occipital lobes and the right superior temporal gyrus was found [33]. After application, measured the activity of natural killer cells in the spleen, gene expression in the hypothalamus, and the activities of antioxidative enzymes in the hypothalamus, liver and red blood cells. The EA treatment increased natural killer cell activity in the spleen by approximately 44%. It also induced genes related to pain, including 5-Hydroxytryptamine (Serotonin) receptor 3a (Htr3a) and endothelin receptor type B in the hypothalamus, and increased the activity of superoxide dismutase in the hypothalamus, liver, and red blood

cells [34]. Five canonical pathways including alpha-linolenic acid metabolism, d-glutamine and d-glutamate metabolism, citrate cycle, alanine, aspartate, and glutamate metabolism, and vitamin B_6 metabolism pathways were acutely perturbed, and fifty-three differential metabolites were identified[35], increased normal cell telomere[36],H_3K_9 acetylation seen[37]. Nitrous oxide signal transduction and the cholesterol-lowering effect seen with ST40[38].

Why, acupuncture effects so common? And, how it is possible, for instance you sunk the needle into skin in the food, and brain is getting stimulate? From the physicist point of view, piezoelectricity as a fundamental property of biological tissues, pressure electrification [39]. It is normal for all cells. For instance, hydroxyapatite nanocrystals in natural form are a major component of bone, a well known piezoelectric material. Even if hydroxyapatite crystals also exhibits pyroelectricity and ferroelectricity effects [40]. Why is so important for us. Because, if you touch somewhere in your body, piezoelectric effect starts and you could stimulate another part of your body easily. And ourbody, our skin, acts as an antenna. Again, mesodermal tissue take part of its role, because collagen carry on piezoelectric, pyroelectric and ferroelectric specifity. Second, cell to cell stimuletes occur. And body rythm starts, and body do what it needs? As, how an undifferentiated stem cell, while divided sometimes is being two new stem cells, sometimes also a stem cell and a differentiated cell is capable of providing? Or why same originate cells and organs act different? Likewise basic epigenomic studies aims. At the atomic level, matter has a dual aspect: it appears asparticles and as waves. Which aspect it shows depends on the situation. In some situations the particle aspect is dominant,in others the particles behave more like waves; and this dualnature is also exhibited by light and all other electromagneticradiation [10].

Additionally, one thousand and seventy-five literatures, shows that the acupoint catgut-embedding therapy has an extensive application in all departments illness. Especially, epigastric pain, obesity, epilepsy, asthma, abdominal pain, facial paralysis and constipation of the internal medicine, low back pain and leg pain of the surgical department, psoriasis of the dermatological department and blepharoplasty of the department of ophthalmology and otorhinolaryngology are considered as the dominant diseases for acupoint catgut-embedding therapy [41]. With this mind, in chronic illness course embedded amount of stem cells could be more effective, instead of sunk the needle into specific acupuncture points. Because, force and matter, particles and waves, motion and rest, existence and non-existence-these are some of the opposite or contradictory concepts which are transcended in modern physics. Of all these opposite pairs, the last seems to be the most fundamental, and yet, in atomic physics we have to go even beyond the concepts of existence and non-existence. This is the feature of quantum theory which is most difficult to accept and which lies at the heart of the continuing discussion about its interpretation. At the same time, the transcending of the concepts of existence and non-existence is also one of the most puzzling aspects of Eastern mysticism [10]. Nature and body, has a

dynamic balance, not stable. Simply, could only be understood in theirs' entirety. Yin and Yang. And only stimulus.

Funding

No external funding sources were used for this study.

Competing Interests

No compeing interest was declared by the author.

References

1.Cheung, L.;Li, P.; Wong, C.,"The Mechanism of Acupuncture Therapy and Clinical Case Studies.''1st ed. Taylor and Francis, London:Taylor and Francis Press; 2001.

2.Hedge, S.,"Music-based cognitive remediation therapy for patients with traumatic brain injury.''Frontiers in Neurology, vol. 5, no. 34, pp. 1-7, 2014.

3.Pichler, A., and Pichler, M.,"Music therapy in cancer patients: Factor fiction.''Future Oncology, vol.10, no. 15, pp. 2409-2411, 2014.

4.Krajnik, J.,Kollndorfer, K., Notter, L. A., Mueller, A., and Schöpf, V.,"The impact of olfactory dysfunction on interoceptive awareness.'' Psychophysiology,vol. 52, no.2, pp. 263-268, 2015.

5.Jaen, C.,and Dalton, P.,"Asthma and odors: The role of risk perseption in asthma exacerbation.''Journal of Psychosomatic Research, vol.77, no. 4, pp. 302-308, 2014.

6.Butti, E.,Cusimano, M., Bacigaluppi, M., and Martino, G.,"Neurogenic and non-neurogenic functions of endogenous neural stem cells.''Frontiers in Neuroscience,vol. 8, no. 92, pp. 1-11, 2014.

7.Mennini, A.,"The Neurobiology of Olfaction.'' In: Pignatelli, A.; Belluzi, O., eds. Neurogenesis in Adult Olfactory Bulb. Boca Raton (FL): CRC Press; 2010:119-141.

8.Lanfranco, R. C.,Canales-Johnson, A., and Huepe, D.,"Hypno analgesia and the study of pain experience: from Cajalto modern neuroscience.'' Frontiers in Psychology,vol. 5, no. 1126, pp. 1-7, 2014.

9.Shiue, I., "Adult taste and smell disorders after heart, neurological, respiratory and liver problems: US NHANES, 2011–2012.''International Journal of Cardiology,vol. 179, no.0, pp. 46-48, 2015.

10.Capra, F., "The Tao of Physics, 25th ed.Boulder, Colorado: Shambhala Publications;2000.

11.Güngör, S.,Erdal, S. M., and Özdin, D.,"Biophysical methods used to assess the structure and the permeability of skin.''Turkish Clinics Journal of Dermatology,vol. 22, no. 1, pp.25-29, 2011.

12.Dabiri, F., and Shahi, A.,"The effect of LI 4 acupressure on labor pain intensity and duration of labor: A randomized controlled trial.''Oman Medical Journal, vol. 29, no. 6, pp. 424-429, 2014.

13.Gay, W. C.,Robinson, M. E., George, S. Z., Perlstein, W. M., and Bishop, M. D.,"İmmediate changes after manuel therapy in resting-state functional connectivity as measured by functional magnetic resonance imaging in participants with induced low back pain.''Journal of Manipulative and Physiological Therapeutics,vol. 37, no. 9, pp. 614-627, 2014.

14.Öztürk, G.,"Structure and functions of the skin.''Turkish Clinics Journal of Cosmetology,vol. 2, no. 1, pp. 1-8, 1999.

15.Schepeler, T.,Page, M. E., and Jensen, K. B.,"Heterogeneity and plasticity of epidermal stem cells.''Development, vol. 141, no. 0, pp. 2259-2267, 2014.

16.Freedberg, I. M.;Eisen, A. Z.; Wolf, K.; Austen, K. F.; Goldsith, L. A.; Katz, S. I.,"Fitzpatrick's Dermatology in GeneralMedicine.''6nd ed. McGraw-Hill Companies, USA; McGraw-Hill CompaniesPress. 2003.

17.Amini-Nik, S.,Cambridge, E., Yu, W., Guo, A., Whetstone, H., Nadesan, P., Poor, R., Hinz, B., and Alman, B.A.,"Beta catenin regulated myeloid cell adhesion and migration determine wound healing.''The Journal of Clinical Investigation, vol. 124, no. 6, pp. 2599- 2610, 2014.

18.Joo, K.M., Hwang, J.H., Bae, S., Nahm, D.H., Park, H.S., Ye, Y.M., and Lim, K.M.,"Relationship of ceramide, and free fatty acid cholesterol ratios in the stratum corneum with skin barrier function of normal, atopic dermatitis lesional and non lesional skins.''Journal of Dermatological Science, vol.77, no.1, pp.71-81, 2015.

19.Abu-Humaidan, A. H.,Ananthoju, N., Mohanty, T., Sonesson, A., Alberius, P., Schmidtchen, A., Garred, P., and Sorenson, O.E.,"The epidermal growth factor receptor is a regulator of epidermal complement component expression and complement activation.''Journal of Immunollogy,vol. 192, no. 7, pp.3355-3364, 2014.

20.Nanba, D.,Toki, F., Barrandon, Y., and Higashiyama, S.,"Recent advances in the epidermal growth factor receptor/ligand system biology on skin homeostasis and keratinocyte stem cell regulation.''Journal of Dermatological Science,vol. 72, no. 2, pp. 81-86, 2013.

21.Schauber, J.,and Gallo, R. L.,“The vitamin D pathway: A new target for control of the skin’s immune response?’’ Experimental Dermatology,vol. 17, no. 8, pp. 633-639, 2008.

22.Xiao, Y.,Williams, J. S., and Brownell, I. “Merkel cells and touch domes: More than mechano sensory functions?’’Experimental Dermatology,vol. 23, no. 10, pp. 692-695, 2014.

23.Faure, S.,and de Santa Barbara, P.,“Molecular embryology of the foregut.’’Journal of Pediatric Gastroenterology and Nutrition,vol. 52, no. 1, pp. 2-3, 2011.

24.Sadler, T. W.,“Langman’s Medical Embriology.’’12 th ed. Philadelphia, PA, USA:Lippincott Williams & Wilkins;2012.

25.Türsen, U.,“Stress, hormones and skin.’’Dermatoz,vol. 2, no. 2, pp. 308-319, 2011.

26.Ekblom, P.,and Aufderheide, E.,“Stimulation of tenascin expression in mesenchyme by epithelial-mesenchymal interactions.’’The Internal Journal of Developmental Biology, vol. 33, no. 1, pp. 71-79, 1989.

27.Evain-Brion, D.,“Growth factors and embryonic development.’’Reproductive Nutrition Development,vol. 28, no. 6B, pp. 1681-1686, 1988.

28.Moresi, V., Marroncelli, N., Coletti, D., and Adamo, S.,“Regulation of skeletal muscle development and homeostasis by gene 3 imprinting, histone acetylation and micro RNA.’’ Biochimica et Biophysica Acta, vol. 1849, no. 3, pp. 309-316, 2015.

29.Boyce, T. W.,and Kobor, M. S.,“Development and the epigenome: The ‘synapse’ of gene–environment interplay.’’Developmental Science,vol. 18, no. 1, pp. 1-23, 2015.

30.Li, L. and Li W.,“Epithelial mesenchymal transition in human cancer: comprehensive reprogramming of metabolism, epigenetics, and differentiation.’’Pharmacology and Therapeutics,vol. 150, no. 0, pp. 33-46, 2015.

31.Vasquez, K. M.,and Wang, G.,“The Yin and Yang of repair mechanisms in DNA structure-induced genetic instability.’’Mutation Research,vol. 743– 744, no. 0, pp. 118– 131, 2013.

32.Kumar- Bali, K.,and Kuner, R.,“Non coding RNA_s: Key molecules in understanding and treating pain.’’Trends in MolecularMedicine,vol. 20, no. 8, pp. 437-448, 2014.

33.Li, L. M.,Lu, F. J., and Gou, Z. J.,“Effect of acupuncturestimulation of Zusanli (ST 36) on cerebral regional homogeneity in volunteer subjects with different constitutions: a resting-state fMRI study.’’ ZhenCi Yan Jiu,vol. 38, no. 4, pp. 306-313, 2013.

34.Wong-Rho, S.,Gi-Soon, C., Eun-Jung, K., Sun-Kwang, K., Youn-Seop, L., and Hye-Jung, L.,“Molecular changes in remote tissues induced by electro-acupuncture stimulation at acupoint ST36.’’Moleculer Cells,vol. 25, no, 2, pp. 178-183, 2007.

35.Yan, G., Zhang, A., Sun, H., Cheng, W., Xiangcai, M., Liu, l., Zhang, Y., Xie N., and Wang, X.,“Dissection of biological property of Chinese acupuncture point Zusanli based on long-term treatment via modulating multiple metabolic pathways.’’Evidence Based Complementary and Alternative Medicine,vol. 2013, no. 2013, pp. 1-10, 2013.

36.Omura, Y.,Chen, Y., Lu, D. P., Shimotsura, Y., Ohki, M., and Duvvi, H.,“Anatomical relation ship between traditional acupuncture point ST 36 and Omura's ST 36 (True ST 36) with their therapeutic effects: 1)inhibition of cancer cell division by markedly lowering cancer cell telomere while increasing normal cell telomere, 2) improving circulatory disturbances, with reduction of abnormal increase in high triglyceride, L-homocystein, CRP, orcardiac troponin I andT in blood by the stimulation of Omura's ST 36 Part 1.’’Acupuncture Electrotherapy Research Journal,vol. 32, no. 1-2, pp. 31-70, 2007.

37.Shu-Ping, F.,Su-Yun, H., Bin, X., Chen-Jun, H., Shen-Feng, L., Wei-Xing, S., Yan, H.,Hao, H., Qian, L., Ning, W., Xuang-Liang L., Fanrong L., and Bing-Mei, Z.,“Acupuncture promotes angiogenesis after myocardial ischemia through H3K9 acetylation regulation at VEGF gene.’’PLoS One,vol. 9, no. 4, pp. e94604, 2014.

38.Li, L.,Tan, G. H., and Zhang, Y. Z.,“Modulated expression of genes associated with NO signal transduction contributes to the cholesterol-lowering effect of electro-acupuncture.’’Biotechnology Letters, vol.34, no. 7, pp. 1175-1182, 2012.

39.Shamos, M.H., and Lavine L.S.,“Piezoelectricity as a fundamental property of biological tissues.’’Nature, vol. 213 no. 5073, pp. 267-269, 1967.

40.Lang, S.B., Tofail S. A., Kholkin A.L., Wojtas, M., Gregor, M., Gandhi A. A., Wang, Y., Bauer, S., Krause, M., and Plecenik, A.,“Ferroelectric polarization in nanaocrystalline hydroxyapatite thin films on silicon.’’Scientific Reports,vol. 2, no. 2215, pp. 1-6, 2013.

41.Zhang, X. P.,Jia, C. S., Wang, J. L., Shi, J., Zhang, X., Li, X.F., Xu, X.K., Qin, L., Zhang, M.L., Kang, S.G., and Duan, X.D.,"Acupoint cat gut-embedding therapy: superiorities and principles of application.''Zhonqquo Zhen Jiu,vol. 32, no. 10, pp. 947-951, 2012.