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REVIEW

Mechanism of acupuncture regulating visceral sensation and mobility

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Abstract **Chinese ancient medical scientists have long focused on the internal and external contacts between acupoints on the surface of the body and the viscera. The Miraculous Pivot (it is one of the earliest medical classics in China) stated, "Twelve regular channels belong to the *zang-fu* organs internally, and connect to the extremities and joints externally." Traditional Chinese medicine considers acupoints as defined areas where the Qi of viscera and meridians are transfused. These include the reaction points of visceral diseases on the body surface as well as the acupuncture trigger points that promote the flow of Qi and blood, and regulate visceral function. Chinese ancient medical scientists classified the specificity of the main acupoints in the body based on the meridian doctrine, which has been instructing clinical application for about 2000 years. Laws on the domino effect of acupoints have mainly focused on conclusions to clinical experiences. Indications of some acupoints exceed the practical paradigm since the excessive extension occurred during theory derivation. The current research direction on acupuncture focuses on three aspects: the effectiveness of acupuncture and moxibustion; the relevances and associations between meridians and viscera; and the physical and chemical properties and relevant physical basis of acupoints. The relevance between meridians and viscera is the central theory in the meridian doctrine, and acupoints are regarded as an important link in the relationship between meridians and viscera. Specific relationships between acupoints and target organs exist. Stimulating different acupoints on the body surface can help deal with different diseases, especially visceral diseases. In addition, acupoints have a dual function of reflecting and treating visceral diseases. There is no systemic research available on acupoint specificity, despite current knowledge and clinical experiences, which results in a weak foundation for acupuncture theory. This study focuses on the relevance and associations between meridians and viscera. A summary of the mechanisms of acupuncture regulating visceral sensation and mobility and the specific relationships between acupoints and their target organs are presented in this review.**

Keywords acupuncture; somite; visceral pain; somato-visceral connection; meridian

Somite and meridian

The somite of vertebrates makes up a structural function unit. Every somite includes osteocomma, sarcomere, dermatomere, and homologous nerve segment, in addition to the segmental innervations of sympathetic nerve innervating body, blood vessel, sweat gland and arrector pili muscle, and the visceral organs innervated in the same segment of the spinal cord. One nervous segment exists in one somite, connecting every part of its own somite as well as the viscera, and is arranged correspondingly. One segment of the spinal cord could control one viscus through the visceral nerve, or relate with skin, muscle, and so on, via the somatic nerve. Biologic characteristics of acupoint effectiveness are closely related to somites.

Mechanism of acupuncture inhibitory effect on visceral pain through noxious input signal

Acupuncture has a remarkable antinociceptive effect on visceral pain through three levels of the central nervous system pathways: the dorsal root of the spinal cord [1,2], the dorsal column nucleus of the medulla oblongata [3,4], and

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ventral posterolateral thalamic nucleus [5]. Acu-stimulation of different parts of the body has different analgesic effects. Homo-segmental stimulation proved to have the best effect when produced at the spinal level; lower effect is produced at the thalamus level; and the least effect is produced at the medulla oblongata level. In acute spinalized animals, homo-segmental acu-stimulation still produced analgesic effect, indicating that the spinal cord plays an important role in acupuncture analgesia [6–8].

Such effects may be attributed to the convergence and interaction between the inputs of visceral nociception and acupuncture at the level of the spinal dorsal horn.

On the pattern of rectum and colon pain, neuronal activity reaction caused by visceral pain could be inhibited by acupuncture stimulation and moxibustion stimulation [9,10].

In neuroscience, the inhibitory effect of acupuncture on the pain activity of neurons is related to the inputs of Aδ-fiber and C-fiber activated by acupuncture. At the level of the spinal dorsal horn, manual acupuncture stimulation could inhibit wide dynamic evoked neuronal discharge caused by hetero-typic nociceptive stimulus, as disclosed in the methods of electrophysiology and immunohistochemical analysis. The Aδ-fiber and C-fiber inputs are involved; thus, the strong antinociceptive effect of acupuncture is manifested [11,12].

The impact of colorectal distention (CRD) on the spinal dorsal horn neurons at the spinal dorsal horn wide dynamic range (WDR) neurons involved the addition of neuronal discharges at 180.93 times/20 s, which were an increase of 323.09% from 56 times/20 s of background activity. The spinal dorsal horn neurons can be activated by harmful level input from the viscera of the same nervous segment. The influences of acupuncture on acupoints to the inactivated reaction of neurons by CRD could be observed based on the stable inactivated spinal WDR neurons caused by CRD.

Furthermore, the effect of acupuncture on acupoints (Zusanli (ST36) and Sanyinjiao (SP6) of the same side) in the excitable cell receptive field to CRD on spinal dorsal horn WDR neurons can be investigated [2].

At a pressure of 100 mmHg CRD, the inactivation of WDR neurons were added rapidly to 20.31 ± 1.86 spikes/s from 4.75 ± 1.26 spikes/s of background activity. Excess acu-puncture to acupoints in peripheral receptive fields could further increase the reaction with additional 1.41 ± 0.51 spikes/s based on the CRD reaction. The convergence of input from acupoints in the peripheral receptive fields and harmful input from the viscera would completely react at the level of the spinal dorsal horn.

The inhibitory effect that appeared on the inactivated reaction to CRD, that is, the acupuncture in the acupoint of Zusanli (ST36) in the non-receptive field of the contralateral side, decreased to 5.16 ± 0.56 spikes/s from 15.48 ± 1.36 spikes/s, of which $(68.61 \pm 6.86)\%$ was restrained. The inhibitory action to visceral harmful input by acupuncture in acupoints of the non-receptive field lasted for some time since the acupuncture applied. To explain the inhibitory effect of the spinal cord above the center to the visceral noxious reaction induced by acupuncture, the effect of acupuncture on CRD before and after spinalization should be observed. In normal conditions, acupuncture restraint resulted in an activated reaction to CRD (around 60%), while the inhibition mostly disappeared after spinalization.

Acupuncture and visceral noxious input signals converge and interact at the level of the spinal cord. Acupuncture on the acupoints restrains the spinal dorsal horn neuron reaction activated by the visceral noxious input. The spinal cord plays an important role in acupuncture in restraining the visceral noxious input, and keeping the super spinal center intact is necessary [3].

In this study, 45 out of 269 recorded dorsal column nuclei (DCN) neurons responded to the noxious reaction caused by CRD. Out of the 45, 36 DCN neurons were excited, and 31 appeared to exhibit the electroacupuncture effect on excited DCN neurons. The average background action potential was 3.68 ± 6.92 spikes/s for the 31 DCN neurons. Neuron discharge increased rapidly when 80 mmHg CRD was given, and formed a stable activated platform in several seconds, with average activated amplitude of $(199.29 \pm 27.20)\%$. The influence of electroacupuncture (intensity of 1 mA, 2 Hz, 5 min) acupoints (mainly Zusanli (ST36)) of the receptive field to CRD activated the reaction in 20 neurons. The average activated intensity of CRD reaction decreased from 7.03 ± 2.16 spikes/s to 6.17 ± 2.26 spikes/s immediately after electroacupuncture. The inhibitory rate of electroacu-puncture to DCN neuron is 12.12%. These results indicate a weak but effective inhibitory outcome of electroacupuncture to the activated reaction of CRD neurons caused by the viscera at the DCN level.

The relationship between DCN and visceral sensation, especially pain, has long been an issue in the field of neuroscience. DCN simultaneously accepts information from the surface of the body and viscera. They can interact with, and restrain each other; translational modification to visceral sensation exists, and the inhibitory effect of acupuncture to visceral noxious reaction was limited [4].

The 78 visceral input convergence neurons that reacted with CRD were recorded in the ventroposterior lateral (VPL), and all receptive fields were found in the peripheral parts of the body, mainly located at the lower waist and sacrum segment, back limbs, and rump.

Background discharge can be found in most VPL neurons. Spontaneous activity frequency of VPL in recorded 27 neurons was 12.10 ± 1.81 spikes/s. The VPL discharge could be increased rapidly by CRD. Neuron activation stayed at the platform stage during the stable stress period, which is different from the activation of VPL neuron at different surface acupoints. Acupuncture on the acupoints in the front limbs (distant segmental relationship) restrains the activity of VPL neuron to some degree (the inhibitory rate was 14.75%). On the other hand, the simultaneous activation of the background VPL neurons occured in the periphery of the

back limb to some degree (activation degree was 21.80%). Manual acupuncture in three different areas of acupoints of the front limbs, back limbs, and in the periphery of the back limbs restrains the activation of the reaction of VPL neuron to CRD. The inhibitory rate of the front limbs was (26.78 ± 3.20)%, the back limbs was (31.20 ± 4.46)%, while the most obvious inhibitory effect of (33.37 ± 5.42)% appeared in the accretive fields. Statistical difference exists in every group of data [5,7].

Generally, the spinal dorsal horn is the most important part that produces the inhibitory effect on visceral pain by acupuncture, VPL is a less important center, and DCN is the least important.

Research on dual adjustment effect of acupuncture on visceral function, visceral segmental innervations and relationship, and laws among acupoints

Acupuncture stimulation has facilitative or inhibitory effect on gastric motility depending on the different stimulated acupoints of the body. Homo-segmental acupuncture stimulation, with the same innervations of the stomach, produces inhibitory response in gastric motility. The sympathetic efferent nerves and the propriospinal circuit are involved since the effect disappeared with sympathetic neurotomy, but appeared with acute spinalization. Non-segmental acustimulation with different innervations from the stomach induced facilitation response, which depended on intact vagal nerves. Acupuncture regulation of gastrointestinal mobility is effective only under excited fine Aδ/C fibers. In acute spinalized animals, the regulation of non-segmental acustimulation on gastric motility was disrupted, indicating the participation of the super spinal center [13,14].

The method of electrophysiology was adopted in this study [13,14]. The relationship between the acupoints of the stomach meridian and acupoints of non-meridian in the surface of the body, the innervations of gastric segment, and the application of this kind of relationship in acupuncture were discussed. The influence of acupuncture on different acupoints to intragastric pressure (IGP), and the different effects of acupuncture on varied conditions were observed. IGP was measured by a transducer fixed into the pyloric area via abdominal operation. Acupuncture was conducted on acupoints of non-stomach-meridian (part), including Juliao (ST3), Sibai (ST2), Qihu (ST13), Rugen (ST18), Liangmen (ST21), Futu (ST32), Zusanli (ST36), Feishu (BL13), Geshu (BL17), Weishu (BL21), Xiaochangshu (BL27), Qihai (CV6), Quchi (LI11), Sanyinjiao (SP6), Zhongwan (CV12), and the ear-stomach point. Acupuncture lasted for 30s, and then the variation of IGP and gastric motility was observed.

The time of acupuncture on different acupoints of the stomach meridian, for example, acupoints above Ruzhong (ST17) and below Guilai (ST29) improved gastric motility and strengthened IGP. The inhibitory effect of gastric motility was seen when acupuncturing acupoints from Rugen (ST18) to Wailing (ST26). IGP was decreased when stimulating acupoints on the rats' abdomen (Liangmen (ST21), Qihai (CV6), and Zhongwan (CV12)) and the back (Geshu (BL17), Weishu (BL21)). A contraction appeared as the trend weakened during the exciting effect and IGP was elevated when acupuncture was conducted on acupoints of Qihu (ST13) on the upper breast, Sibai (ST2) and Juliao (ST3) on the head and face, on the four limbs, (Zusanli (ST36), Futu (ST32), and Sanyinjiao (SP6)), ear, and Feishu (BL13) on the back. Acupuncture on Rugen (ST18) slightly reduced IGP and mildly increased Xiaochangshu (BL27) [13].

The influences of stimulation on each acupoint to gastric movement were generally inconspicuous at an electroacupuncture intensity lower than Aδ, except for some inhibitory effects in acupuncture on Liangmen (ST21). When electroacupuncture intensity was higher than Aδ but lower than C, all reflective effects on gastric movement appeared by stimulating each acupoint, resulting in a remarkably different effect compared with the electroacupuncture intensity lower than Aδ. The IGP rose when the Quchi of front limbs, Qihu (ST13) of the upper breast, and Zusanli (ST36) of the lower limbs were stimulated. On the other hand, IGP was reduced upon stimulation of Liangmen (ST21) and Qihai (CV6) of the abdomen. At an intensity higher than C, the effects of all acupoints to gastric movement were still strong, but not greater than the intensity between Aδ and C, as shown in [13].

Low-level simultaneous background activity of autonomic nerves proceeded before acupuncture (nerves splanchnicus major: 4.15 ± 0.80spikes/min; gastric vagus nerve: 4.61 ± 0.85spikes/min). The influence of acupuncture on acupoints to the vagus nerve manifested as notable increasing activities of the gastric sympathetic nerve by acupuncture on Liangmen (ST21), Qihai (CV6) of abdomen, Geshu (BL7), Weishu (BL2l) of notum, and Rugen (ST18) of lower breast. It also considered the same direction of the reaction and the inconspicuous influence or slight excitement of the gastric vagus nerve. Despite the inconspicuous influence to the sympathetic nerve, the activities of the gastric vagus nerve remarkably increased upon the stimulation of Qihu (ST13) of upper breast, Feishu (BL13), Xiaochangshu (BL27) of notum, Quchi (LI11), and Zusanli (ST36) of limbs [13].

IGP rose after cutting off the bilateral nerves splanchnicus major and acupuncturing on acupoints on limbs of Quchi (LI11) and Zusanli (ST36). However, no distinct exciting effect was caused by stimulating Quchi (LI11) compared with the time before the nerves were cut, in which a stronger exciting effect and higher IGP to Zusanli (ST36) could be perceived. No distinct IGP caused by stimulating Liangmen (ST21), Qihai (CV6) of abdomen, and Weishu (BL21) of notum occurred, compared with the time before the nerves were cut and existing inhibitory effect disappeared. Inconspicuous variation of IGP fluctuated within the range of 1–3 mmH_2O after cutting the gastric vagus nerve and

stimulating Quchi (LI11) and Zusanli (ST36) on limbs, resulting in the existing exciting effect to disappear. IGP could be reduced by stimulating Liangmen (ST21), Qihai (CV6), and Weishu (BL2l) without any distinct inhibitory effect compared with the time before the nerves were cut [13].

After the spinal cord was traversed, IGP reduction was elicited by stimulating the acupoints of abdomen and Weishu. There was no change to the inhibitory effect of Weishu (BL2l), Liangmen (ST21), and Qihai (CV6) compared with the condition before spinal cordization. More rapid recovery of IGP on Liangmen (ST21) and Qihai (CV6) occurred after acupuncture. IGP could not be influenced by stimulating Zusanli (ST36) of the back limbs. The effect on the rise of IGP disappeared as well [13].

Mustard oil was injected into the gastric wall of a rat and Evans Blue was injected into the tail vein. A blue dot appeared under the skin and mucosa one hour later, with concentration on the lower breast, abdomen, and the area near the middle line on the notum (lower than shoulder joints but higher than hip joints). These points are acupoints treated for gastric and intestinal diseases such as celialgia and diarrhea [13].

Acupuncture on the acupoints innervated by the nerves in or near the same segment of the stomach could restrain gastric and intestinal movement, and reduce IGP. The effect was completed by output fibers of sympathetic nerves from the reflex center inside the spinal cord. Acupuncture on the acupoints innervated by nerves far away from the segment of the stomach could increase IGP, which could be completed by output fibers of vagus nerves as the participation of the spinal cord center. A certain degree of stimulus intensity of acupuncture is required to activate the effect of adjusting the IGP. Thus, the impact on gastric movement by acupuncture on acupoints is closely connected with the dominant relationship between nerve segments.

Effect and mechanism of acupuncture on cardiac input and function

The somatic foci of cardiac pain were mainly distributed along the heart meridian (HM). HM acupoints have been used to treat cardiac diseases since ancient times. The relationship between the heart and acupoints along the HM is closer than that along the lung meridian (LM) is, and more double-labeled spinal ganglion cells have been traced both from acupoints along the HM and from the heart [15]. Compared with LM, acu-stimulation along the HM evoked more sympathetic responses, and correspondingly, stimulation of cardiac sympathetic nerve evoked more reflective myoelectricity propagation along the HM. In articulating the relevant relationship between the heart and the HM, most acupoints correlating with the adjustment to the cardiac function are distributed in the HM because of the nervous segmental accordance of the heart and HM acupoints.

Homo-segmental acu-stimulation could produce remarkable analgesic effect. Non-segmental acu-stimulation facilitates gastrointestinal motility, while homo-segmental acu-stimulation inhibits it. Cardiovascular function could be regulated by acu-stimulation on homo-segmental acupoints along the HM. A discussion on the neuronal science mechanism involved in how referred cardiac pain areas, which are distributed along the inner side of the upper limbs, are concerned with the heart's mechanism of the generation of referred pain supplements the findings.

Three kinds of fluorescents (fast blue, propidium iodide, and benzoylimino) were injected into the acupoints in the HM, LM, and the heart. The distribution of the marked cells in the spinal nervous ganglion from C6 to T5 were observed. The average number of marked acupoints in the two sides of HMs and double-labeled cells were higher than the acupoints in the LM and double-labeled cells of the heart. However, only double-labeled neurons in the left heart and LM acupoints to the heart expressed statistical distinction. The number of double-labeled cells in the left HM was greater than that in the same segment of right side was [16].

Stimulating acupoints of HM and LM by a series of impulses of the same intensity may induce varying degrees of activating reaction of the cardiac sympathetic nerves. The heart vagus nerves discharge were evoked by stimulating acupoints on both sides of the HMs and were stronger than in the LMs.

Electromyoreaction in the HM was induced at various stimulation degrees, but remained weak in the LM. Electromyoreaction in acupoints of both meridians exemplified an ascending trend following the increase of stimulation intensity [17].

The bifurcation phenomenon appears at the axon of the ganglion spinal. One branch locates in the heart, and another is in the upper limbs. This phenomenon is the foundation of the nervous morphology correlating body surface and viscera, and of meridians and viscera. The dominant phenomenon of ganglion spinal cell bifurcation phenomenon was more apparent between the coasting line of the HM and the heart, which suggested the relative specificity of the heart, referred cardiac pain and connection with the heart, and the neuron base that is dense with nervous segments. Compared with acupoints of the lungs, greater excitement of the heart vagus nerve could be induced by electroacupuncture stimulation. On the other hand, the greatest electromyoreaction in acupoints of the HM can be evoked by stimulating the heart vagus nerve.

Stimulating the cardiac sympathetic nerve could evoke reflexive electromyoreaction in the coasting area of the HM, while still weak from being evoked in the coasting area of the HM with segmental distinction. This not only suggests a clear segmental distribution trend in the sympathetic-motor reflex, but also presents vast discrepancies in the degree of density to the distribution of the nervous fiber. In medical practices, cord-like tissues can be subcutaneously touched in the

meridian-acupoint area associated with the contracting of the skeletal muscle. These phenomena are generally associated with visceral pathological changes. Visceral referred pain is mainly manifested as muscular hyperalgesia, accompanied by segmental muscle spasm. Local internal organ pathological changes controlled by the sympathetic nerves usually lead to muscular spasm in the relevant nervous segment. The mechanism of segmental sympathetic-motor reflex might be the effect input of the sympathetic nervous system acting on muscle spindle and controlling the contractive function of the muscle fiber. The base of specific connection of the HM, the psychogenic referred pain and the heart is the same as that for the nervous segment and the relative intensity of the nervous fiber distribution. The base of the psychogenic referred pain overlaps with the innervations of the cardiac afferent nerve, and acupoints in the HM and along the channel of reflex.

Conclusions

Acupuncture has been widely used in treating diseases. It may induce pain relief by changing regional blood flow through the somatosympathetic reflex [18]. In addition, it modulates the functions of visceral organs by inducing the activation of somato-visceral reflexes and changing the autonomic nervous system [19–22].

Nonetheless, acupuncture remains a field that needs to be explored. Conducting case studies on the effects and mechanism of sensation and motion of viscera such as the heart and the gastro-intestine still needs to be considered. Previous studies have focused on the separation of the sensation index and motion response. In investigating the effect of acupoints, the choice of acupoints should be greater than 30 to obtain varied and conclusive results. This paper aimed to supply new and distinct instructive principles for the choice of acupoints in clinical acupuncture, and thus, establish the regularity of acupoints based on modern science and technology.

Each individual was observed simultaneously with regard to the reactions of acupoints to the visceral sensation, motions of visceral, peripheral nerve, visceral nerve, and nervous centrals mentioned in this research. Furthermore, the scientific basis of the acupuncture effect and its specific law with a joint research of analgesia mechanism, adjusting the effect to visceral function, regulation and mechanism of acupuncture, and deriving a more systemic result were explored.

Systematic research on the inhibitory effect of stimulation on acupoints to visceral pain from the peripheral, spinal, medulla, and thalamus levels was carried out, as well as a comparative analysis of the contribution of the different parts of the central nervous to the effect of analgesia by acupuncture. In conclusion, the most important inhibitory effect on visceral pain by acupuncture is the spinal level. This study is the first of its kind to investigate an acupuncture and visceral pain at multiple levels and multiple target spots.

Acupuncture on acupoints in or near the same segment of the stomach could restrain stomach movement and reduce IGP. Although not every one of these acupoints belongs to the stomach meridian, the inhibitory effect is clear. These acupoints activate the sympathetic nerve, and the effect after the spinal cord is intersected presents advantages and indicates the output of the reflex activity as it passes through the stomach sympathetic nerve while the reflex center is in the spinal cord. When acupuncture occurs on acupoints in distant segments, whether these acupoints belong to the stomach meridian, the IGP would increase at different levels but on a consistent reaction direction. At the same time, acupuncture activates the output activity of the vagus nerve. The absence of such effect if the spinal cord was intersected demonstrates the reflex activity through the gastric vagus nerve, which requires the spinal upper center.

This paper comprehensively and systematically discussed the regulatory function of acupoints at every part of the body to gastric sensation and motion, as well as the differences among all the acupoints. It seeks the most suitable acupoints for easing gastric diseases; explained the transmission path of acupuncture signals and principles of action to this kind of specific effect; and attempted to solve the most urgent question in clinical work on acupoints in terms of choice and principles. Acupoints from different nervous segments have distinct influences on gastric motions, despite all of them belonging to the stomach meridian. When all acupoints are in the same nervous segment with the stomach, IGP could decrease and restrain gastric motion. The results of this paper will supply academic reference to acupoints in terms of choice for treating different gastric motor diseases using acupuncture.

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