

Reviewing Zang Heart to Create a New Comprehensive Anatomico-functional Model

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Chinese Medicine (CM) conventionally described Zang organs according to the Zangfu manifestation theory. Current CM studies demonstrated that myocardial contractile strength and efficiency may represent Zang Heart-Qi. While it illustrates how in CM the Zang Heart directs circulation, little has been shown how thereby it carries the spirit, as CM describes it houses Shen. The controversy as to whether the brain or the heart directs ('governs') the Shen mastery still remains unsolved, and diverges CM thoughts. This paper reviews how the Zang Heart could mean the same anatomical organ but with an added dimension. Re-inclusion of its connections up to the cortical-autonomic system would help to restore the anatomical functional tie. The one Cortical-autonomic-medullary-heart Complex may be taken as the Zang Heart. Its lower medulla-autonomic-heart system reflexively stabilizes the circulation while connections up the higher cortical autonomous system provides regulation for situational circulatory responses, motive or emotive as necessary, likened to its CM-described capacity to transform Shen (into different modes of mental mastery). Zang Xiang (external manifestations) may be expressed as functional features of that one structure as it integrates emotional and cognitive components of the mind with autonomic cardiovascular control, related with intestinal absorption for capacity of body perfusion, and its connection to the whole central nervous system and the body, as neural and circulatory networks evolve together with repeated remodeling since development. Remodeling of their interactions produces patterned responses to stimuli or stress, so that perfusion and nervous activity can be in balance and matched during endeavors or actions. These mechanisms together with neuroendocrinal interactions with the thermal regulation would work for perfusion needs so that, when working well to adapt to the environment, the Heart synchronizes with all organs and the whole works with mastery and efficiency, in a state demonstrated as psychophysiological coherence with the whole body in optimal function: analogous to CM describing that "the Heart holds the office of sovereign, whence the bright spirit emanates". There are evidences that information and perfusional elements go hand in hand. From reviewing mind-body interactions remodeled during development, it is found that the tone and dynamics of the whole, in stabilizing circulation and perfusion during support of endeavors and performance, provide mechanisms to adaptations to face life. These correspond well with the described Zang Heart, and meet its essential meaning more closely than previous models, eliminating the controversy over the brain-heart split. This paper illustrates for the first time in CM literature how the mind-body, perfusion, brain-heart, body heat, temperament, and climatic thermal environment can interact and influence each other, just like what is observed in Nei Jing and supported with current research literature. This anatomico-functional model can better interpret CM literature and be easily understood by current science.

Key words: Zang Heart, heart-brain split, Zang Xiang, anatomical functional structure, organ complex, modern medical science

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1. Introduction

Traditional Chinese Medicine (CM) mechanisms need be understood in scientific terms. Understanding Zang Xiang or Zangfu manifestation theory is highly important to clinical CM. Current researchers that reinterpret them have used a network of body functions to refer a Zang organ as a set of interrelated distinct parts rather than one anatomical organ. As these current descriptions of Zang organs are not matched for function with anatomy, two articles have been written, on Zang Kidney and Zang Spleen [1,2], to clarify how one single structure which the ancient people should have referred to, can explain more comprehensively and comprehensively the described Zang Manifestations or Zang Xiang over each Zang starting from Huang Di Nei Jing. One single structure re-defines the ought-be-present but missing Zangfu organ "situated internally"[3]. The grouping of many other functional entities in the network would then additionally expand the explanations of Zang Xiang manifesting externally. With that depiction, the match between anatomy and function of the Zang organ is more acceptable to modern science.

It remains to see whether, besides the Zang Kidney or Zang Spleen, each of all Zang Organs can be ascribed to one single structure to elucidate the Zang Xiang. This paper is a continuation of this process by describing the Zang Heart similarly in modern terms. By reviewing the CM Zang Heart, understanding the limitations of current models, and reinterpreting the Zang Heart by identifying meaningful modern anatomico-physiological homologues and states that match CM Zangfu networks and functions, a useful model can be deciphered. That would be important for framing future research.

A note to clarify the terminology used. CM texts capitalize the first letter to denote a word significantly different from modern medical usage. Here, for clearer and easier reading, Zang Heart, Zang Kidney, Zang Spleen, Zang organs are abbreviated with prefix as zHeart, zKidney, zSpleen, zOrgans respectively [4]. Similarly, other Zangfu organs will be given the same prefix.

2. Ancient and Orthodox Zang Heart Model: From Anatomy to Function

To start with, it can be presumed that CM and

western medicine essentially started with the same body bio-physiological features, being different only after long cultural separation. Here it is believed that the ancient sages started with essentially the same anatomical organ but with a wider dimension [1,2,5].

To review, it is first notable that CM ancient literature anatomically described many body parts. Internal Zang-fu were classified as five Zang organs, six Fu organs and six extraordinary Fu organs. That was an anatomico-functional classification, describing the Zang or zOrgans as solid organs, and the Fu or zViscera as hollow through organs. Anatomy was emphasized in the ancient classics [6]. Nan Jing described the zPericardium in comparison [7] as not a solid Zang and without a form. In discussing pairing for Zangfu, which is an important part of the Zang Xiang theory, the heart was noted distant to the small intestine and the lung distant to the large intestine as compared to other Zangfu pairs [8]. That must mean an anatomical distance. In fact the word 心 (heart) in Chinese is a pictographic word, an anatomical simile. The heart was referred anatomically in Nei Jing: "the lung is the canopy of the heart" [9]. In Nan Jing, the heart anatomy is briefly described as "weighing 12 liang, having 7 orifices and 3 chords" [10]. A scholarly CM description in Ming Dynasty described clear anatomy of the heart in position and shape [3]. In CM, same as in modern physiology, the zHeart directs circulation. However, it also has a dominating influence on the Shen, mastery of spirits.

Zang solid organs and Fu hollow organs form the core while the other body parts are functionally related to them. "The Zangfu organs are situated internally, and manifested externally (physiological and pathological features reflected externally) as Zang Xiang" [3]. By ancient Chinese scholars' observation, the body as a whole varies with environment in adaptation, or expressed in holistic terms, varies with nature according to Yin Yang and harmony principles [12]. Diseases would be due to disturbances of nature on poor body constitution and adaptation. Then, the interrelationship between various body parts was used to account for inner harmony and its disturbance. This is the Zangfu manifestation (Zang Xiang) theory. Xiang, or manifestations, in Chinese refers to the picture as well as the equivalent symbolization of things.

As Xang Xiang is clinically important, current workers tried to understand it through

diseases and from clinical methods being used. Nevertheless, the concepts of Zang organs and Zang Xiang were developed since ancient time. Over the course of time after Nei Jing, CM described the body in terms of functional entities away from anatomy matters. At present, with insignificant correlation between anatomy and functional physiopathology, the Zang organs are essentially different from terms of western scientific medicine. The zKidney and zLiver are not exactly the anatomical kidney and liver.

Different interpretational positions had allowed later scholars to attribute each function under study either to zOrgan itself or to Zang Xiang in general, as they seem fit. Thereon, later in Ming dynasty, inspired by new anatomical understanding of the western functional view of brain in the skull from the expatriate missionary [13], Li Shizhen remarked that "the Brain is the house of the original spirit", drawing analogies from Nei Jing in his famous book [14]. This set up a controversy that escalated over the centuries.

It looks as if the original scripts of Nei Jing described both "Heart directing the Shen mastery" as well as "Brain directing the Shen mastery (model A)" concepts. The verses "the Heart, the sovereign of all organs, and the source of intellect" [15] support the former, while "the head, the house of the discerning intelligence" [16] supports the latter. Many CM scholars throughout the centuries thereafter already attributed the Shen to the head [17–19]. Then after Li Shizhen, the Brain specifically took over as the site attributed [14,20].

As the descriptions that the Heart directs the Shen are more dominant in Nei Jing [15,21,22], this concept (model B) is more prevalent in scholarly dissertations throughout the ages. Thus the zHeart directing circulation is viewed with general consensus, but there are diverse ideas concerning whether the zHeart or Brain directs the Shen mastery. To note, the phrase 心神 (heart-Shen or spirit in the heart), has been a common term used by current as well as ancient CM scholars [17].

3. Modern Zang Heart Model

The word Zang currently takes a rich meaning, including its many interrelated body parts and their functions, and its relationship with other body parts, demonstrating the mutual positive and negative influences among the body

systems. In the last few decades, researchers in China from the integral, organ, cellular and microscopic levels to investigate for the essential meaning of Zang Xiang, have generally move from a solid organ representation of Zang away to a network representation. Even so, there are still many who seriously believe and wish to find the anatomical correlates [23–25].

For present CM scholars, the Heart-circulation model has been used. Taking the perspective that the zHeart directs circulation and thereby carries Shen (model C), and noting that zHeart-Qi deficiency and zHeart-Yin deficiency are the commonest syndromal dysfunctions, the study of the essential nature of zHeart has been positioned towards the circulatory system and its diseases. Measurement of the myocardial contractile strength and efficiency were used as proxy indices of zHeart-Qi [26–29], short of finding a proper animal model [30]. Deficiency of zHeart-Qi was associated abnormal left heart function [31–45] including shortened LVET (left ventricular ejection time), prolonged PEP (pre-ejection period), increased PEP/LVET ratio [32], and the STI (systolic time interval) indices correlated with the degree of zHeart-Qi deficiency [34,45,47]. It was noted that zHeart-Qi deficiency, zHeart-Yin deficiency, and zHeart-Yang deficiency are incremental stages of a series of deterioration [35,47] and increased PEP/LVET ratio can be used to distinguish the stages [38]. Cardiac Doppler also helped [48,49], and demonstrated that zHeart-Qi deficiency would manifest similarly regardless of noncardiac or coronary conditions [50]. Notably, contraction and/or dilatation dysfunction can simply occur in zHeart-Qi deficiency [51], with dilatation dysfunction usually preceding contraction dysfunction [52]. Other circulatory and blood flow indices were also studied. While increase in blood viscosity is more related to Blood-Stagnancy, there are in zHeart-Qi deficiency various degrees of prolonged microvascular stasis associated with reduced VPE (ventricular pumping effectiveness) [53]. In zHeart-Qi deficiency subjects, the microcirculation is dulled and distortedly sluggish [54], while that in zHeart Yin deficiency is linear in flow and accelerated [55,56]. In short, reduced cardiac contractility, reduced outflow, and pump dysfunction are the basic patho-mechanisms and useful indicators of zHeart-Qi deficiency. These cardiac functional indices, notably worse in zHeart-Yang deficiency than zHeart-Yin deficiency, and this in turn

worse than zHeart-Qi deficiency, are found useful to distinguish between them [38,57,58].

Thus, after decades of hard work and research activities, formation of a core of modern understanding of zHeart has been achieved. Yet the bulk of modern understanding of all Zang Xiang were mainly attempts to verify and rationalize it with indices of Western medicine, whereby the actual Zang Xiang theory remain undeveloped [59]. There is need to expand on the substance of theorization in Chinese medicine until its proficiency produces input to the scientific world. Regarding the zHeart, taking the model and perspective that the zHeart directs circulation thereby carrying Shen and influences the mind, researches have elucidated the circulatory part of zHeart but not much on its part with the Brain. As was found useful, much was done with hope to use immunoreactive antinatriuretic peptide irANP as an index for zHeart-Qi deficiency [60] to bridge that heart-brain link, but with poor success. There still need a model and perspective to develop studies to elucidate how zHeart could direct Shen mastery.

Whether the Heart or Brain directs the Shen mastery or intelligence, the concerning divergent ideas seem not reconcilable. The Ming controversy stayed the last several hundred years and still affect the present academia. In the last century, Zhang Xichun (1860–1933), CM trained and also learned in western medicine, believed that both the heart and brain together direct the Shen mastery” [61]. More recently, some began to appeal that it is the Brain directing Shen, while the Heart directing Shen is misleading [62]. Up recently, Chen Shi-kui published the view that the "Brain directing the Shen mastery" concept should reform the orthodox "Heart directing the Shen mastery" view to breakthrough over CM modernization difficulties [63,64]. Others supported [65]. Shen is seen as the highest consciousness, and in general, consciousness is usually related to the brain. After all, this seems more acceptable in modern medicine to move away from any heart-brain myths.

There were as expected strongholds from other scholars. Deng Tie-tao soon reaffirmed that the Heart directs Shen [66], holding that CM is macroscopic and the difficulty to modernize it in microscopic terms should not be the reason to refute its concepts long verified by practice. Yet how "the Heart directs the Shen mastery" still remains unexplainable in modern terms. Attributing it simply to yet-unexplained meri-

dians [67] was not helpful. To affirm, a lot of funds had been put in [68–76], but not much resolved.

This controversy not resolved, the modern zHeart model has not been definitive in modern medicine or CM terms despite much research done to expose the zHeart syndromes and diseases. One expression of zHeart in current CM literature describes its main physiological functions and features [77]: “In CM, the zHeart is the house of the mind, the master of blood, and the director of the vessels. The main CM physiological function and features of the zHeart are: (1) governing blood in vessels; (2) carrying the master spirit Shen; (3) opening through the tongue, associated with pulses in the body, manifesting externally in the face and complexion, as joy in the emotions, as sweat at night; and (4) mutually internal-externally interconnecting with the small intestine, with Meridian connecting.

4. Blind Spot in Modernizing Zang Heart Concepts

To review effectively, the limitations of modern CM framework obscured by blind spots must be recognized [1,2,5]. The above controversy in CM literature notably started only after western medicine was introduced in the Ming dynasty. Western medicine once followed a reductionist path to understand the body part by part and component systems. In describing the circulatory system, the nervous system was separate. This reductionist classification has caused blind spots limiting proper conceptualization of, for example, the zKidney and zSpleen when CM workers put in orthodox western medical framework to justify. In justifying Zang Kidney conceptualization, it lost the important associated musculature [1]. In Zang Spleen, it misled to separate the intestinal-mucosal immunological system out during discussion of the digestive processes [2]. Re-emphasis of the separated hind-end musculature or intestinal immunology helps in restoring understanding of zKidney and zSpleen. The reductionist days in the west were a time seeking to understand anatomico-functional physiology. The western Cartesian mind-body dualism, viewing the two as essentially separate entities since Descartes [78] would make matters worse [79]. That blinded scholars to see how, during endeavors in living, nervous activities and perfusional

support are actually closely coupled together to accomplish it. That would obscure how core directives for life necessitate the heart and brain to evolve and work together as a unit to bring forward the whole person to live for life. The ignorant reliance of the reductionist brain-heart split established in western framework placed a gap and obstacle to restore meaning and understanding of Zang in a modern context when CM workers used this western framework in the construct of zHeart.

In fact, the western scientific world is making great strides to revive from that former reductionist split. Recently, the heart and brain once taken separate is more and more taken as one unit for consideration in dedicated fields of neurocardiology or behavioral cardiology [80–82]. Early in the 1980s, an editorial in the Mayo Clinic Proceedings highlighted neurocardiology as a field come of age [83]. In 1994, the concept of functional ‘heart brain’ was introduced, noting the heart’s nervous system, with around 40,000 neurons, gathers information about the heart to the brain medulla and the higher brain centers to influence perception, decision making and other cognitive processes [84,85]. With growing literature in this direction, the Second International Conference on Heart & Brain 2014 [88] aimed to unite cardiologists and neurologists to study it. Neurocardiology refers to (patho)physiological interplays of the nervous and cardiovascular systems [87].

It is believed that the ancient started with essentially the same anatomical organ, heart, but with a wider dimension [1,2]. The importance of this brain-heart complex in understanding zHeart has been briefly introduced in a previous article [88] and will be explained in greater depth here.

5. New anatomico-functional Zang Heart Model

Let us presume that in ancient CM, the zHeart was essentially started or defined as a structure with a name and configuration consistent with anatomy, while the frame model of Zang Xiang, generalizing manifestations of physiology and pathology, were added on top of it later¹. Then by finding out the initial ancient anatomico-functional structure of zHeart, the derived Zang Xiang functions can be reviewed in a better perspective.

5.1. Domains of the brain essentially part of

Zang Heart

Much has already been studied in classical western literature to clarify the stabilizing homeostatic mechanisms of the circulation in body motion and activities. Only recently is it clearer that the higher cortical autonomic network in the brain is important [89]. Its processes support the heart for anticipatory reactions to demanded emotional and social environments over the basal circulatory motivity mode. Not just efficiency, but also adaptability is needed for redistributing perfusion in expectant situations.

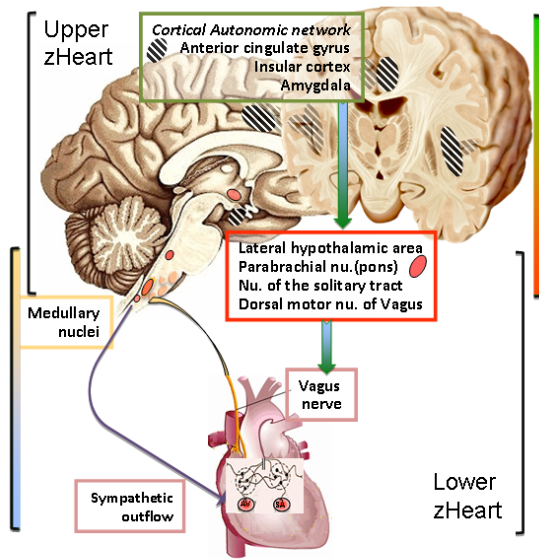
While it has long been thought that conscious awareness originates in the brain alone, recent scientific studies suggest that consciousness could emerge from the brain and body acting together [90]. Studies have noted how the brain and heart interact in a mode not separate. The pattern of the heart’s rhythm would reflect the emotional state [91]. Changes in cognitive and emotional state produce changes in autonomic cardiovascular control producing what has been called “brain-body harmony” [92]. The brain’s alpha, beta rhythms, and lower frequency brain activities exhibit increased synchronization with the cardiac cycle during the mode of “psychophysiological coherence” [93], a global coherent state of performance-enhancing interactions within and among the physiological, cognitive, and emotional systems. To rediscover the anatomico-functional zHeart, there is need to re-include its synchronizing brain parts in the actual anatomical zHeart structure in reframing its theoretical framework.

5.2. Defining the functional anatomical Zang Heart

The Zang Heart, in ancient CM, could mean the same anatomical organ but with added dimension. The organ mass with the heart and its associated nervous complex with connections up to the cortical centers is taken as ONE single functional structure that could be the zHeart (figure 1). Its perfusion capacity is intimately related to the intestinal absorption.

This is one functional structure, because it can be seen as one integral, closely interactive, closely inter-coordinated complex. Blood circulation and perfusion of essential and regulatory materials are Intrinsic Functions of that functional structural complex. It maintains stable circulation, and mediates the comprehensive motive and emotive functions during anticipation and endeavors. The word

heart in old days means the pumping heart as well as the perceptive and emotive heart.



Figures 1. Zang Heart, Functional Structure

Fig. 1. Zang Heart, functional structure

This view with a structural base allows a coherent construct of the zHeart and Zang Xiang manifestations can then be reunderstood in three inter-reacting levels: the zHeart Anatomical Structure, its Intrinsic Functions, and supporting Internal Interactive Mechanisms. Essentially it serves: circulation, body perfusion, related intestinal absorption, dynamics for transporting essential and regulatory materials, and functions for mental control during mastery for life. The internal support would be a host of neural, perfusional, endocrinal, receptor mechanisms among others to achieve homeostasis. As these interact to cater for energy and life needs, the whole body displays varying states of neural-perfusional balance which when synchronized would produce mental mastery for directing life and living. These would produce external observable Zang Xiang manifestations.

5.3. Better understanding supports the internal Zang in the zHeart Present Model

This present view of zHeart, as a functional structural complex closely interacting with supporting mechanisms, would be able to embrace known features and current findings that in the new light also become evidences for this model. This one functional structural complex includes the heart and the associated nervous complex with connections up to cortical centers working with body directives and

perfusion. For processing functions, it may be taken as two parts interacting.

One part of the zHeart complex, the heart with its associated lower nervous with connections up to medullary centers (figure 1, lower zHeart), provides the needed stabilizing mechanisms to maintain circulation. The integral body needs essential materials transported all over, and circulation is well described in western medicine (while the mechanisms to guarantee perfusion are more complicated). This needs be constant as cell and tissue metabolism is a continuous process, and this is supported by maintenance of a steady arterial pressure.

Circulatory dynamics are maintained by intrinsic structural functional characteristics of the heart, including (i) its functional relationship between myocardial contraction energy and diastolic filling (Starling's Law) as this provides inbuilt properties to enable the heart to adjust stroke volume (SV) to varying rates of filling related to venous return decreases or increases as in exercise, and (ii) cardiac response to arterial pressure changes (an after-load effect) to enable the heart to adjust SV to maintain arterial pressure. These have been the parameters that modern CM researches on zHeart-Qi were concentrated in.

The integration centers in the medulla, connecting the heart, are part of the autonomic nervous system (ANS) of the brain. The sympathetic and parasympathetic ANS regulates inflow-outflow of the heart and blood vessels, and is particularly important for regulation of arterial pressure. Cardioexcitatory and cardio-inhibitory centers are reciprocally innervated and mutually inhibitory to control autonomic outflow to the heart. They are also connected to mutually inhibitory medullary vasomotor centers that control sympatho-adrenal outflow to vascular smooth muscle as reciprocal vaso-constrictor and vasodilator centers.

This ANS is classically regarded as an "involuntary" system regulated by hypothalamic centers and beyond direct conscious control [84,94,95]. This lower medullary zHeart complex is concerned with regulation for stabilization of the basal circulatory dynamics. These receive afferent nerves from receptors, high-pressure baroreceptors (pressoreceptor) in the carotid sinus and aortic arch, to monitor systemic arterial pressure and its rate of change. The effect of stimulation would activate medullary vasodilator center and medullary cardio-inhibitory center, and reciprocally inhibit the

vasoconstrictor and cardioexcitatory centers. The net effect of stimulation is to reduce systemic arterial blood pressure. Decreased pressure at the baroreceptors would produce the opposite effect.

High-pressure baroreceptor reflexes are important for immediate short-term regulation in stabilizing systemic arterial blood pressure. A low-pressure baroreceptor is present also, in the heart atria, which regulates venous pressure and body fluid volume through renal physiology. The baroreceptor with aortic body and carotid body, and the renin-angiotensin system with renal juxtaglomerular apparatus provide the most important reflex systems for homeostasis.

These processes act on peripheral vascular resistance, the heart's SV and cardiac output to regulate circulation. That corresponds to what CM described as: zHeart governing or directing blood vessels and pulses [9], vessels carrying blood, and all features of Blood are related to zHeart [96]. Blood in CM is a material form of Qi, transporting nourishment and also vitality. Blood is the basis for the formation of skin, bones, muscles, and organs. It may be said that these features are related to perfusion.

The second part of the zHeart complex, the further connections up higher cortical autonomous system (figure 1, upper zHeart), provides circulatory responses by situational recognition primed with past experiences and memories. Conscious effort can mode cardiovascular function through the classical involuntary ANS [84,94,97]. Cortical function through projections, to autonomic control centers [98] having direct control over sympathetic and parasympathetic activity, provides mechanisms for volitional control of cardiovascular function [84,99–107]. These cortical regions include the insular cortex, the somatic and motor sensory cortex, the medial prefrontal cortex (PFC), and the anterior cingulate cortex (ACC).

These central components are a part of the limbic brain, which regulates autonomic and endocrine responses in response to emotional stimuli, setting the level of arousal. The insular cortex has a “representation of the ANS” [84] as well as “viscerotopic and cardiac sensory inputs” [95]. The ACC, which integrates the emotional and cognitive activities with body physiological responses, has projections to autonomic control centers [98,108]. The network consisting of the insular cortex, ACC, and amygdala has been shown by positron emission tomography and functional magnetic resonance imaging to

play a crucial role in the regulation of central autonomic nervous system [80]. The ACC and PFC together integrate emotional and cognitive components of the mind with autonomic cardiovascular control [92].

Some relevant interactions are briefly explained (figure 2 a,c). Emotional stimuli from the environment or from memory are presented to the amygdala or orbitofrontal cortex which are trigger sites for emotion. Emotional reactions are released through hypothalamus, the basal forebrain, and the nuclei in the brainstem tegmentum, with visceral response and associated heart changes. In reverse, reacting from threat, stress or kindness, visceral sensations reach the anterior insular cortex with the stimulating event represented, and then reach the ACC for second-order mapping and reflective coding. Circulatory modes are driven by the resolution signals from the cortical-autonomic-system, and memory is a feature of the setup. The person's life and living history, current climate, and environmental exposures may all affect the behavior in actuation and adaptation (figure 2b, d). Central and lower medullary autonomic centers then interact for further processing regulatory dynamics.

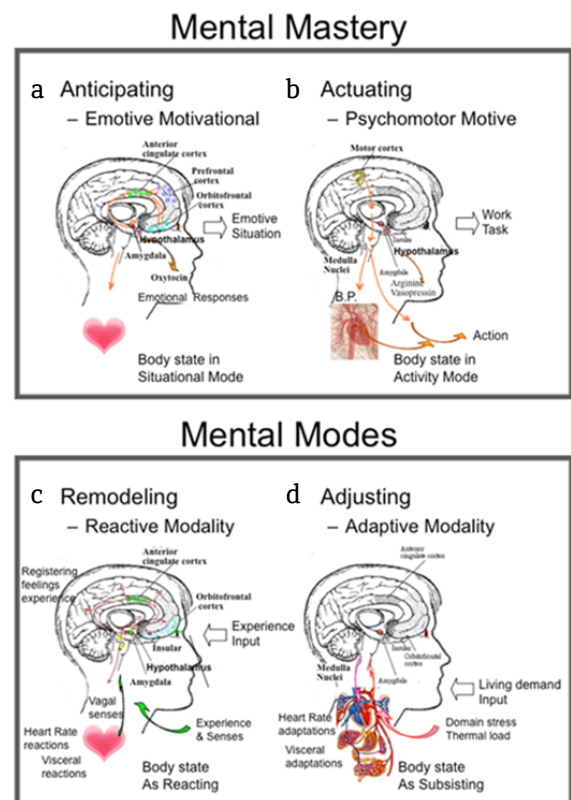


Fig. 2. Zang Heart, transforming spirit master

Transforming between emotive and motive modes, the zHeart as CM described is in the highest faculty, carrying or housing the Shen [10,21], and is responsible for its alteration [109]. Shen, with no exact western translation, has been translated variously as soul, consciousness, spirit, mind, psyche, vigor, etc. Here, let it first be understood as Mental Mastery [88], which governs mental activity and domain attentiveness. It is a feeling of mastery of integral uprightness, or integrity, as if it has good control of the whole body. The CM zHeart could thus be taken as functioning to transform different mental mastery or modes in response to environment, according to coded memory for situations.

5.4. Better derivations supports External Manifestations in the zHeart Present Model

The interactions between cortical-ANS, medullary-ANS and heart are of course not a self-contained closed loop. Matters of the mind related to zHeart are further related to closely interactive mechanisms connecting these structures with the rest of the nervous system and the whole body.

First, the nervous system receives afferent messages from the heart, with meaning. Notably, ice cream chills the circulation deep felt in the heart, and in fearsome situations, the heart felt chilled. In another scenario, many often use beta-blockers that decrease heart rate to control their anxiety to cope with stressful performances. Simply controlling the physiological symptoms help the anxiety. Heart rate variability (HRV) is considered a measure of neurocardiac function that reflects heart-brain interactions and ANS dynamics [91], and rather than the heart rate, it is the distinct heart rhythm patterns that characterize different emotional states. The use of HRV coherence biofeedback similarly helps as an alternative to control stressful performances [110]. In a way, intrinsic nervous mini-system of the heart independently operates and processes information (and feelings) to send up to the brain.

Next, the cortical-autonomic-medullary-heart complex (zHeart) and the whole central nervous system are connected, and the whole body is connected in neural and circulatory networks. Particularly, nerves, arteries and veins travel together in the body in neurovascular bundles, rather than nerves and blood vessels independently. Information and perfusional resources go hand in hand, a body principle to be

reemphasized.

Furthermore, there is evidence of a genuine physical and reciprocal connection between the mind and the body defined by physiological pathways and organic structural elements that remodeling of their interactions demonstrates, whereby a view away from the classical body-mind split view can be renovated [111].

Then the mind relating to zHeart can be better appreciated. Rather than previously viewed as purely brain-generated mental expressions, emotions are now known to be associated with the body as much as the brain. The brain is constantly sampling the internal and external environment for matching patterns, and, neither the structural cause-and-effect model nor the existential-phenomenological model of how the mind and perception work is sufficient [112]. Currently many neuroscientists and psychophysicists view that the emergence of emotional experience results from ongoing interactions between the brain, the body, and the external environment [113,114]. When perceiving an expected change in patterns (as in anxiety from repeated confrontations), the mind, the senses, and the body systems would be all alerted that a change from normal has occurred and may be repeated. This activates the body's alarm system, including emotions, physiological responses, and perceptions [112].

In confronting stress from the internal and external environment, the heart, brain, and body together work in concert in response [115], having emotional feelings tied with cognitive and physiological changes. There is evidence that mind-body interactions evolve with repeated or sustained stress, and cytokines can act as neural trophic factors. This remodeling may reorient the state of the systems governing mind-body interactions to produce a correct or a biased response patterned to stimuli or stress [110]. Biased or deviated responses occur in those with early life trauma, having significant increases in baseline and stress-induced neuro-immune activation [116]. Biased responses are also seen in depression when episodes follow a pattern of repetition, suggesting evolution of pathways that progressively facilitate a depressed mood [117].

While brain-heart interactions are not yet completely understood, these features pertaining to the CM-described Shen can be appreciated. Also, the heart is partly an endocrine organ, the Yin aspects in CM. ANP produced and released by the heart is a hormone exerting

effect on the blood vessels, on the kidneys, the adrenal glands, and on a large number of regulatory regions in the brain. The heart also contains "intrinsic cardiac adrenergic" cells [118,119] that release noradrenaline and dopamine, neurotransmitters like those produced by neurons. The heart also secretes oxytocin in concentrations as high as those found in the brain [120]. Oxytocin, apart from functioning in childbirth and lactation, is also involved in cognition, tolerance, adaptation, complex sexual and maternal behaviors, learning social cues and the establishment of pairing bonds [121]. There could be many more humoral and hormonal mechanisms identified connecting the heart and brain interactions. The vascular endothelial growth factor (VEGF) is a prototypic example of this cross talk between nerves and vessels. VEGF, originally described as an angiogenic factor, is now well established to play a crucial role in the nervous system as well, during development, health, and disease. Neurogenesis and angiogenesis are closely intertwined, with endothelial cells in vascular niches releasing cues for neural stem cells [122]. Information and perfusional elements go hand in hand.

Referring to CM for comparison, modern Zang researches showed that zHeart-Qi deficient patients have a reduced respiratory rate, and impaired postural heart responses relative to normal, as well as prolonged heart rate recovery after exercise, thus indicating impaired ANS regulation and sympathetic function [123]. Additional zHeart-Yin deficiency showed impairment of cortical inhibitory processes and hyperexcitatory ANS function [124], similar to Yin deficiency in general [125]. They also have increased serum dopamine- β -hydroxylase activity indicating hyperexcitatory sympathetic function. In zHeart-Qi deficiency, it is reduced indicating hyperexcitatory parasympathetic function [32]. Both zHeart-Qi deficiency and zHeart-Yin deficiency have varying ANS dysfunction depending on stage [126].

When working well, all these neural-cardiac-endocrino-perfusional setup and interrelationships allow what has been called psychophysiological coherence [93], a heart brain coherence [127,128], a state when positive emotions, stress reduction and performance in health are geared for. Intentionally generating positive emotions can help to maintain positive states, with sustained co-

herent heart rhythm patterns, which leads to increased synchronization between heart rhythm and activity of multiple bodily systems. Heart rhythms, respiratory rhythms, and blood pressure oscillations, other biological oscillators, including very low frequency brain rhythms, and skin electrical potentials can become synchronized. Production of this global coherent state of optimal function, with increased synchronization, harmony, and efficiency in the interactions among all systems, is analogous to CM describing "with the zHeart, as sovereign ruling all organs, discerning spirit (Shen) takes mastery" ("the Heart holds the office of sovereign, whence the bright spirit emanates") [15]. Then one can think fast and respond readily with clarity of mind. The better the perfusion and resourceful directives, the better the cardiovascular peace and heart-mind mastery. With psychophysiological harmony, one feels joy in the emotions, as what Nei Jing described with zHeart [135].

Such state as the zHeart synchronizes with all organs in mastery is contributed by central directives coordinated with unblocked flow and good perfusion of tissues all over the body. Regional perfusion is well known as being autoregulated. Local perfusion is affected by many factors. Notably, arterioles in the nervous system lay in intimate contact with foot processes of glial cells and nerve terminals. This neurovascular unit allows blood vessels to match oxygen and glucose delivery with neuronal metabolic demands [129]. Neurons also regulate neuronal perfusion indirectly through release of glutamate that stimulates astrocytes to secrete vasoactive substances [130]. Perfusion goes hand in hand with nervous activity. Another close interaction between neuronal and vascular cells is the innervation of flow resistance arteries by autonomic nerves [131,132]. During development, to form a pressurized circulation, certain arteries became innervated to allow proper control of the distribution of flow to vital organs [132]. The embryonic neural crest contributes directly to the formation of both autonomic nerves, and smooth muscle cells and pericytes over the large thoracic arteries and forebrain vessels [133,134].

The perfusional and hormonal interactive mechanisms together with its essential and regulatory materials support neural and brain activities in synchrony. Blood provides material support for mental activities, while the zHeart governs moods, wills and emotive thoughts, and

all perceptive understanding, CM describes. It says that the zHeart carries vascular circulation, and in this resides the Shen ("heart houses the pulse, and in this resides Shen") [135]. Perfusional activities carries information resources. Dry assertiveness or endeavors by simply willing and pressing forward is not vigor, cannot last long and toils the brain, while with heart-felt discretion, the matters are carried out and through. For this, CM says that the zHeart is the organ responsible for performance at will [135].

CM describes the zHeart supporting endeavors and Nei Jing remarked that: acting on the corpus and the spirit, "performance on matters at will is expressed with the Heart. The Heart's desire is expressed with Intention. Intentions willed up are expressed with Will Commitment." [135]. From Intention forming meaningful context, the person acquires ambitions and aspirations while sustaining oneself as Will, firm when decisive with Commitment. It goes on to describe how pertaining to Will comes Consideration, and caring for the future comes Deliberation. Finally, "to be deliberate on matters is expressed by Wisdom." [135]. All these Intention, Commitment, Consideration, and Deliberation (意, 志, 思, 慮) are based with the heart, even in word formation. The zHeart is the zOrgan perceiving and handling various stimuli. Discretion is an act of judgment by weighing all relevant matters. In real life, mental discretion may not be as successful as discretion by heart for an individual. Discretion by heart involves those experiences the individual lived and the sum total heart-felt aspirations and will commitment generated for that individual. Such discretion offers better cause for personal success. With the zHeart rightly kept, motives and emotive frameworks would be well shaped, and mental vitality would be facilitated, ministering effectively, flexibly, promptly and smoothly [3].

The mind-body interactions, that evolve with repeated remodeling, developed early from interactions between mothers and infants, a mammalian heritage. Humans however are the very species where early social play around the matching of socio-affective facial signals is seen. Infants even at the third month of life begin face-to-face interactions that are marked by synchrony of non-verbal cues, including mutual gazing, co-vocalizations, and the matching of affective expression [136]. Infants' gaze synchrony (matching social gaze between parent and child), and affect synchrony (matching affective expression) during inter-

action with parents, set the framework for social relatedness and contribute to cognitive growth [137] and development of self-regulatory capacities [138]. Time-series analysis and bootstrapping analysis showed that mothers and infants adapt one to another their heart rhythms within lags of less than 1 second, even without any physical touch [139].

Through these endeavor-performance remodeling mechanisms, such synchrony in interactions plays an important role in the maturation of brain circuits that support social engagement, and contributes to cognitive, social, and emotional growth [140-142], in childhood and adolescence [143,144]. These self-actualizing interactions in nurturing environments facilitate biological and physiological synchrony between the mother and infant's heart rhythms, support the development of infant's physiological regulation, autonomic response and ANS maturation [145,146], and provide the foundation for the infant's physiological, social, and emotional growth [147]. In essence, remodeling mechanisms for synchrony facilitate a more adaptive autonomic response to stress [148].

In summary, the internal closely interactive heart-brain mechanisms as a series of vascular, neural and hormonal messages between heart and body facilitate modulation of circulatory homeostasis for body and mental actualization, influencing the growth, the physique and organ development, and are constantly remodeled since infancy. The whole zHeart complex is coupled with external association mechanisms allowing discretionary discernment originating from the self image of integral entirety, remodeled for recognizing situational provision of perfusional or informational resources to cope with matters over surrounding domain, and built for timely matching with environmental needs. By promoting a body endeavor-perfusional feed-forward balance since infancy, molding of the whole heart-brain apparatus and whole body neural-perfusional mechanisms allows gradual assumption of full function by many other maturational changes. Enrichment of the immediate environment can affect the formation of patterns. At steady states, even the matured adult recognizes and directs diverse self-determined and environmental driven acts and endeavors in promoting life and homeostasis. With the cycle from anticipating, actuating, adapting, to remodeling, and reprocessing again (figure 2), the brain and heart are coupled

to tune to self-mastery. This mechanism is analogous to the CM description that zHeart is the basis of life, as it is the transformer for different mental modes (“as it is responsible for changes of the spirit”), directing Shen to achieve psychophysiological mastery [109]. Also, CM describes the zHeart, by its own, associated with sad or glad emotions [135]. The hippocampus in the limbic system is not only active in encoding memories but also in retrieving them. When confronting environment, sad past events may well up to manifest with melancholy. Positive reactions produce joy. CM describes that zHeart when decidedly firm would produce joy [22,160]. The heart-mind is the part just below cortical ration and action. Joy would be sensed when ration and action are congruent with neural-perfusional-endocrinal synchrony of body and mind.

The heart pangs, pulse races in apprehension, love and other emotional behavior. The zHeart governs a delicate subliminal reflexive system to condition freewheeling of the circulation [88]. The heart-mind represents patterned emotional body reactions. The upper zHeart-ANS centers monitors circulatory dynamic responses through cortical sampling of direct sensed environmental and retrieved past-stored data and senses how the body is feeling. Resolution signals are sent down to the medulla and heart to adjust situational circulatory modes. It may just well be that the heart is uniquely positioned as a powerful central mediating point inter-connecting body and mind, motivity and emotion. Unhappy emotional events, threatening life situations and motivational plans referring to previous memory banks for a charted course are registered with adaptive changes of heart and body arousal, enabling the body to face emotional events or stress environment. Basic circulatory stability is regulated and maintained by the underlying medullary-autonomic lower zHeart complex. The limbic systems in the upper zHeart above set the level of arousal and are involved in motivation and reinforcing behaviors. On top, the heart provides the necessary motive power for supporting perfusion for activities as the body transforms between emotive or motive modes. With body parts well perfused and irrigated, whether in motion or emotion, the body is prepared to be readily maneuverable by the brain for adaptation and actualization. The balance to be motive or emotive depends on its emphasis and strategic position. The brain senses and works out for the

body itself for that environment to determine its mobility or motivation as directed by motives or emotive moves according to their importance, even "fight or flight" responses. The heart is that delicate organ which becomes the chief sensor up-brain for body state and the chief brain-down effector such that the body can be congruent with the mind to meet living demands, while the brain senses and coordinates with them. The whole zHeart complex enables responses and some decision systems, and makes prepared perfusional support, all in a way reacting for self-preservation. Finally, motility or emotional reactors with neuroendocrinal and circulatory effectors interact with perfusional states between the body core and surface, and all these together form key mediators of whole person homeostasis, affecting and are affected by body organs.

5.5. Further understanding enlightens the CM climate related zHeart

Apart from situational responses in motive or emotive states, ongoing physicobiological stimuli also have demands on the system. Externally in the environment, heat changes interact with the circulatory system and body perfusion homeostasis. Temperature has been considered an ‘ecological master factor’ for its profound effects on physiology, having ramifications on the behavior and ecology of a species [149,150].

As temperature increases, the standard metabolic rate (i.e. the lowest metabolic rate) would steadily increase [151]. The Fick equation describes the circulatory mathematics, relating tissue oxygen consumption to the product of cardiac output (CO) and the arterio-venous oxygen difference. When tissue oxygen demand increases, such as during aerobic exercise, after feeding or with increased temperature, the primary means to transfer more oxygen to tissues is by increasing CO. Blood pressure is needed to drive circulatory heat exchanges. Thermoregulating mammals in the mean have blood pressure six times higher than poikilotherms [152]. When cold and getting lower than the critical temperature limit, the body must reduce perfusion to body surfaces by limiting vascular flow resistance to prevent heat loss. On the other hand, with external heat load and a high metabolic heat load during intense exercise, core temperature steadily increases and requires more oxygen delivery and increased tissue perfusion. At high temperature,

possibly limited by oxygen transport [153,154], maximum metabolic rate is constrained for performance.

The built-in surface insulation may become the limit for heat loss in high temperature and even become a risk factor when temperature rises over the high critical point. When rate of metabolic heat production out-matches heat dissipation, thermoregulation requires an adaptive shift of blood volume between surface and core. During prolonged exercise in the heat, cardiovascular drift, especially in the associated fatigue, would manifest with a directly associated steady upward drift in heart rate [155]. Heat dissipation requires much surface blood flow increase, without compromising muscle blood flow for exercise if that is to continue unimpaired in continued heat load. A reduction in splanchnic and renal blood flow along with a gradual change in compliance of the capacitance vessels [156,157] brings forth this allowance. Inadequately met, CO would have to increase further [158].

Facing environmental heat, acclimatization mechanisms program the body with the heart having higher CO and surface vasodilatation in summer, and less in winter. Any behavioral or environmental change that alters oxygen uptake typically involves a change in CO. As aerobic scope represents all processes above living (e.g. for locomotion, immune system), it can be used to denote the amount of aerobic energy beyond that required that can be allocated to activities that contribute to lifetime fitness (e.g., for growth, activity and reproduction). Extreme temperatures can limit the aerobic scope for energy allocation [159] for endeavors above the lowest cost for basic existence.

Over all these thermal climate effects, the ancient had great expertise to define and delineate and had passed on refined calendars for general living. In CM, Nei Jing kept its emphasis on climate influence of zOrgans, even the heart, and described "Heat, produced in the south...., for the body subsists the pulsing circulation, and subsists the zHeart for organs"(also translated "The south generates heat...., in man's body it is the vessels, among the depots it is the heart") [160]. Body thermal core adaptation, along the varying but repetitive patterns of the climate, acclimatizes the zHeart, by central circadian circulatory rhythms [161,162] patterned for climate perfusion function, to vary with nature according to Yin Yang and harmony principles. From the basal circulatory tone, the balance of

the body as a basic life unit would be affected by any added ways to change it, including tissue perfusion thermal environments.

Understanding how the whole body reacts and adapts in its environment in integral terms would help understanding its basic need for reflexive monitoring and control of good perfusion. When circulatory shifts are needed in motion or emotion, the zHeart with its transforming ability would prepare a body-mind ready for the expectant and regulated adaptation and actualization for the endeavor. Matching perfusion with activity is crucial. Poor synchrony means poor internal health and risks. When compared to other supportive mechanisms not so dependably facilitated, the close link of these mechanisms to the zHeart structure as one functional complex can be appreciated.

Over these basics, other zHeart Zang Xiang manifestations can now be understood. On sweating, CM scholars often view that sweat and blood come from the same source. In fact, the zHeart is related to one of the many functional mechanisms of sweating. Nei Jing described how through nutritious pulses, sweat can be generated, while requiring warmth (Yang), and the action of other zOrgans on fluids, in particular, zHeart for sweat. Another zOrgan manifestation concerns the face. All these warmth-perfusion and mind-body synchrony of zHeart are featured over the face. Discrepancies in synchrony are well manifested as tarnished complexion, and worrying looks. In fact, the three most important CM differential diagnostic tools, namely face, tongue and pulse, all belong to functional features of zHeart. CM describes that the tongue is governed by the zHeart [160], associated at least with its high vascularity. Also CM describes that the zHeart-Qi communes to tongue [168]. Apart from the expected control from the heart-mind, this feature can now be better appreciated by the neurovascular bundling or the interrelatedness of perfusion and nervous activity described above, noting that this is a richly neurovascularized highly differentiated part of the body.

In conclusion, the Zang Heart can be perfectly expressed by a functional anatomical zHeart, which anatomical mass is made up of the Cortical-Autonomic-Medullary-Heart Complex acting on the circulatory system and perfusion. Its functional expressions or external Zang Xiang is observed in the associated interactive components, with the brain-heart-body inter-

acting and remodeling. From anticipating, actuating, adjusting and remodeling (figure 2), and the process recycled, the body-mind or Shen fits various living domains. The whole complex serves all functions described under traditional Zang Heart:- to achieve endeavor-perfusion balance even in different thermal environments, to enhance preparedness in emotive and motive modes to encounter new and past-similar situations, as these maintain a dynamic interface, related intestinal absorption for enriching perfusion, and maintenance, regulation and disposition of a circulatory-perfusional system for essential and regulatory materials all over the body for achieving good energy and vegetative balance for nourishment of endeavors in life. The internal support would be a host of neural, perfusional, endocrine, receptor mechanisms among others to achieve homeostasis and to cater these needs. Their action domain during work, exercise, endeavors and reactions may subserve the circulatory homeostasis and body perfusion, and, influence dynamics of the whole body and internal organs, transportation of blood and materials in circulation, physical strength, body endeavor-perfusional feed-forward balance, and endeavor-performance remodeling mechanisms to cater for life. This present model views the heart and brain at their best producing synchrony in nervous and circulatory tone after homeostatic balances over well resolved motivational motive or emotive directives, in control and adaptation, achieving at the same time coherent synchrony in rhythms and functions of organs and of the whole body, towards an integral mastery.

6. Functional anatomical Zang Heart, evidence and validation

Three main approaches stand out in past studies on Zangfu physiopathology: to review the original CM classics on theory and applications, to expose classical knowledge of traditional CM with modern interpretation and experimental proof and to research by clinical studies. The key is to keep them relevant to, and consistent with, the ancient texts and current usage in disease and therapy relating to zHeart. This present model will be reviewed for its supporting evidences in contrast with the past models, including "the Brain directing the Shen" (model A), "the Heart directing the Shen" (model B), and "the Heart direct circulation and thereby carrying Shen" (model C). To note, the past

models discuss the nervous or cardiac events as being dominantly directing rather than one structural complex with interactive circulatory and perfusional consequences as the present model.

6.1. Validating with ancient texts

To validate it, its meaning may be checked for consistency (true/false) with ancient texts. To reduce comparing through the tremendous volume of many ancient texts, Nei Jing and Nan Jing may be used as the 'gold standard'. For any modern model, two points are essential for any modern model (Table 1).

Table 1. Comparison of Models with meaning in Nei Jing and Nan Jing (T: consistent, Indirect (with explaining), Split (with Heart/brain dichotomous): inconsistent).

	Nei Jing, and Nan Jing	Models A	Models B, C	Present Model
1.Zangs, solid zOrgans in contrast to Fu, hollow zViscera	T	Indirect	T	T
2.Zang Heart refers to matters around heart-brain	T	Split	T	T

The Present Model and the Past Models B and C (except A) are acceptable as they are consistent with its usage in Nei Jing and Nan Jing. The Present Model has one solid Zang to explain matters around heart and mind. In model A, one has to split brain and heart when referring to matters around heart and mind.

The next validation step is to check for any word "heart" appearing throughout Nei Jing and Nan Jing. The word heart when used in the context to mean a center (e.g. center of palm) or inclination (e.g. just to please the heart) not concerning zHeart would be not included. Then taking aside its use in Heart Meridians, any such word with context and meaning inconsistent with the current interpretation would be incongruent and treated as an outlier. The less the number of outliers, the more representative this present model would be. Going through Nei Jing for incongruence, in time for example, one may come across "In the summer three months....let wills (even ambitions) be without

anger...Let vim be vented....This is summer climate's adaptation, a principle to nurture growth and development. Opposing it harms the zHeart"("The three months of summer.... let the mind have no anger...Cause the qi to flow away...This is correspondence with the qi of summer and it is the Way to nourish growth. Opposing it harms the zHeart") [163]. Here temperament, body nurture, the circulatory features, and the summer climate are tied in one verse. This can be justified by the neural-circulatory-perfusional remodeling mechanisms influenced by thermal climate as depicted in the present model. One may again come across with "The Heart, life's capital, transforming spirits, with luster manifesting in the face, suffusing with blood and circulation....concerted with summer therms"("The heart is the basis of life; it is responsible for changes of the spirit. Its effulgence is in the face. Its fullness manifests itself in the blood vessels....It communicates with the qi of summer.") [109]. Here the consciousness, the circulatory features, and the summer heat are tied in one verse. It can be justified by the situational cortical-autonomic, and the basic circulatory-perfusional regulatory mechanisms, working together with thermal climatic adaptation as one whole as depicted in the present zHeart model but not in past models. To go completely just through Nei Jing would need to be covered in another article. Similarly, after Nei Jing, one can validate the same with other ancient texts.

6.2. Supporting the Model with pathophysiology understanding

One may go through the list of understanding in zHeart pathophysiology in ancient texts, and see how the past models or the present model cover and comprehend better in attributing function or dysfunction to their components (+ present, - absent).

Model A splits Brain from Heart, and re-words "heart" in the context of deliberations. Model C is unclear on points addressing the Shen, hoping clarifications with due research. Model B refers to the ancient texts on Heart features. Going through the list (Table 2), the present model is more plausible as it better explains more of the points listed. It portrays the Zang Xiang manifestations more comprehensively. The standard text described the zHeart as the house of the mind [22], the master of blood [96], governing blood in vessels [9,135], carrying the master spirit Shen [21,164,165], opening

through the tongue [168], associated with pulses in the body [9,135], subsist with pulsed circulation, manifesting externally in the face and complexion [96,109], as joy in the emotions [135], as sweat at night [167], and internal-externally interrelating with the small intestine [8,166]. Now there really is a Zang organ "situated internally".

Any future observations obtained by being enlightened by this model frame would further support its usefulness. In this context, it would be easier to go by having a postulate from the above discussion of the present model. It may be seen that nervous directives and perfusion that go hand in hand are needed for new changes over the existing balanced life unit. Yet the balanced system would have a certain resilience and reserve, a zHeart Capital, that sustain and tolerate a certain degree of change by just nervous directives alone. Over this heart-brain Capital, some change unless great may not affect the psychophysiological synchrony. Significant change over that becomes dry assertiveness when unsupported by perfusional resources, or becomes over-perfusion when the endeavor is not actuated. Observations from this conception would be seen as being enlightened. One example in Nei Jing is its observation that "the brain working in dry worry for a problem first days" is covered by the body capital. "After some days", the brain overused would be compensated by increase in heart perfusion, with "the zHeart heated up. The face over the area is hyperperfused" [169]. Another example in Nei Jing pointed out "among five zOrgans' aversion, the zHeart would not tolerate heat" [164]. The perfusional maladjustment that worsens with thermal heat would affect the circulation and psychophysiological coherence. The concept would also explain for the observation in Nei Jing that "ecstasy raptures zHeart" [162], as the mental mastery falls apart when its Capital is overwhelmed with nothing to carry [135].

The model illustrates how the mind-body, heat, brain-heart, perfusion, temperament, and climatic thermal environment can interact and influence each other, just like what is observed in Nei Jing. With these closely interrelated, the concept should predict that the brain particularly the central autonomic regulatory centers would have concomitant problems when related elements are disturbed. In fact, heart problems may cause brain problems. Stroke occurs as a mismatch perfusion to assertive behaviors, commoner in jeopardized patients

Table 2. Features (+ present, - absent, split (with Heart/brain dichotomous) in Models as related to pathophysiology in texts.

	Model A	Model B	Model C	Present Model
1. The zHeart, the sovereign ruling all organs; from it the discerning spirit Shen derives [15]	reword	+	unclear	+
2. In the zHeart, being the sovereign of five Zang and six Fu, Shen with essence resides [22]	reword	+	unclear	+
3. The zHeart carries (houses) Shen [10,21,164,165]	reword	+	unclear	+
4. The head, the house of discerning intelligence [16]	+	indirect	unclear	+
5. When zHeart broken, Shen loses mastery [22]	reword	+	unclear	+
6. The zHeart governs blood and circulation [9]	split	+	+	+
7. The Heart concerted with the pulsed circulation, emanating in luster [96]	split	+	+	+
8. All features of Blood are related to zHeart [96]	split	+	+	+
9. The zHeart, core of life, transforms Shen (into different mental modes) [109]	reword	+	unclear	+
10. The zHeart, manifesting luster in the face, suffusing with blood and circulation.... concerted with summer therms [109]	split	+	+	+
11. Thermal heat, for the body subsists the pulsing circulation, and subsists the zHeart for organs [160]	split	+	unclear	+
12. Interrelating with the zSmall-Intestine as a pair [8]	split	+	unclear	+
13. The Heart as Yang organ, Small Intestine ministering [166]	split	+	unclear	+
14. In summer months, pursuit not in anger, vim be vented: adaptation, a principle to nurture; opposing it harms the zHeart [163]	(-)	+	unclear	+
15. The zHeart governs sweating [167]	split	+	+	+
16. The zHeart carries vascular circulation (pulses), and in this resides the Shen [135]	(-)	+	unclear	+
17. The zHeart governs the tongue [160]	split	+	+	+
18. The zHeart-Qi communes to tongue [168]	split	+	+	+
19. Performance at will on matters is expressed with the Heart [135]	reword	+	unclear	+
20. The Heart's desire is expressed with intention [135]	reword	+	unclear	+
21. The zHeart associated with joy in the emotions [135]	reword	+	unclear	+

with large vessel or small vessel disease. Cerebrovascular accidents (CVAs) and transient ischaemic attacks (TIAs) are often caused by cardiac arrhythmias or congestive heart failure [170,171]. Atrial fibrillation with associated poorer perfusion may result in cognitive disorders even before the occurrence of TIAs or CVAs [172-175]. A heart-brain tie is demonstrable even in the absence of manifest stroke, as notably atrial fibrillation is a risk factor for cognitive impairment and hippocampal atrophy. Furthermore, the insular cortex (of upper zHeart) tends to be vulnerable to cerebrovascular disease [80]. Converse brain-heart concomitant problems are also seen. Subarachnoid bleeding may lead to serious electrocardiographic changes and even ventricular fibrillation with QT-interval

prolongation [176,177]. Panic disorders and emotional distress such as the Takotsubo syndrome may give rise to supraventricular tachycardias with associated transient left ventricular dysfunction [178-181]. Further demonstration of circulatory-perfusion balance to climate in man would support the heart-therm model. For example, hospitalization for cardiac decompensation with heart failure would increase in the cold winter/spring seasons [182,183]. When having left ventricular dysfunction, to maintain tissue perfusion, patients would be in a delicate balance between preload reduction and relative hypervolemia to augment cardiac contractility, and this balance gets disturbed when they travel from cooler climates to tropical areas. Conversely temperature reduction when going to colder

countries, can cause physiological changes from increased heart rate and total peripheral resistance with increased afterload, and decrease transpiratory and perspiratory water loss with changed total extracellular volume [184]. These temperature shifts can lead to increased levels of hypertension, higher rates of myocardial infarction and acute arrhythmia [185]. All these brain-heart-heat relationship, with or without relevant heart dysfunctions, are borne out in current literature and support the present model.

6.3. Validating with usage in disease therapy

Success with zHeart therapies has to be present as supporting evidence pointing to zHeart dysfunction being treated (Table 3). To start with, distinction should be made between diseases that are internationally categorized, and zHeart dysfunction as a body state that can be coexistent with various diseases.

Table 3. Effectiveness (+, -) on zHeart dysfunction with therapy on Model Components.

	Model A	Model C	Present Model
1. Regardless of disease types, sweating dysfunction or lethargy associated with zHeart deficiency can be remedied with herbs.	(-)	+	+
2. Mental problems can be remedied with zHeart herbs.	+	(-)	+
3. Clearing of vascular blockages [186] alleviate heart and brain disorders such as in coronary heart diseases [187] and in stroke [188,189].	+	+	+

Thus mental problems of insomnia and/or prostration even when not related to heart diseases can be remedied with zHeart herbs. Common zHeart herbs such as Spina date seed (Suanzaoren), silk tree Albizzia bark (hehuanpi), Acorus gramineus (shichangpu), and lotus seed (lianzi) have effects on insomnia. Here the present model would need more experimental support. In the model, the zHeart-Qi is one important key for the endeavor-perfusion balance, which imbalance causes dry assertiveness. Massage of the body is noted to

improve anxiety and depression, possibly by easing the same endeavor-perfusional mechanism. Recently exercise training, electrical neurostimulation, and music therapy have become options in the treatment of angina pectoris, heart failure, and hypertension [190–192]. When it is noted that agitation from dry assertiveness with subsequent zHeart heat can be soothed by heat-clearing zHeart herbs, such as Lotus Plumule (lianxixin), the concept of the present model is again strengthened. Modulation in thermal environmental stress should also help, as air conditioning reduces overexcitement and agitation in hot climates. Other studies to illustrate the importance of zHeart for mental health from reducing dry assertiveness would be useful. Studies to demonstrate the interactive function between the associated mechanisms of zHeart and brain perfusional lag time would strengthen its validity.

In the present model, the neural-circulatory-perfusional interrelationship would synchronize when each and every component feed in positively, even with herbs and lifestyle change that strengthen the zHeart capital. Short of virtuous interactive components, the prevalence of depression increases sharply with the severity of heart failure symptoms, and depression leads to worse outcomes in heart failure [193]. Heart failure patients with depression have four times risk of death [194]. To clarify further, the degree of the closeness of the interactive neural-circulatory-perfusional links can be explored by the degree of smoothness in internal facilitation over that of other less linked mechanisms.

7. Concluding Remarks

This approach by no means refutes scientific findings of previous workers. Previous compromise retains the circulatory only or heart-brain split mechanisms to achieve any necessary anatomico-functional coherence. The present approach consolidates the concept with the anatomical base and internal interacting mechanisms into one single coherent structural-functional complex. This is made possible by recognizing the importance of the interrelated processes between endeavors and perfusion, as these require circulatory support as well as situation-discretionary regulating neural mechanisms. This understanding helps in the formation of an entity with the components of a stabilizing circulatory unit closely tied with its connected neural structures for discretionary

regulation, and the extended entirety with a whole body unit closely interacting with internal mechanisms for neural-circulatory-perfusional balance and thermal homeostasis. The entity illustrates the Zang inside while the entirety manifest external features of Zang Xiang. The interplay of the components in the complex affects each other and the whole body in life.

7.1. Advantages of the present anatomico-functional model over previous models

7.1.1. It would be easier to understand the CM classic as it referred to one single structure.

7.1.2. This single structure supports functions including circulation, perfusion, related intestinal perfusion, circulatory regulation, situational discretionary support, internal regulatory system for endeavors, activation system for motivity and emotivity in social circumstances, and maintenance of neural-circulatory-perfusional balance and thermal adaptation for life demands and challenges. The internal support would be a host of vascular, neural, humoral, tissue receptor mechanisms among others to achieve homeostasis and to cater for self-actuation and life needs. Most if not all of the corresponding described functions of the zHeart can be explained.

7.1.3. The discretionary dynamics of the circulation on top of the stabilizing, perfusional, and transporting functions of the basic circulatory system can be understood.

7.1.4. This structure now includes the cortical autonomic system, which being in the limbic system, embraces mechanisms and control functions highly related to the Shen mastery associated with zHeart. This has not been embraced in previous models.

7.1.5. Understanding the whole body entirety for a person's integrality over social situational and thermal homeostasis helps to further understand regulatory and perfusional disorders associated with zHeart.

7.1.6. This illustrates for the first time in CM literature how the mind-body, perfusion, brain-heart, body heat, temperament, and climatic thermal environment can interact and influence each other, just like what is observed in Nei Jing and supported with current research literature.

7.1.7. The physiology and pathology of the internal supportive complex of neural, circulatory, neuroendocrinal and receptor function can be used to explain the external manifestations of Zang organ networks and

Zang Xiang features.

7.1.8. The statement that "the Heart as Yang zOrgan, Small-Intestine ministering" ("the small intestine serves as its messenger") [166] about the CM zHeart-zSmall-Intestine pairing, can now be better understood in terms of integral perfusion, since the amount of absorption from the small intestine directly influences the capacity of body perfusion and its irrigation. Besides, in terms of thermal heat, Tai-Yang channels, which in the arm is the zSmall-Intestine channel, refers to the body area most exposed to the sun, a maximal heat-receiving area that warms the body for the zHeart to dispose. In a way, the pair relieves thermal loads mutually. It is only in current times that Chinese medicine workers over-generalized the association pair as related all by meridians.

7.1.9. The statements in Nei Jing concerning summer heat, wills without anger, transformation of spirits, suffusing for vascular circulation, and, venting for adaptation concerning zHeart [109,163] can now be more easily understood as to how they are tied together.

7.1.10. The statements in Nei Jing that "zHeart carries vascular circulation ("The heart houses the pulse"), and in this resides the Shen" [135] can now be better justified. This is best appreciated by paraphrasing it with: "perfusional (vascular circulation) and information resources (for Shen) go hand in hand under zHeart".

7.1.11. This model provides a match between anatomy and function of the Zang organ. This is more acceptable to modern science. This platform can pull ancient Zang concepts to modern medicine and will allow elaborations on zHeart and diseases in plain words. (Plainer translations of difficult CM texts in the lifted-up platform in this article could be better from those common translations [195] in bracketed quotes behind them).

This anatomico-functional structural formation is an integrated system. It is richer in breadth and depth than former models. The anatomico-functional model would expand our framework to probe for more useful research and observations to understand and utilize the CM concepts, and build CM models based on scientific acceptable structures to elaborate ancient literature on health and diseases of zHeart. The important past observations are retained, the split brain-heart controversies eliminated, while the present model offers a more stable comprehensible entity. This should help to settle the heart vs. brain controversy

over zHeart started since the Ming dynasty that followed blindly the reductionist frame of western medicine that time. This paper, together with the similar paper on zKidney [1] and zSpleen [2], help to redefine Zang and Zang Xiang in terms of a functional structural complex as the internal Zang, with its Zang Xiang manifestations expressed externally, and illustrate an approach [5] applicable to understand all the five Zangs. This functional structural complex as the internal Zang may be viewed more succinctly as an “organ complex” [2]. Western medicine describes organs and systems; with the word organ meaning a fully differentiated structural and functional mass in one unit specialized for some particular function, and system meaning a related organ group interactive for some particular specialized function. In contrast, this “organ complex” means an extended series of connected organs packed together in one formation, being closely interactive for some related specialized function. Organ connectedness could have phylogenetic origin in which close interactions such as nervous and perfusional directives and development are mutually evolving.

7.2. Help further understanding

Previous findings can now be re-interpreted with this model. Further studies should relate how treatment to strengthen the regulated neural-circulatory-perfusional synchrony and thermal homeostasis would strengthen the zHeart and alleviate zHeart symptoms.

CM zHeart dysfunction relates to the heart itself, the blood channels and the mind. Main symptom of zHeart dysfunction includes heart diseases, cardiovascular unrest with integral perfusion disorders and loss of heart-mind mastery as a range of functional psyche disorders. These may manifest as heart diseases, palpitations, arrhythmia, fright, insomnia, cardiac neurosis and cerebrovascular diseases. Alterations in heart Yin-Yang dynamics may be seen in deficiency of zHeart-Qi and deficiency of zHeart-Yang. The motivity propagatory energy of and from the heart is called zHeart-Qi, and its deficiency may cause cardiac palpitation, shortness of breath and chest tightness that are aggravated by physical exertion, a pallid complexion, weariness with weakness, and spontaneous sweating with a pale tongue. Palpitation and chest discomfort are prerequisite for this diagnosis [196]. The heart's control over blood and the blood vessels depends both upon

zHeart-Qi for motivity force and upon zHeart-Yang for warming against stagnancy. In addition to the above symptoms, zHeart-Yang deficiency will have cold-aversion, cold limbs, heart pain, pallor of the complexion, and cyanotic lips with a pale and plump tongue and thready indistinct pulse. Insufficiency of zHeart-Blood, common in chronic illness with loss of nourishment for the heart, mind and the entire body, causes palpitation, insomnia, dream-disturbed sleep, forgetfulness, pale lips and tongue and a thready feeble pulse. In zHeart-Yin deficiency, there is additionally heat in the palms and soles, flushed cheeks, recurrent feverishness, night sweat, and oral aphthous ulcers with tongue red and dry. Emotive problems often come when lacking the sustaining Yin substances, and dry assertiveness suffers with consequent worries, palpitations, and temperamental changes. Worsened, zHeart-Fire may blaze and disturb the mind and the blood and meridian channels, causing restlessness with insomnia, aphthous sores, flushed face, thirst, difficult and painful deep-colored urination, dry constipation, yellow coated red tongue, rapid pulse, and even worsening with hematemesis, epitaxis or agitation with delirium. To note, the zPericardium that covers the heart [7], which when deranged has associated mental symptoms in CM, is not described here as it was very little described in Nei Jing except along with Meridians. It protects the heart and in CM its dysfunction affecting the zHeart could be related to channel problems.

With the model, these classical syndromes could be further delineated with modern anatomical structures and physiological mechanisms at those many interrelated levels. In general, the zHeart disorders may occur from the brain in endeavors following motive or emotive directives, from the heart in performing motor and motional with circulatory problems, and during adaptive problems of both brain and heart reciprocally according to homeostatic or situational demands. These need be supported by zHeart-Qi to circulate blood well, zHeart-Yang to prevent blood stasis, Yin nourishment and no vascular blocks, wherewith deficiencies cause problems. Developing tests for stability or facilitative cohesiveness of internal interactive mechanisms of zHeart, including neural-circulatory-perfusional dynamics on one hand and neuroendocrinal receptor aspects on the other hand, may develop good indices to measure zHeart strength and how use of

massage and environmental enrichment, or thermal management, may strengthen it. Oxytocin levels and receptor functions [197,198] over the heart and brain may help differentiating zHeart-Yin nourishment and deficiency states, and assessment of VEGF may be useful to clarify angiogenic and lymphangiogenetic status [199]. Additional anatomical and physiological assessment by brain functional scans in addition to tests of parasympathetic and sympathetic activity [200] over heart contractility, and evaluation of thermal and social factors, should improve defining the different zHeart dysfunction syndromes and the state of the circulatory regulation and operation over various defined situations. The person's self-adjustment and mastery in behavior and capital of neural-circulatory-perfusional synchrony and thermal homeostasis may be useful assessment areas. A diagnosis of zHeart dysfunction would then, apart from the diagnostic label of zHeart Qi, Yang, Yin, or Blood deficiency, comprise of the fuller diagnosis with the various levels of derangement specified. All these may allow better clinical differentiation and application in treatment, with the Zang organ and Zangfu manifestation theory in concert with modern medicine.

Therapy is based on the clinical syndrome diagnosed, and therapy under the present model allows manipulation and treatment at the various levels. CM therapy of zHeart dysfunctions has been useful to treat circulatory and mental disorders. Other modules of treatment could then be explored and coordinated with herbal treatment or with acupuncture for the type of zHeart deficiency. How heat-clearing zHeart herbs help soothing heated mental agitation could be explored experimentally. Here the present model should predict that further study on therapy on heat would strengthen the heated zHeart in regaining perfusional adaptation. There can also be local assertion-perfusional dysfunctions. To note, Armand clematis (mutong), which clears zHeart heat through the zSmall Intestine, would besides soothing the disquieted heart also help with oral ulcers. To note, Mutong and Shengdi (Rehmannia root) are used in concoction in the therapy of zHeart heat translocated to zIntestine in the syndrome of daochi powder. Perfusion characteristics are improved that heat is redistributed and calmed by diuresis (as CM describes mutong drives downwards to facilitate urination thereby clearing zIntestine

fire), and perfusion is somehow also helped by Rehmannia. By the same token, *Boswellia carterii* (ruxiang) another heat-clearing zHeart herb, besides alleviating pain, is used to treat ulcers, non-healing boils and gangrene. Notably, Nei Jing described how pain and boils are related to the zHeart [201] and can be appreciated in the present model as irrigational malperfusion with heat and is open to treatment. All these emphasize that perfusion should be taken account of when addressing any zHeart model.

Diseases of the actual organ of the heart or brain are more complex and related to many zOrgans, not only zHeart deficiency. Cerebrovascular diseases under CM assessment would manifest with a variety of mixed syndromes, from phlegms to blood stagnancy, and from zHeart to zLiver and zKidney dysfunctions [202,203]. Worth noting though is that before cerebrovascular events, there can be CM signs and syndromes traceable [204]. Heart failure is similarly complex. Correcting basic attributes such as cardiac contractility related to zHeart-Qi deficiency would help. For zHeart-Yang deficiency, there basically exist circulatory-perfusional reactions similar to those reacting to prolonged cold temperature. Besides herbs, modulation in thermal environment should also help as expected in the model. In the summer heat, zHeart-Yang deficient patients often find some relief. Patients with congestive heart failure, with progressive severity of disease, lose their autonomic control and diurnal variation of parasympathetic/sympathetic balance [205-208]. Starting here, while modern workers would consider managing vegetative dysfunction of motivational to motional mismatch, CM specialists would try to clear the channels [186] while strengthening the neurocirculatory capital through whole body synchrony to achieve good Yin-Yang reperfusional dynamics [209, 210].

In the present model, the neural-circulatory-perfusional interrelationship should synchronize when each and every component feeds in positively. Thus the current therapeutic strategy by the current model-A advocates to treat both heart and brain can still be used. Interventions to strengthen the zHeart capital and alleviate adaptational dysfunction by restoring normal autonomic control include herbs and lifestyle change. It is often observed in practice [211] that treating ill patients their whole body for strength and relieving painful sites and nuclei, the body harmony or synchrony can be more

easily achieved. Interruption of the cascade of autonomic and proinflammatory pathways helps preventing depression and stress responses and heart disease [111]. Interventions at the higher nervous system level, experimentally, may also be beneficial during heart failure [212,213]. The paraventricular nucleus of the hypothalamis could contribute to the neurohumoral excitation commonly observed in heart failure [214]. Addition of herbs acting on the limbic system for modulation of emotions can be considered [215]. Restoring the functional balance of the vegetative nervous system would help other multi-organ disturbances. On circulatory dynamics, mismatch between the tissue demand for oxygen and the supply capacity of the circulatory system can get progressively worse in thermal demand, adverse environment or dry assertiveness, so that tissues became hypoxemic, or the body reacts seriously to compensate. The endeavoring achievement and cardiac performance may not suffice for the body needs, with an increasing likelihood that the cardiovascular system is compromised and limits tissue oxygen delivery to important structures. Reviving the neural-circulatory-perfusional match for the body should help preventing pathology. Therapy should consider modulating the surface and border-zone perfusion (a CM principle [216] “when zHeart is harmed”), and, reversing hemodynamics beyond limits threatening one’s ability to maintain adequate cardiac output and perfusion, through decreasing the magnitude of body stress responses, and reversing a mismatch perfusion to assertive behavior. Patients need to commit time and lifestyle change to reduce imprudent mismatch. Discretionary dispositions in lifestyle through programs interacting with an ecological system matched to host ability may be worked out, in addition to prescription, facilitated with various forms of environmental manipulation and situational experiential reprogramming. The re-mastery of the zHeart with mastery of the pattern of motivational and emotional behavior would allow one to become prudent, improving return of psychophysiological synchrony with increased capital and reserve for tolerating changes. Development of the self for the person from infancy to adulthood should install in himself a match by neuro-endocrinal and circulatory adjustment along his own original balanced self-integrity profile for a zHeart capital and capacity for his environment. It consolidates the need for the concept that

the whole system is meant for circulation and situational endeavors.

CM somehow saw in ancient times that link as a whole between the mind and heart, which reciprocal interactions are established with recent advances. CM literature illustrates how the mind, body, heat, brain, and thermal environment influence each other. The body with variable motivity and emotivity in terms of integral needs has to be perfused to fulfill its adaptation and actions for functional actualization. The understanding of zHeart should raise possibilities for research in adapting mainstream medicine to the overall clinical and investigative approach to patients with heart and mind problems to augment therapies.

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綜論中醫心臟以重建解剖與功能 關連之結構模組

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本文以現代醫學理解的層面描繪傳統中醫學說中的[心]臟。傳統中醫學說以「臟象學說」演繹臟腑。過去數十年的現代研究中醫[心]臟理論，展示了心臟收縮力與效能代表心氣，這顯明中醫心主血脈，但研究上未能證實由此可帶出心主神明，是為中醫學現代化的結——心主神還是腦主神兩觀念使中醫分歧而對立。按中醫學說中“臟”指本來部位以外之維度，本文綜論[心]臟，以血循環基層機能及策外對應的調節層面切入，具體把中醫[心]臟的結構與功能互相連結，將由心(器官)連至大腦的自主神經系統的機組，視為「居於內」的[心]臟。這機組的下部分的延腦心臟自主系統會管理血液循環穩定性；上部分的大腦自主系統則管理情勢需要的血脈循環反應，具備用心或用力的變化狀態，好比中醫的「神之變」；這個結構與全腦全身一體聯繫，配合小腸供液功能，一統自主血液循環與神緒中情感及理智等功能的表現可視為「觀於外」之[心]臟的臟象。神經及血液循環網絡在發育過程中，會隨著不同環境變化，互相調控以適應人體謀慮及行動的需求，而最終化育為成熟的系統。該系統藉由神經、內分泌、熱能管理及血液循環等機理互應，心與其他臟器可以發揮精良的功能並且互相同步調節，而促進精神自主，好比中醫所謂「心者君主之官也，神明出焉」。情緒/動機或動作-神經-循環-血液灌注-環境整體張力及動態，互為配合來穩定支援個體機變行動(中醫所謂任物)來應付生命。這[心]臟範式與中醫學的心臟本質意義相距不遠，但比過去的模式更為貼切，去除心腦對立觀念，更能成全主流基本要求標準，因其中解剖與生理的密切關連。這是中醫文獻首次演繹內經一體所說及精神、身體、血流、心腦、熱能、情緒、環境天時的互相影響，亦有以現代研究支持。因此，這模型比起過去的理論模型，較易為現代科學的同儕所認受，其中提出臟器群的特色可供主流醫學參考。本文亦介紹古籍及現代研究複證的方法，有助於中西醫學發展，並帶來獨特及具啟發性的看法。

關鍵字：中醫心臟、心主神與腦主神之分、臟象、功能解剖結構、臟器群、現代醫學

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