Acupuncture and Heart Rate Variability: A Systems Level Approach to Understanding Mechanism

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Recent research has elucidated several different mechanisms for acupuncture. However, the interrelationship between these mechanisms and how acupuncture affects complex physiological systems is still not understood. Heart rate Variability (HRV), the beat-to-beat fluctuations in the rhythm of the heart, results from the regulation of the heart by the autonomic nervous system (ANS). Low HRV is associated with increased risk of all-cause mortality and is a marker for a wide range of diseases. Coherent HRV patterns are associated with increased synchronization between the two branches of the ANS, and when sustained for long periods of time result in increased synchronization and entrainment between multiple body systems. There is strong evidence from randomized placebo controlled trials that acupuncture modulates HRV. This may represent a mechanistic pathway for global physiological regulation, which is congruent with East Asian medical theory. The ability of acupuncture to improve HRV could be used as a tool in acupuncture research and practice to monitor treatment effectiveness and the impact on quality of life.

Key words: Heart rate variability, acupuncture, global physiological regulation, translational research, acupuncture mechanism

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MECHANISMS OF ACUPUNCTURE

Over the past three decades, a great deal of research has examined proposed mechanisms to explain the effects of acupuncture. Much of this research has focused on the role of the nervous system, specifically the secretion of a range of neuropeptides, such as endorphins and monoamines.[1,2] Neuroimaging studies have shown that acupuncture can modulate several regions of the brain including the somatosensory cortices, limbic regions, the anterior and posterior insula, and the prefrontal cortex.[3-6] Studies examining the connective tissue surrounding acupuncture points and along the length of acupuncture meridians suggests that these regions are associated with increased thickness of connective tissue, which forms vertical connective tissue planes.[7-9] The connective tissue has been shown to be the basis of needle grasp (de qi needle sensation) and the propagation of mechanical and chemical signals both local and distal to acupuncture points. There is some evidence to suggest that meridians and points have reduced electrical resistance and impedance and higher capacitance compared to surrounding controls, although the general poor quality of studies of this theory has prevented any substantive conclusions.[10,11] Collagenous bands are found to be significantly associated with lower electrical impedance, which may account for reduced impedances previously reported at acupuncture meridians.[12]

Despite the various above-described studies we still lack a clear picture of how acupuncture works.[13] In particular, it is poorly understood how these various mechanisms may work together, and there are no models reflective of global physiological regulation that would be compatible with traditional East Asian medicine theory. In this article we propose that Heart Rate Variability (HRV), which is the way in which the time intervals between heart beats changes over time and is reflective of autonomic nervous system function, may have a role in global physiological regulation and could be used as a biomarker for acupuncture.

Systems theory as it is applied to biology proposes that living systems are composed of numerous interconnected, dynamic networks of biological structures and processes. Unlike the reductionist view of the body, the systems view proposes that the parts work together in an integrated fashion with many levels and layers of information being communicated to facilitate optimal functioning. Such a perspective has many parallels with traditional East Asian medicine theory[14] and the way in which the heart and coherent HRV patterns[15] may reflect the dynamic interplay between various physiological processes in the body. The ability of acupuncture to modulate HRV could imply that acupuncture may function by regulating and integrating the various physiological systems in the body.

In this sense acupuncture could be viewed to function as a global physiological regulator, which would be congruent with traditional East Asian theory that is based on the notion that everything in the body is interconnected. The acupuncture meridian system facilitates the movement of qi, which has been proposed to be information that allows interconnection and communication.[14,16] The Heart in Traditional East Asian medicine is termed the monarch organ, reflecting its superior role

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ISSN 1550-8307/$36.00

doi:10.1016/j.explore.2011.12.002

and as discussed below is compatible with recent research demonstrating the multifunctionality of the heart organ. As biology increasingly embraces theories originally proposed to describe complex systems (systems biology), the concept of global physiological regulation by subtle interventions such as acupuncture may be explored as a putative mechanism for both organism regulation and acupuncture biomechanism. In a recent NIH National Center for Complementary and Alternative Medicine (NCCAM) sponsored workshop focusing on the application of the principles of complex systems to integrative medical research[17] the importance and value of capturing the global state of a system through parameters like HRV was emphasized. We propose that future research into the mechanisms of acupuncture should potentially focus more on HRV and other systems-level markers of physiological function rather than on specific molecular markers more appropriate for investigating less complex interventions.

In this article we explain what HRV is and its physiological and pathological significance. An argument is presented to support the notion that acupuncture treatment improves HRV based on the literature analyzing this issue in randomized placebo controlled trials. The parallels between acupuncture as a global physiological regulator and traditional East Asian medicine and systems theory are discussed. Finally, we explain the ways in which HRV could be used as a multifaceted translational research tool.

HEART RATE VARIABILITY

Heart rate variability refers to the beat-to-beat fluctuations in the rhythm of the heart, or the way in which the time intervals between heart beats change over time.[18] This variation results from the regulation of the sinoatrial node of the heart by the sympathetic and parasympathetic (vagal) branches of the autonomic nervous system (ANS). HRV therefore reflects the activity of the ANS and is affected by internal and external stimuli that regulate the ANS. Examples of internal stimuli include respiration, thermoregulation, humoral regulation (rennin-angiotensin system), blood pressure, and cardiac output. External stimuli include environmental factors and our reaction to them (emotional, psychological, and physical stress and conditions that engender calmness). Age and gender also affect HRV.[19,20]

Physiological and Pathological Significance of HRV

Heart rate variability is a predictor of morbidity and mortality, and has been investigated in the context of many medical conditions.[21] A high degree of HRV is preferable as it indicates that the body has greater flexibility and adaptability in response to changing conditions. It has been recognized for many decades that low HRV is associated with increased risk of all-cause mortality, and low HRV has been proposed as a marker for disease.[22] The relationship between HRV and morbidity and mortality associated with diabetes, hypertension, and cardiovascular disease is well recognized.[23-26] More recently evidence has been presented for vagal regulation of three systems associated with physiological regulation and allostasis: glucose regulation; the hypothalamic-pituitary-adrenal (HPA) axis system; and inflammation.[27] As the authors state, these systems are all critical to the wear and tear on the physiological systems associated with health and disease, and as such may explain the association of low HRV with increased morbidity and mortality in a growing list of diseases. Evidence has been presented in support of vagally mediated HRV in the regulation of affective and cognitive processes as well, indicating that low HRV is a risk factor not only for pathophysiology but also psychopathology.[28]

HRV Analysis

HRV analysis is a powerful, simple, accurate, and reliable tool for assessing ANS function. The source information is the continuous beat-to-beat measurement of interbeat intervals using an electrocardiograph (ECG). Twenty-four-hour ambulatory measurements using a simple, small, unobtrusive device permit continuous measurement of ANS activity and balance within the context of normal day-to-day activities in the subject's usual surroundings and also take into account sleep and circadian rhythm data. Two types of analysis of HRV data are typically undertaken: time and frequency domain analysis. Time domain measures are the simplest to calculate but unlike frequency domain measures do not provide information about the different branches of the ANS and their circadian rhythms. Time domain measures describe how much variability occurs in the heart rate over a 24-hour period and involve statistical analysis of the fluctuations in sinus RR intervals.[29] The most important time domain measures are the heart rate, the SDNN (standard deviation of all normal sinus RR intervals over 24 hours), the SDNN Index (the mean of the standard deviations of all normal sinus RR intervals for all 5-minute segments), and the RMS-SD (the root mean square of successive differences between normal sinus RR intervals).

Frequency domain or power spectral density (PSD) analysis yields information about the amount of the variance (power) in the heart's rhythm explained by periodic oscillations of heart rate at various frequencies. These frequencies, when grouped together in bands, provide a detailed view of cardiac autonomic modulation.[18] A standard approach is to calculate power in four bands: high frequency (HF) (0.15-0.4 Hz), low frequency (LF) (0.04-0.15 Hz), very low frequency (VLF) (0.0033-0.04 Hz), and ultralow frequency (ULF) ($<$0.0033 Hz).[22] HF is mediated by the parasympathetic (vagal) nervous system.[22] LF is mediated by both the parasympathetic and sympathetic nervous system.[30,31] The ratio of LF/HF is often used as a measure of sympathovagal balance,[32,33] but because LF includes both parasympathetic and sympathetic, this can be misleading.[34] Although the physiological mechanisms associated with the VLF and ULF are not well understood, the VLF is believed to reflect activity of the sympathetic nervous system.[35,36]

ACUPUNCTURE AND HEART RATE VARIABILITY

Numerous studies have investigated the impact of acupuncture on HRV in both humans and animals. In 2010, a systematic review of human studies was published.[37] This review only included randomized controlled trials that compared acupuncture to a sham (placebo) acupuncture intervention. Of the 12 studies that met the inclusion criteria for the systematic review, five showed that the subjects in the acupuncture group had improve-

Table 1. Summary of Randomized Placebo Controlled Trails Examining Acupuncture and Heart Rate Variability

Study (by Last Name of First Author)	Subjects: Healthy (H)/Diagnosed (D)	Clinically Valid Intervention	Sham (Placebo) Intervention[b]	Modulate HRV[d]	HRV Outcome[e]
Agelink	D: minor depression and anxiety	Yes	MPnAP	Yes	VA - ↓ LF/HF vs SA
Backer	D: migraine	Yes	MPnAP	Yes	VA - ↓ HF vs SA during 1st and 12th session Both VA and SA - ↓ LF in subjects who had ↓ headaches in response to VA or SA
Lee	D: post stroke insomnia	Yes	NPAP	Yes	VA - ↓ LF/HF vs SA
Kristen	D: congestive heart failure	Yes	NPAP (S)	Yes	VA ↑ SDNN vs SA
Hwang	H + night shift stress	No	PnAP	Yes	VA - ↑ HF, ↓ LF, ↓ LF/HF vs SA
Li	H + fatigue	No	MPnAP	Yes	VA - ↑ HF, ↓ LF, ↓ LF/HF vs SA
Kang	H + mental stress	No	MPnAP	No	No change
Park	H + mental stress	No	MPnAP	Yes	VA - ↓ LF, ↓ LF/HF vs SA
Jeong	H + caffeine	No	MPnAP	No	No change
Chang	H	No	MPnAP, no EA[c]	No	No significant change
Haker	H	No	MPAP	No	Both VA & SA - ↑ HF & LF
Wang	H	No	PnAP	Yes	VA - ↑ HF, ↓ LF vs SA
Huang[a]	H	No	PnAP	No	VA - ↑ nHF vs no treatment Both VA & SA - ↑ mean RR interval vs no treatment
Rheu	H	No	MPnAP	No	No significant change
Streitberger	H	No	NPnAP (S)	No	Minimal significant change
Carpenter	H	Yes	NPAP	Yes	VA - ↓ LF/HF vs SA

[a]Only study that included a no treatment control.

[b]MPnAP – minimal penetration on nonacupuncture point(s); NPAP—no penetration on real acupuncture points; MPAP—minimal penetration on real acupuncture points; PnAP—penetration on nonacupuncture points; NPnAP—no penetration on nonacupuncture points; (S) Streitberger needle.

[c]Only study that used electro-acupuncture (EA) in the real acupuncture group, no EA was used for the placebo control.

[d]Comparing verum acupuncture to the placebo acupuncture control.

[e]HF— high-frequency; nHF—normalized high frequency; LF—low frequency; LF/HF—low-frequency high-frequency ratio; SA—sham (placebo) acupuncture; SDNN—SD of all normal R-R intervals during 24 hours used as a marker of overall hear rate variability and sympathetic tone; VA—verum (real) acupuncture.

ments in HRV following acupuncture compared to subjects in the placebo control group.[38-42] Of the remaining seven studies two studies showed improvements in HRV in both the acupuncture and placebo control groups.[43,44] Although the overall conclusion based on meta-analysis was that there was "no convincing evidence for the effectiveness of acupuncture in modulating HRV," there were a number of significant problems with these studies, as noted by the authors and discussed below. Since this systematic review was published, four randomized placebo controlled trials investigating acupuncture and HRV have been published, all of which showed that acupuncture improved HRV.[45-48] All randomized placebo controlled trials (a total of 16) undertaken thus far are presented in Table 1. Taken together, the data suggest that acupuncture improves HRV as discussed below.

Of the 16 randomized placebo controlled trials (Table 1), 11 of these studied healthy subjects at their normal baseline state or under conditions of artificially induced stress, one studied healthy subjects following the stress associated with three consecutive days of night-shift work, and four studied subjects with medically diagnosed conditions (depression and anxiety, migraine headaches, poststroke insomnia, and congestive heart failure). One issue with studies involving healthy subjects is the degree to which it would be reasonably expected that acupuncture would improve HRV, especially if the subject already had a healthy high level of HRV. The problems associated with using healthy subjects upon the validity of acupuncture trials has been raised by several leading acupuncture researchers.[49]

Only 3 of the 16 trials investigated the association between the impact of acupuncture on HRV and improvements in the medical condition that the subjects were being treated for. All of these trials showed that acupuncture can modulate HRV, and that the improvement of HRV is correlated with improvement of their medical condition. Bäcker et al.[41] examined subjects with migraine headaches. Across all subjects there was significant improvement in headache symptoms and quality of life. However, there was no significant difference between the acupuncture and placebo control group. Acupuncture (real and placebo) induced significant changes in HRV that were different between the real and placebo subjects, and between the subjects that did or did not have an improvement in headache symptoms. Differences between real and placebo acupuncture groups was in the HF power of HRV, with real acupuncture inducing a stronger decrease in HF power, and was independent of the headache response to treatment. Differences between the headache responses to treatment were in the LF power of HRV, with responders exhibiting a decrease in the LF power of HRV. Taken together, the authors conclude that the therapeutic effect of real

and placebo acupuncture in migraine might be related to an overall decrease of sympathetic nerve activity.

Lee et al. (2009)[50] looked at the impact of acupuncture on post-stroke insomnia. The group that received real acupuncture showed significant improvements in insomnia and a significantly greater reduction in the LF/HF ratio of HRV compared to the placebo control group. The authors concluded that the acupuncture treatment used in the study appeared to reduce sympathetic hyperactivities and may be a useful therapeutic method for poststroke insomnia.

The third study examined the effect of acupuncture on subjects with congestive heart failure.[46] Subjects receiving real acupuncture showed significantly increased ambulated 6-minute walk distance, postexercise recovery after maximal exercise, ventilatory efficiency, and quality of life compared to the placebo control group. Subjects in the real acupuncture group also showed significantly improved HRV (as measured by SDNN) compared with the placebo control group.

Another critical limitation associated with the majority of studies included in Lee et al.'s[37] systematic review and the additional studies published since then (Table 1) was the very low dosage of acupuncture that was used. Seven of the 12 studies on healthy subjects used just one acupuncture point,[38,43,44,51-54] three studies used two acupuncture points,[40,42,55] one study used four acupuncture points,[48] and the remaining study[45] used 10 acupuncture points. All 12 studies on healthy subjects only gave the subjects one acupuncture treatment between the pre- and postacupuncture HRV measurements. Acupuncture treatment that accurately reflects clinical practice usually includes 4 to 10 (or more) acupuncture points given in each of six (or more) acupuncture treatments. In Table 1 an assessment of the studies as to whether they included a clinically valid intervention is presented.

Interestingly, in the four studies on medically diagnosed subjects, three of the four studies[39,41,46] involved administering a course of acupuncture treatments (10 to 12 treatments, using 5 or more acupuncture points per treatment), and the fourth study[47] used intradermal acupuncture needles for three days All of the protocols used in these four studies resemble usual clinical practice and all of these studies showed that acupuncture could modulate HRV compared to the placebo control group. However, of the 11 studies using healthy subjects with low doses of acupuncture, only 4 studies demonstrated a change in HRV in the acupuncture group compared to the placebo control group. Thus, inadequate dosing appears to have substantially confounded the results of many of these studies.

Much has been written about the difficulties of designing effective placebo or sham acupuncture interventions.[49,56] All types of placebo acupuncture interventions have been criticized and argued to be capable of eliciting therapeutic effects. The general consensus among highly experienced acupuncture researchers is that placebo control groups are not a reliable way of determining the effectiveness of acupuncture, and that acupuncture interventions also need to be compared to no treatment or usual care control groups.[49] Only 1 of these 16 studies included a no treatment control group,[44] and this study showed that acupuncture did improve HRV compared to no treatment, but not when compared to the placebo control. Additionally, another study, not included in the systematic review because it did not include a placebo control group,[57] reported significant effects of acupuncture in improving HRV compared to the no treatment control group in subjects with hypertension.

With regard to these 16 studies there are a couple of interesting trends in relation to the placebo control. First, the impact of a possible therapeutic effect from the placebo is more likely to negatively influence trial outcomes when the dosage of acupuncture is low. This is because a low dosage of acupuncture is likely to have only a small amount of therapeutic benefit, which when compared to a placebo control (that itself may have a small amount of therapeutic benefit) is likely to result in nonsignificant differences between the two. Eleven of these 16 trials used a very low dosage of acupuncture. Of these 11 trials, only four showed that real acupuncture modulated HRV compared to the placebo control. Interestingly, an additional two showed that both real acupuncture and placebo acupuncture modulate HRV. This is to be compared to the five trials that included clinically valid acupuncture dosages, which all showed that real acupuncture modulated HRV compared to the placebo control. Second, placebo acupuncture interventions vary as to their validity as a negative control. Validity is determined by the degree to which they are truly inert and therefore do not deliver any therapeutic benefit. The best placebo acupuncture intervention thus far is the Streitberger needle.[58] This is an acupuncture needle where the shaft of the needle collapses into the handle upon "insertion" and therefore results in no real insertion. This is believed to be the most inert placebo acupuncture control. Two of the 15 trails used the Streitberger needle and both of these showed that real acupuncture did modulate HRV compared to the Streitberger needle placebo control.

When these various methodological issues are taken into account, the results of these 16 randomized placebo controlled trials strongly suggest that acupuncture can improve HRV, especially when acupuncture is delivered in clinically valid dosages to subjects with a medically diagnosed condition and with the inclusion of an inert placebo control.

GLOBAL PHYSIOLOGICAL REGULATION AS A PUTATIVE MECHANISM OF ACUPUNCTURE

Acupuncture Mechanism and the Role of the Heart Organ from a Traditional East Asian Medical Perspective

An explanation of physiology and pathology from a traditional East Asian medical perspective is beyond the scope of this article. However, a brief overview of traditional East Asian medicine concepts related to global physiological regulation and the role of the Heart organ are relevant in the consideration of HRV in relation to a possible putative mechanism of acupuncture.

A fundamental principle of traditional East Asian medicine is interconnection.[16] Unlike in Western philosophy, traditional East Asian medicine is not rooted in linear cause and effect, but rather the notion that disease reflects disharmonies present on multiple levels of the system both physically and psychoemotionally. The signs and symptoms, even those that may appear unrelated, are registered as aspects of a presenting disease pattern in the context of the whole system. In this sense traditional East Asian medicine theory has parallels with systems theory.[14] The

acupuncture meridian system is an "invisible" lattice that links together the physiological components and functions of the body and is thought to embody a kind of informational network.[14,16] Recent research[7-9] suggests that the anatomical basis of the meridian system may be the contiguous fabric of connective tissue, and through connective tissue signaling the maintenance of homeostasis and potential to correct imbalance may occur. From this perspective the most fundamental mechanism of acupuncture would appear to be global physiological regulation. Perturbation of the meridian system, by stimulating points or areas in the lattice, sends a signal through this interconnected system to restore normal function to a disharmonious state.

There are some intriguing early findings in the scientific literature supporting this notion that acupuncture operates physiologically through a global regulatory mechanism. For example, of interest with regard to HRV and the ANS is the research demonstrating the role of the sympathetic nervous system as the mechanistic basis of acupuncture for treating polycystic ovary syndrome[59] and cardiovascular conditions such as hypertension and myocardial ischemia.[57,60] Likewise, the findings from neuroimaging studies that acupuncture affects a wide range of different brain regions and their associated functions may also be reflective of acupuncture being a complex intervention which works at least in part by eliciting sensory, affective and higher cognitive/evaluative effects upon the brain.[13]

Qi is the vital force stimulated by acupuncture and is defined as "form" and "function." So, too, the internal organs have "form" and "function": the Heart shares anatomical features and certain functions in common with the biomedical understanding of the heart organ. However, in traditional East Asian medicine the Heart is considered the most important organ, described as the "ruler" or "monarch" of the internal organs.[61] The Heart is responsible for the vessels and the circulation of Blood. The Heart houses what is called "shen," translated as spirit, mind, consciousness, that is, mental activities: ability to think, be present and lucid, to be measured, appropriate, and paced in response.[62] Although the Heart is thought to be damaged by sudden fright, shock, or excess excitement, the Heart registers any and every emotion because the Heart in traditional East Asian medicine is the only organ that "feels." So ongoing stress or overstimulation can injure the function of the Heart, which is not only related to its "beat" but its ability to reign and maintain global homeostasis.

HRV as a Marker of Global Physiologic Regulation

HRV patterns that are organized as a stable pattern of repeating sine waves with a very narrow, high-amplitude peak in the LF region are termed coherent.[63,64] Coherence implies connectedness and consistency in the system where the emergent whole is greater than the sum of the parts. Systems require global coherence to function efficiently and effectively. When HRV shows coherence there is increased synchronization between the two branches of the ANS and a general shift in autonomic balance toward increased parasympathetic activity. Research has shown that when coherent heart rhythm patterns are sustained for long periods of time there is increased synchronization and entrainment between multiple body systems.[65] The term psychophysiological coherence is used to describe this effect manifesting on the physiological, psychological, and behavioral levels.

HRV coherence is associated with many physiological benefits in the system including improved short-term blood pressure control and respiratory efficiency, increased vagal afferent traffic, which inhibits pain signals and sympathetic outflow, increased cardiac output and efficiency, improved cardiovascular flexibility, and increased temporal synchronization of cells throughout the body.[65] This wide range of physiological benefits and the psychological and behavioral benefits are probably attributable to the fact that the afferent networks that connect the cardiovascular system with the brain are far more extensive than the afferent systems associated with other major organs.[66] Recent research has shown that the heart is much more multifunctional than previously thought. In addition to its role in pumping blood, it also functions as a sensory organ and as a complex information encoding and processing center. The emerging field of neurocardiology has demonstrated that the heart has an extensive intrinsic nervous system termed the "heart-brain" containing over 40,000 neurons, which can sense, regulate, and remember, and act independently of the central nervous system.[67,68] The heart is also part of the hormonal system synthesizing and secreting a number of hormones and neurotransmitters.[68-72] In addition to the neurological and biochemical modes of heart function, this organ also communicates through biophysical (pressure and sound waves) and energetic (electromagnetic field interactions) means.[65] This multifunctionality enables the heart to have a unique role in synchronizing the activity of multiple body systems across different levels of organization, "reigning" much like the function of the Heart in traditional East Asian medicine.

HRV AS A TRANSLATIONAL TOOL FOR ACUPUNCTURE RESEARCH AND PRACTICE

We have argued that acupuncture operates at least in part as a systems-level regulator of physiological function, and that HRV is a potentially useful tool for measuring and describing this type of regulatory function. We further propose four ways in which HRV could be developed as an important translational tool for acupuncture research and clinical practice:

1. *Basic science ⇔ clinical medicine–insight into the mechanistic basis of acupuncture.* As discussed above the ability of acupuncture to modulate HRV may be reflective of a global physiological regulation mechanism elicited by acupuncture, which facilitates the optimal interaction of the various systems in the body. It may also provide insight into how the various putative mechanisms for acupuncture relate to each other and provide a foundation for a more holistic understanding of acupuncture mechanism.
2. *Clinical studies ⇔ clinical practice–the impact of acupuncture on stress and quality of life.* In clinical practice it is common to observe that the effects of acupuncture extend beyond those directly relevant to the main complaint. Often patients experience improvement in a range of health related parameters (overall quality of life), for example, sleep, mood, energy levels, stress levels, etc. Patients may be highly satisfied

with the outcome of their acupuncture treatment even though their main complaint may have only improved to a limited degree or even not at all. However, the improvement in their overall health and/or aspects of their health that were especially bothersome, but which they had not chosen to address with acupuncture treatment, may have significantly improved. In such patients an improvement in HRV may well be the underlying reason why their overall health improved and could be used as a tool to monitor such effects both in clinical trials and in clinical practice.

3. *Predictive outcome tool–research findings from clinical trials should serve to inform and define best practices.* If improvement in HRV following acupuncture is correlated with improvement of disease status (reduced symptoms, etc.) then HRV could be used as a tool to differentiate patients into those that are likely or unlikely to benefit from acupuncture. That is, a tool to facilitate optimal treatment choice. For this application, baseline HRV would be compared to HRV measurements taken after appropriate acupuncture treatment. An improvement of HRV could then be used to confirm the choice of acupuncture as an appropriate intervention and justify continued treatment.
4. *Tool to inform the design of controlled trials.* The partial and fragmented understanding of acupuncture mechanism hinders clinical research into acupuncture. It is currently not possible to use mechanistic understanding or outcomes to facilitate clinical trial design. If HRV became accepted as a mechanistic outcome measure, then it may be possible to use it to improve the design of acupuncture clinical trials. For example, much of the acupuncture clinical research has been criticized as being inadequate due to a range of characteristics associated with the acupuncture intervention, such as; the choice of points, the dosage of acupuncture, the use of a fixed acupuncture point protocols for all subjects (fixed protocol bias) and a number of issues surrounding placebo acupuncture controls and whether they are truly inert. HRV being a simple and inexpensive marker of physiological effect could be used routinely in clinical trials to assess the effectiveness of the acupuncture intervention. If the chosen acupuncture intervention is effective, and the placebo intervention completely inert, then a significant proportion of the subjects receiving the real acupuncture should have an improvement in HRV, above that of the subjects in the placebo control group. This HRV outcome measure could function as an internal control of the trial, independent of primary and secondary outcome measures related to the condition being treated.

CONCLUSION

In this paper we propose that acupuncture may function by mediating global physiological regulation through improvement of HRV and synchronization of the two branches of the ANS. As a complex intervention we propose that such a view of acupuncture mechanism is conceptually aligned with systems and complexity theory and is more compatible with traditional East Asian medical theory. It also provides a potentially valuable framework for integrating the various mechanisms that have thus far been proposed to explain how acupuncture works. Given that there is sufficient evidence in the literature to support the effectiveness of acupuncture in improving HRV, we propose that HRV could be used as a translational tool for acupuncture research and practice.

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