

## Abstract:

**Background:** Prevention of disease is a pillar of the practice and teaching of Traditional Chinese Medicine (TCM). In modern medicine the concepts of “health” and “resilience” are less relevant because they are not measurable. Applying tools of complexity science to TCM, these concepts may be quantifiable. Heart Rate Variability (HRV), a noninvasive measure of autonomic balance and considered a tool of complexity science, has been applied to acupuncture studies in both humans and animals typically over a period of minutes/hours, to weeks/ months. A year time frame is considered for this study of HRV data collected in 6 migraineurs.

**Objective and Hypothesis:** HRV data collected as part of an ongoing protocol development project was examined in a group of successfully treated migraineurs. Hypothesis was that their HRV would improve over time.

**Materials and Methods:** Patients monitored in the acupuncture clinic during treatment from the first visit. **Protocol:** Monitoring for 5 minute baseline, during needling and resting for 20 minutes needles in place. Needling protocols varied based on TCM principles and from acupuncture research protocols known to invoke vagal enhancement. HRV analysis of 3 minute segments during treatment over several HRV parameters. Representative 9 minute HRV segments were charted for each treatment.

**Results:** 6 acupuncture patients with definitive reduction in migraine frequency demonstrated an overall improvement in their HRV in the first year of treatment.

**Conclusions:** HRV monitoring showed a general increase in HRV over the first year of treatment in migraineurs with implications for overall “health” and “resilience.”

## Introduction

Traditionally, Acupuncture and Chinese Medicine were used as a preventative health strategy as well as a means to alleviate clinical conditions. Because the objective was to balance energy and optimize health from within, it was taught that the best physicians kept their patients healthy and only second-rate physicians helped them once sick. But in the era of evidence based modern medicine, proof is essential. To show efficacy of prevention, cohort or double blinded well powered studies are required. These are extremely expensive and can be fraught with difficulties in execution. This is particularly true for acupuncture studies where the nonspecific effects are large and the threshold for demonstrating an effect beyond placebo has hindered acceptance of academic studies. Furthermore, the concepts of “wellness” or “resilience” are seldom valued or even recognized by modern academia because they are considered vague and unquantifiable.

But with recent advances in tools derived for “complexity science” these states may, perhaps, be measured. A report from joint workshop convened over a decade ago to explore how complexity science might be applied to Complementary and Alternative Medicine (CAM) research<sup>1</sup> states

*“complexity-based tools may present a revolutionary bridge between qualitative and quantitative measures. Terms such as adaptability, robustness, or health were previously considered qualitative terms and thus were quantitatively intractable. Yet, complexity science has identified analytical methods that can help assess these features...”*

The discussion goes on to identify HRV as a promising technology that is based in complexity science and may help to measure these qualitative states.

*“Because heart rate is dynamically balanced through many elements, including the autonomic nervous system, respiration, hormones, and other physiologic systems,..This capacity to capture the global state of a system or an individual suggests these complexity-based measures may act as surrogates for concepts that were traditionally difficult to measure but considered important for CAM research (e.g., “health” and “adaptability”)”.*

A few recent studies have recognized the potential for HRV to reflect health status in a more global sense. A recent paper called for the implementation of routine HRV monitoring as a biomarker for health and disease.<sup>2</sup>

*“Epidemiologically, high vagal activity, indexed by greater heart rate variability (HRV), independently predicts reduced risk of Global Burden of Disease (GBD)... Biologically, the vagus nerve inhibits oxidative stress, inflammation and sympathetic activity”...*

Another study found that HRV correlated with self-rated health (SRH) better than inflammatory, glycemic or lipid markers. *“We showed that a global measure of SRH is associated with HRV, and that all measures of ANS function were significantly more strongly associated with SRH than any other biomarker.”*<sup>3</sup>

HRV is uniquely suited to academic research since it can capture physiologic shifts over seconds, minutes, hours or days. Because it is a noninvasive measure of autonomic balance, it is useful in clinical settings as well. Autonomic balance affects sleep, mood, pain tolerance, immunity<sup>4</sup> and inflammation and perhaps longevity. Inflammation alone has been linked to multiple health conditions, cancer and heart disease among them. In affecting autonomic balance, there is the promise of improving health in a number of ways. HRV has been extensively studied and a recent literature review concluded that *“Results generally showed negative associations between indices of HRV and markers of inflammation... Overall, we propose that indices of HRV can be used to index activity of the neurophysiological pathway responsible for adaptively regulating inflammatory processes in humans.”*<sup>5</sup>

Interest in the autonomic nervous system’s role in acupuncture goes back decades<sup>6</sup> and we now have a abundant research pertaining to acupuncture’s effect on it. Academic acupuncture research has defined some of the physiology of manual and electro acupuncture on the autonomic nervous system from periphery to specific brain centers<sup>7</sup> which then relay to the vagus nerve, sympathetic system, and the pituitary<sup>8</sup> adrenal axis<sup>9</sup>. There is keen interest in acupuncture’s effect on inflammation<sup>10</sup> through vagal activity. Acupuncture has been shown to

improve autonomic balance in animal studies<sup>11</sup>, healthy volunteers<sup>12 13 14</sup>, and in some clinical studies directed at specific conditions<sup>15</sup>.

In addition, there is some evidence that it may be a biomarker for effective acupuncture treatment from clinical<sup>16</sup> studies showing that HRV improves after needling in patients most likely to respond to treatment<sup>17</sup>. Furthermore, there is some evidence that HRV improves over weeks to months with continued acupuncture treatment.<sup>18 19 20</sup> This study is to explore data from an even longer period, i.e. one year.

This study is a case series of patients successfully treated with acupuncture for migraine. Migraine is characterized by episodic attacks. In stabilizing the system with acupuncture, one would theorize that migraine attacks would be fewer, or non-existent, which was the case in this group. Data was chosen to represent one year or more. Migraine patients are ideal for this type of case study because their results are very clear and measurable as recorded in their diaries. Once migraine patients achieve results, most are motivated to continue treatment so longer longitudinal data sets are possible. The data was collected as part of an ongoing project to develop a workable protocol for HRV measurement in the acupuncture clinic. The focus of the project is to evaluate different needling and related therapies for their effect on HRV during the half hour of treatment. This data was repurposed and examined to represent a snapshot of patient's HRV during an inactive, resting part of treatment. The hypothesis was these patients, might show an overall improvement in these segments over a longer period of time, i.e. one year. Even though this is a small case study, the longer time frame of one year makes the data, hopefully, of interest to the research community. If the hypothesis holds, this might have implications for utility of acupuncture as a true preventative treatment and HRV a metric for improved "health", "resilience" and "adaptability".

## **Materials and Methods**

### **Study Participants:**

Migraine patients included for study presented initially with at least one migraine per week. All patients had decisive clinical improvement within the 6 weeks of treatment as represented by their migraine diaries.

### **Consent**

Written consent was obtained for monitoring and treatment.

### **Acupuncture Treatment**

Needling protocols were based on TCM principles with points added from published studies shown to be effective for migraine and for autonomic balance. Needles used were DBC™ Spring Ten Acupuncture Needles .25X30 and .16X30. Typically 10 to 20 needles were used, twisted 3 to 5 times, no de qi elicited. Treatment varied because short term HRV response was of interest

also. During some treatment days, transcutaneous auricular vagal nerve stimulation (TAVNS) was added for study purposes. Different treatment protocols are not designated in the data for this study for simplicity of presentation. Treatment frequency was 2 treatments/week for two weeks and then weekly for two more weeks if possible. For longer term patients, frequency was at least monthly, sometimes weekly as shown in data results.

### **HRV Monitoring and Measurement**

**Patient Monitoring:** Patients were monitored for ~5 minute baseline then during needling (4 to 7 minutes) and then for 20 min with needles in. Patients were monitored and treated in the supine position.

**Data Capture:** Nonin OEM Evaluation Program Rev. 15, from Nonin Medical, Inc. was used either on the right forefinger or right first or second toe for heart rate measurement connected wirelessly to a standard laptop computer for heart rate capture. The heart rate data was stored as a text file and then uploaded to Vivosense Heart Rate Variability Analysis 2.4 software from Vivonoetics, for analysis. Each tracing was examined for artifact and corrected on a beat by beat basis. The data was divided into time windows with a 5 minute baseline, a needling segment, and then 3 minute segments of time on the table with needles in.

### **HRV Data Analysis**

HRV was quantified using registration of percentage changes in R–R intervals in the time domain (TP, RMSSD and Pnn50) as well as the changes in the frequency range (HF, HF norm, LF, LFnorm, LF/HF) by analysis of pulse form power spectra. Parameters are recommended by the task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology<sup>21</sup>. Calculation of pulse oximeter peak-to-peak measures of power spectra are thought to provide a representation of the contributions of the sympathetic and parasympathetic systems on HRV. It is known that vagal and sympathetic activities affect low frequencies (LF:0.04-0.15 Hz), whereas vagal tone only affects high frequencies (HF: 0.15-0.4Hz). Nonlinear measures were measured (Sample Entropy, Poincaré plots, DF $\alpha$ 1) also, but not reported for this study.

For this study, LFnorm/HF norm was graphed as well as Sample Entropy multiplied by HFnorm to incorporate a nonlinear measure to capture additional nuance of response.

The time window for assessment was chosen to represent a quiescent 9 minute period during treatment after the effects of needling had diminished.

### **Clinical Assessments**

Clinical outcomes were patients' self-reporting of migraine incidents.

### **Results**

#### **HRV Parameter Definition and Significance:**

## Frequency Measures

**LF/HF** a measure of **sympathetic/parasympathetic tone** → **lower is healthier**

## Complexity X Parasympathetic Measure

Sample Entropy a nonlinear measure of **complexity** combined with HFnorm → **higher is healthier**

## HRV Values over a year.

Cases are presented on an individual basis due to the constraints of clinical practices and individual patient circumstances, i.e some patients had more treatment over the year than others.

The trend toward improved HRV over the course of the year is not smooth nor pronounced in all cases. The uneven trajectory in most cases is hardly surprising given that this data is collected in the clinic with no control for time of day, caffeine consumption, exercise before, poor sleep, nor other mitigating influences that are routine controls in academic studies. The HRV improvement did not necessarily correlate with clinical improvement in all cases since all patients had clinical improvement during the first 6 weeks of treatment, yet the HRV charts showed jagged, but continued improvement over the year.

A recent issue of Medical Acupuncture was devoted to acupuncture's role in preventative care emphasizing its ability to optimize health and to promote longevity. The editors also announced the opening of a new institute, The World Health Science Organization (WHSO), which proposes to address the global health crisis by using modern advances to explore the nature of health not only the manifestation of disease.<sup>22</sup> In a separate publication an author asks,

*"Traditional theories of acupuncture predict whole body effects. Does this permit the possibility of applying treatment to target overall health improvement of the patient rather than the symptom?... How can one measure these effects?"* .<sup>23</sup>

This study suggests that there may be some measurable, global effects of acupuncture over the first year of treatment. As mentioned earlier, this has been shown in shorter time frames, but data spanning a year is rare. In this group of migraineurs successfully treated with acupuncture, HRV improves over the course of the first year of treatment. Further study is needed to see if patients successfully treated for other conditions might have the same result. There is some evidence that migraineurs have more autonomic sensitivity than the population at large so patients with other conditions may respond differently<sup>24,25</sup>. This is an uncontrolled study so the effect of the acupuncture itself is unsure.

HRV is challenging to use as a clinical monitor because it is influenced by many inputs, internal and external. As is apparent in the data, it is not a smooth trajectory over the course of the year. Many inputs can confound the results: time of day, caffeine, poor sleep, etc... But even so, there is a trend towards improvement in HRV. Controlled academic studies could control for these factors, and, indeed often do.

There have been other recent studies that investigate whether acupuncture confers some autonomic stability. Two studies have been done in animals in which animals are given acupuncture and then startled<sup>26 27</sup> The animals receiving acupuncture have a blunted autonomic response compared to control animals. PTSD is thought to be, partly, a dysautonomia and acupuncture applied preventatively in earth quake survivors over a 3 week period developed less PTSD than controls<sup>28</sup>.

Stabilizing autonomic activity as a way to engender resilience is a burgeoning field in the area of “electroceuticals” or neuromodulation with the advent of implanted or peripheral nerve stimulation for improving vagal tone. These approaches are being used for immune conditions such as rheumatoid arthritis, but also epilepsy and depression. The interaction of the peripheral nervous system and immune response is the focus of intense interest with obvious parallels to acupuncture treatment.

*“Sensory and autonomic neurons of the peripheral nervous system (PNS) play a critical role in regulating the immune system during tissue inflammation and host defense. Recent studies have identified the molecular mechanisms underlying the bidirectional communication between the nervous system and the immune system... Nociceptor sensory neurons detect immune mediators to produce pain, and release neuropeptides that act on the immune system to regulate inflammation.”<sup>29</sup>*

Even the field of cancer metastasis embraces the concept of “seed and soil” with a recognition, that the “soil” or body’s environment can be a key to the establishment of metastases<sup>30</sup>.

Just as in other huge challenges facing us in the modern world such as environmental degradation, there is an affinity for “technological solutionism”, meaning a willingness to fund glamorous, elaborate solutions rather taking steps to prevent the problem in the first place. Likewise in modern medicine, curing diseases is always more exciting than prevention. The hope is that with biomarkers such as HRV, development of sophisticated tools of complexity science, and institutes such as the WHSO we can make prevention quantifiable and hence more tangible and exciting. The best physicians will, again, be devoted to keeping their patients well.

## Conclusion

In conclusion 6 migraineurs successfully treated with acupuncture displayed a general increase in their HRV over the first year of treatment supporting the hypothesis. This data should be considered descriptive since it is uncontrolled, so the clinical/physiological effect of acupuncture is not firmly established. But the length of time included in this study makes the

data set unusual and, hopefully, of value and interest. There is a need for quantitative measures of “health” and “resilience” and HRV may be useful in this regard.

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