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# Qigong, Parasympathetic Function and Fibromyalgia

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**Abstract**

Fibromyalgia (FM) is characterized by widespread pain and multiple other symptoms; underlying mechanisms include central sensitization, dysregulation of the stress response system, and autonomic nervous system dysregulation. Alterations in the sympathetic nervous system have been variably implicated, but a reduction in parasympathetic nervous system (PNS) activity is now becoming more clearly implicated. Qigong, a traditional health and wellness practice that is also considered as mindful exercise or meditative movement, has been shown in several controlled and uncontrolled trials to be of marked benefit in FM, with effects that are sustained over time. Several hypotheses have been considered to account for the benefits of qigong practice, including autonomic regulation. The current article proposes that qigong, as a self-practice, leads to enhanced PNS activity, and this underlies benefits in FM and contributes to other health benefits that occur with extended practice. This hypothesis could be tested: (a) by exploring benefits of non-invasive vagal nerve stimulation (this should mimic effects of qigong), (b) by demonstrating that qigong practice produces changes in PNS activity, (c) by demonstrating that other non-pharmacological therapies that have been shown to be of benefit in FM also modulate PNS activity. The hypothesis is amenable to direct testing.

## Fibromyalgia and the Autonomic Nervous System

Fibromyalgia (FM) is a chronic condition involving widespread pain, fatigue and multiple other symptoms, all of which contribute to a diminished quality of life [1,2]. FM is also known as a syndrome, reflecting the prominent involvement of other symptoms in addition to pain. FM was recognized as a clinical entity in the early 1990s with the American College of Rheumatology proposal of classification criteria; these criteria were modified in 2010 [3,4]. There is overlap between FM and several related conditions (e.g. chronic fatigue syndrome or CFS, irritable bowel syndrome or IBS, headache disorders), and a unifying concept has been to consider these as central sensitivity syndromes or CSSs [5-7]. FM is also prevalent in other chronic pain conditions [8]. Mechanisms contributing to FM include: 1) sensitization in central pain pathways, with amplification in pain transmitting mechanisms, reduction in inhibitory pain modulation, and neurotransmitter, neurotrophic and neuroplastic changes; 2) dysregulation of the hypothalamic-pituitary-adrenal axis and the stress response system; 3) genetic factors; 4) psychological and traumatic factors [1,2,9-12].

Autonomic nervous system dysfunction in FM and related conditions (CFS, IBS) was first proposed in the 1990s [13,14], and subsequent studies have continued to provide support for such dysfunction. The autonomic nervous system is a complex adaptive system that regulates vital functions (e.g. blood pressure, heart rate, respiration) and maintains homeostasis; it includes the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), and these two systems have opposite effects on many bodily functions. The term "autonomic" indicates that the system is not consciously governed, and regulation occurs via multiple feedback mechanisms. More recent reviews of studies assessing SNS function (using heart rate variability (HRV) spectral analysis, sympathetic skin responses, tilt table testing, and other methods) indicate that SNS predominance, together with blunted responses to stressors, is common in FM and CFS [15,16]. With CFS, increased sympathetic activity occurs during the night [15]. On the other hand, reduction in PNS activity, as reflected in decreased high-frequency heart rate variability, also is prominently implicated in FM and is receiving increasing attention [17]. It has been speculated that alterations in the complex adaptive system that the autonomic nervous system represents provides a non-reductionistic and non-linear framework for considering the etiology of FM and explaining diverse symptomology that may not necessarily be explained just by considering central sensitivity [18-20]. In non-linear systems, there is a complex and dynamic relationship between factors, such that cause and effect are not readily discerned.

## Qigong and Fibromyalgia

Qigong has a long history in China, and many forms have been elaborated in distinct domains (health maintenance, medical qigong, martial qigong, spiritual qigong) [21,22]. The scientific study of medical qigong began in the 1950s, and has increased dramatically over recent decades. Qi means "vital energy" or "life-force energy" and gong means "skill", and the practice of qigong represents cultivation of a domain of function. Internal qigong refers to self-practice, while external qigong refers to a projected skill delivered by a master proficient in the practice. The core elements of qigong involve movement, breath and mental practices, and it is traditionally regarded as a self-healing mind-body practice. Contemporary terminology for qigong is "mindful exercise" [23] or "meditative movement" [24,25], and such characterizations are helpful for deconstruction, operationization, and considering mechanisms involved. The main focus of considerations in the current article relate to internal qigong as self-practice.

Several studies have examined effects of different forms of qigong in FM. When qigong is practiced regularly (30 mins, ≥ 5 days a week, 6-8 weeks), there are consistent improvements in pain, sleep, impact, and

mental and physical function following the practice, and benefits are maintained at 3-6 months follow-up [26-29]. The magnitude of effects is notable, with effect sizes (standard mean differences) of 0.5-1.0 and greater observed over several domains, and these are generally maintained at follow-up [30]. Some earlier qigong studies involved weekly sessions of qigong, but practice requirements in between were not required or not stringent and ambiguous effects were reported [31-33]. There is direct quantitative data indicating that benefit is related to amount of practice, as those who practiced per protocol had more favorable outcomes in all measures compared to those who practiced minimally [28]. This difference in outcomes between practice groups was also manifest in qualitative comments on experiences with the practice [34]. There are several recent systematic reviews and meta-analyses of qigong for FM, either alone [35,36] or along with Tai Chi and yoga [37,38]; these are cautious in their conclusions regarding qigong because not all consider the full range of studies that are available, and even when this has occurred, trials were considered as a cohort without stratification for amount of practice.

In addition to randomized controlled trials in which qigong was practiced for a standard regimen, there have also been uncontrolled reports of effects of extended practice of qigong in FM subjects. Thus, there is an extension trial involving qigong practice for at least 1 year [39], and case studies of qigong practiced over even more extended periods (1-3 years) in a community setting [40]. These reports document marked benefits in core FM symptoms (pain, sleep, impact, mental and physical function) as well as other health benefits (e.g. improvement in asthma, sleep apnea, food and chemical tolerance, headaches) as reflected in qualitative comments [30,39,40]. It is important to note that those who undertake extended practice experience initial benefits with the therapeutic regimen, and these benefits motivate the extended practice. Similar initial benefits occurred in those undertaking community-based practice and were a prominent motivator for continued practice [40]. [There is also a report of marked improvements in FM with external qigong with benefits maintained at follow-up 3 months later [41]. However, mechanisms involved in external qigong, by definition, differ from those involved in internal qigong which is the main focus of the current review.]

There are now several reports that qigong self-practice is also of benefit in CFS, another condition regarded as a CSS and exhibiting autonomic dysfunction (section 1). These studies involved two different qigong regimens of instruction, and regular practice over 2-4 months; qigong practice resulted in significant improvements in sleep, fatigue and signs of anxiety and depression following the intervention, and at follow-up at 3 months [42-44]. Furthermore, the amount of practice was significantly associated with improvements in sleep, fatigue, anxiety and depression [44]. [There are also case reports of external qigong providing marked benefit in CFS [45].] An emerging body of information indicates qigong is useful for fatigue, anxiety and depression in a range of conditions [25,46,47]. However, there has been limited consideration of the relationship of amount of practice to outcomes in these studies.

## Qigong Mechanisms

Within traditional Chinese medicine theory, qigong promotes the circulation of vital energy (qi) within the meridian system (vital energy channels) and improves the balance, distribution and free flow of qi within that system [21,22]. Contemporary proposals for the efficacy of qigong, considered as mindful exercise, include the following [23,48-50]: 1) changes in central neurotransmitter systems (neurochemical hypothesis), 2) neuroendocrine modulation and reduction in stress-related hormones (neuroendocrine hypothesis), 3) regulation of neurotrophic factors and central neuroplasticity (neurotrophic hypothesis), and 4) mind-body regulation within a biopsychosocial model. Within the psychosocial model are psychosocial (cognitive behavioural theory, distraction theory, social interaction theory) and physiological (cardiovascular fitness theory, amine theory, endorphin theory) domains [23]. Within the cardiovascular fitness construct, qigong mechanisms may involve regulation of the autonomic nervous system, with stabilization of SNS activity, increases in PNS activity, and enhanced sympatho-vagal balance [23].

In addition to these proposals, contemporary terminology that considers qigong as "meditative movement" [24] allows for the ability to draw upon mechanisms contributing to therapeutic benefits of specific forms of exercise and meditative techniques. Thus, further proposals involving bodily regulation (metabolic expenditure, rhythm, grounding and posture, interoception) and engagement of aspects of central circuitry (imagery, basal ganglia, default mode networks) are possible [25]. Within this framework, the spatial/interoceptive/proprio-ceptive/kinesthetic focus of awareness is considered a defining characteristic of meditative movement practice, delineating it from conventional exercise (which emphasizes flexibility, strength and aerobic function) and some static (seated) meditative and/or mindfulness practices [25]. This defining element is also an important feature of body awareness and other somatic practices that have been developed over the past century in the West [25,51]. It is interesting to note that the neurological substrate for interoception includes sensory input via A δ and C fibres in the lamina 1 system and via vagal input to the brainstem with subsequent supraspinal integration [52-54]. In this regard, exploration of effects of such practices in the context of chronic pain is particularly relevant to further understanding the practices.

## Qigong and Vagal Nerve Activity

The vagus nerve (the "great wanderering protector") comprises a network of neuro-endocrine-immune functioning that maintains homeostasis; it has reciprocal connections to multiple brain regions, integrates interoceptive information, and adapts with modulatory responses [52]. The vagus nerve controls cardiovascular, respiratory, and alimentary systems, and these functions are well recognized; further recent studies indicate regulation of CNS function, mood, pain and inflammation by vagal nerve activity [55,56]. Vagal nerve stimulation, using invasive stimulation methods (iVNS), was approved by the US Food and Drug Administration for the treatment of refractory epilepsy and depression in recent decades [57-59]. Non-invasive vagus nerve simulation methods (nVNS) also have been developed, and there is an emerging literature on efficacy in several conditions beyond those for which they are currently approved, including headache disorders [60,61], and in other diverse conditions (asthma, inflammation, gastric mobility disorders) [55]. In support of clinical observations in pain conditions, nVNS stimulation resulted in reduced sensitivity to pain in a human experimental pain paradigm [62]. Furthermore, VNS produces antinociception in several preclinical pain models, and mechanisms potentially involved in antinociceptive actions have been considered [55,63,64].

Qigong has been proposed, in a general sense, to increase PNS activity and to enhance sympatho-vagal balance [23]. From the perspective of recent understanding of the extent of vagal functions,

which includes regulation of CNS function, pain and inflammation, this hypothesis has merit for several reasons. (1) A reduction in PNS activity is clearly implicated in FM, and this facilitates an understanding of diverse symptomology in FM (section 1). A practice that enhances PNS activity would potentially be of benefit to the core symptoms of FM (pain, fatigue, impact, physical and mental function) because it interacts directly with the dysfunctional system. (2) Qigong practice, especially extended practice, produces additional health benefits beyond the core symptoms of FM. For example, there are several cases where asthma improves with qigong [39] (section 2). Anti-inflammatory effects and respiratory regulation resulting from vagal nerve activity could explain some of these additional effects. There is direct evidence that vagal nerve stimulation improves respiratory function in asthmatics resistant to standard treatment [65]. (3) A defining characteristic of qigong practice includes an interoceptive focus of attention (section 3). The vagus nerve consists 60-80% of afferent nerves and integrates interoceptive information [52-54], and this aspect of its function provides plausibility for a role in the benefits of qigong practice.

## Testing the Vagal Stimulation Hypothesis

### Vagal nerve stimulation (VNS) should mimic effects of qigong

iVNS, using implanted electrodes, as used in epilepsy and depression trials, has been tested in a small cohort of subjects (N=14) with FM [66]. iVNS stimulation over a 3-month interval resulted in benefits in pain and tenderness, and at the end of this acute phase of stimulation, two subjects (of N=12) no longer met widespread pain or tenderness criteria for FM. During follow-up (to 5-11 months), three additional subjects attained the same criteria, suggesting progressive improvements over time [66]. Adverse effects were similar in nature to those observed in other trials (voice changes, neck/facial pain, headache and dyspnea).

With the availability of non-invasive, safer and better-tolerated VNS methods and protocols [67], systematic studies on effects of nVNS in FM could be undertaken. nVNS can be used over extended intervals, and effective regimens, including prophylactic ones, for pain conditions are now being described [61,67]. For FM, controlled trials, outcomes compared to sham interventions (use of device but no delivery of stimulation, or delivery of parameters known to be ineffective), as well as to standard treatment, would provide useful information. Furthermore, with favourable tolerability and safety, extension trials in which stimulation can continue over longer intervals (months) in subsets of individuals could be considered. In addition to considering outcomes in relation to controls, those attaining clinically meaningful changes in core domains (minimal clinically important difference concept) should be identified, as well as those attaining the endpoint of no longer meeting criteria for diagnosis of FM. The latter criterion is interesting to include, as some subjects with iVNS were described as attaining this endpoint [68]. Furthermore, while not always explicitly considered in these terms, several subjects who engaged in extended qigong practice would meet this criterion [39,40]. Finally, with long-term protocols, additional health benefits beyond core FM symptomology should be considered, as such effects are reported with qigong practice (section 2). Qualitative approaches which allow for the detection of diverse effects that are not necessarily the immediate focus of study can be valuable contributors to this exploration.

### Qigong practice should produce changes in parasympathetic nerve activity

Several studies have examined effects of qigong on autonomic function. Much of this interest has developed due to improvements in cardiovascular function with qigong [69], but potentially are generalizable to other conditions as well. (1) Qi-training (for 40 min) in young healthy subjects (N=20 vs 20 sedentary controls) increased high frequency (HF) power and decreased the low frequency/high frequency (LF/HF) power ratio of HRV during practice [70]. Results were interpreted as indicating increased parasympathetic tone and stabilization of the autonomic nervous system during the practice. (2) Qi practice in older subjects in the community (N=47 experimental, 30 controls) who practiced for 12 weeks (3X week, 30 min), reported improvements in several HRV parameters (increased LF and HF parameters) following the practice regimen [71]. (3) External qigong (EQT, external Qi therapy) applied for 5-10 mins (N=30 healthy male volunteers) resulted in decreased heart rate and improved HRV parameters as indicated by a reduced LF/HF power ratio [72,73]. Results were interpreted as indicating EQT stabilizes sympatho-vagal function. (4) Tai Chi qigong exercise (for 5 mins) in cancer survivors (N=11) decreased LF power and increased HF power during the practice; these results were interpreted as an improved HRV profile [74]. (5) There are also reports of a lack of effect on HRV with 12-16 weeks of qigong practice in healthy adults [75] and wheelchair-bound adults in long-term care facilities [76]. Both studies reported favourable physiological and/or psychological effects resulting from practice.

There are a limited number of studies examining qigong effects on HRV, and these are very heterogeneous in terms of populations (age, absence or presence of disease), the nature of the qigong (various styles are reported on), parameters of the regimen (duration, novice or established practice), and the time at which assessment occurs (during, post-practice, at follow-up). While several studies do report improved sympatho-vagal balance and increased parasympathetic tone, many observations are in healthy subjects, and generalizability to groups in which autonomic regulation is compromised is unclear. Future studies exploring effects of qigong on autonomic nervous system function in FM and CFS should assess effective therapeutic regimens on symptoms as well as autonomic parameters, determine pre-, during and post-practice effects, as well as follow-up responses to determine the durability of changes. In addition, the relationship of such changes to clinical outcomes should be evaluated. Particular attention needs to be given to the methodology needed to detect relevant changes in PNS activity [77].

### Other treatments useful for FM improve parasympathetic activity

FM management involves pharmacological, non-pharmacological and complementary and alternative therapies [78-80]. Non-pharmacological therapies include exercise, meditative movement and complementary exercise practices, as well as hydrotherapy. Exercise is known to increase vagal tone and decrease sympathetic tone in cardiac regulation [81], and regulation appears to occur more prominently in those with autonomic dysfunction than in healthy subjects [82]. Exercise modulates autonomic function in fibromyalgia, with favourable modulation of several aspects of function [83]. Tai Chi (also considered meditative movement) improves vagal activity and the balance between sympathetic and parasympathetic activity in Tai Chi practitioners [84,85]. These observations were considered largely in

relation to clinical populations with cardiovascular diseases, but are also potentially relevant to other conditions in which autonomic dysfunction occur. Hydrotherapy improves vagal modulation and decreases sympathetic modulation of cardiac function in FM subjects [77]. Importantly, this study observed an association between improved non-linear dynamics of HRV and the impact of FM on quality of life, and emphasized the need to use non-linear dynamic analysis of HRV. Improvement in parasympathetic function, with or without parallel changes in sympathetic function, has the potential to provide a plausible common pathway / mechanism for explaining how heterogeneous practices and activities lead to health benefits in FM. Future studies which assess clinical endpoints along with autonomic parameters in FM subjects promise to be an interesting and important area of investigation.

## Perspective

FM, with its diverse manifestations and co-morbidities, is a complex condition which is a challenge to model and a challenge to treat. System dysregulation has emerged to account for the diversity of expression (e.g. central sensitization in pathways involved in pain signaling, autonomic nervous system dysfunction). One purpose of considering system etiology is that it allows for treatment strategies to specifically target a system; for example, multiple pharmacological agents target aspects of pain transmission pathways involved in central sensitization. The present article focuses on parasympathetic activity as an underlying construct for understanding FM, and posits that treatment strategies can target this system. This can occur using devices (i.e. non-invasive vagal nerve stimulators), as well as qigong and potentially with other practices which share common elements. Within this hypothesis, there is the implication that these approaches will impact significantly on core domains of FM symptoms (pain, sleep, impact, physical and mental function), and potentially also on other diverse manifestations. The latter may occur with standard regimens that influence core symptoms, or with extended regimens. It is possible to monitor PNS activity such that this general hypothesis is amenable to direct testing.

Qigong is traditionally considered to be a mind-body health promoting practice, with more contemporary terminology being "mindful exercise" or "meditative movement". With the latter terminology, comparisons with other movement forms (certain types of exercise), as well as with meditation, mindfulness and contemplative practices can occur. An additional prominent focus for qigong involves interoception, and this is considered a defining feature of the practice [25]. Thus, further comparative consideration could be with other body awareness practices where interoception, an aspect of embodiment, serves as a prominent component [51,86].

## Declaration

The author has no conflicts of interest relevant to this report.

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