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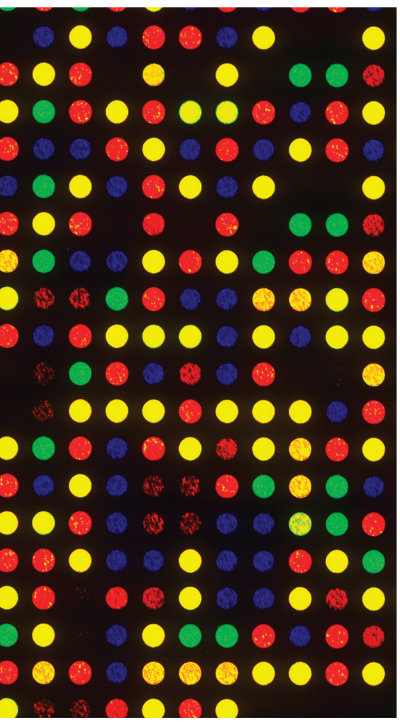
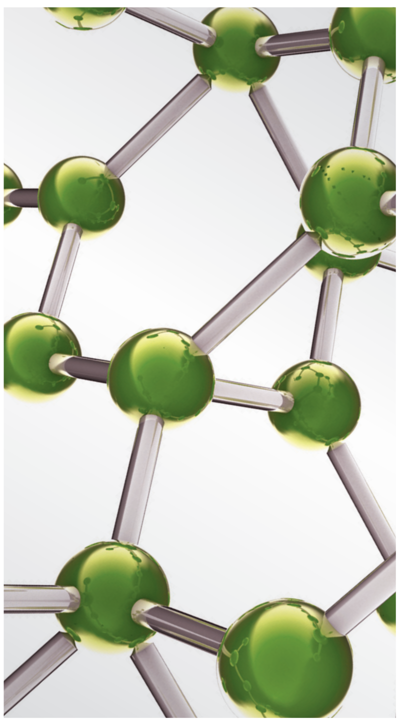
Scientific Basis of Mind-Body Interventions

Guest Editors: Hector Tsang, Cecilia L. W. Chan, Kevin Chen, William Chi-shing Cho, and Myeong Soo Lee



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Editorial Board

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Editorial

Scientific Basis of Mind-Body Interventions

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Mind-body exercise, a form of exercise that combines body movements with mental focus, has a long and winding history around the world. In the two ancient civilizations, India and China, Yoga and Health Qigong/Tai Chi have, respectively, been practiced for thousands of years among healthy individuals or those with a health condition for wellness or therapeutic purpose. In modern times, progressive muscle relaxation, visualization, and Pilates are becoming more and more popular in the western world for health and fitness.

Although different types of mind-body exercises have been practiced by people from different cultures and clinical effects have been observed for centuries, these interventions have been criticized by researchers and practitioners to be lacking in scientific support in two aspects. First, many review articles [1, 2] (Ng and Tsang, 2009; Wang and Chan et al.) reveal that most clinical studies on these mind-body interventions are not well controlled and designed. Many do not even have a comparison or control group. These have posed a lot of difficulties on the generalizability of the results. Second, even effects are well documented. The biological or psychosocial mechanisms underlying the effects are largely unknown [3, 4].

My neuropsychiatric rehabilitation research team at The Hong Kong Polytechnic University has been active doing research in providing scientific evidence to Chinese mind-body exercises for the past decade. I am glad to receive many requests for reprints after the research articles are published. Some even requested for access to the video so that they may replicate the studies or apply these mindfulness exercises in their clinical settings. It is an excitement when I was asked by the editorial office to edit a special issue devoted to the scientific basis of mind-body exercises. This special issue in fact is to fill the knowledge gap that may help promote these activities for clinical practice and gradually attain its mainstream status in modern medicine.

In this special issue, we are happy to present a total of 7 original research papers to augment the evidence base for mind-body interventions. It is impressive to see that mind-body/mindfulness interventions have been applied to different groups of clients including frail elders, patients with major depressive order, shoulder pain, chronic fatigue, acute respiratory infection, and patients in intensive care unit. Articles submitted to this special issue provide further evidence on the clinical effectiveness in various aspects. H. W. H. Tsang and his team showed that the newly developed adapted mind-body exercise for frail elders improved their thinking operations. EEG data from A. S. Chan et al. and P.-C. Lo and C.-H. Chang showed that Chan-based mind-body intervention helped induce positive mood and calm state mind. J. S. M. Chan et al. reported that Wu Xing Ping Heng Gong reduced total fatigue score among chronic fatigue patents. A. L. Baldwin and colleagues showed that energy healing was as effective as manual manipulation physical therapy in treating patients with shoulder pain problem.

A. M. Chiasson et al. realized that patients in intensive care unit found harp music effective in helping them reduce perceived pain. Finally, the mindfulness based stress reduction program by A. Zgierska et al. has been demonstrated to produce improvement in psychosocial functioning among patients with acute respiratory infection.

I hope that the results reported in this special issue will further spark further enthusiasm on scientific research for mind-body interventions in the future so that more clients will benefit providing evidence, clinical implications, and inspiration to clinicians, researchers, and patients.

Hector Tsang
Cecilia L.W. Chan
Kevin Chen
William Chi-shing Cho
Myeong Soo Lee

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Research Article

A Randomized Controlled Neurophysiological Study of a Chinese *Chan*-Based Mind-Body Intervention in Patients with Major Depressive Disorder

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Our previous studies have reported the therapeutic effects of 10-session Chinese *Chan*-based *Dejian* mind-body interventions (DMBI) in reducing the intake of antidepressants, improving depressive symptoms, and enhancing the attentional abilities of patients with depression. This study aims to explore the possible neuroelectrophysiological mechanisms underlying the previously reported treatment effects of DMBI in comparison with those of cognitive behavioral therapy (CBT). Seventy-five age-, gender-, and education-matched participants with depression were randomly assigned to receive either CBT or DMBI or placed on a waitlist. Eyes-closed resting EEG data were obtained individually before and after 10 weeks. After intervention, the DMBI group demonstrated significantly enhanced frontal alpha asymmetry (an index of positive mood) and intra- and interhemispheric theta coherence in frontoposterior and posterior brain regions (an index of attention). In contrast, neither the CBT nor the waitlist group showed significant changes in EEG activity patterns. Furthermore, the asymmetry and coherence indices of the DMBI group were correlated with self-reported depression severity levels and performance on an attention test, respectively. The present findings provide support for the effects of a Chinese *Chan*-based mind-body intervention in fostering human brain states that can facilitate positive mood and an attentive mind.

1. Introduction

Mind-body interventions focus on the interaction between the brain, the mind, and the body with the assumptions that the mind and body are interconnected and that individuals can use the mind to affect physical functioning and mental health. The use of mind-body training has received increasing interest as a complementary intervention method among psychologists and medical professionals due to its documented therapeutic effects on many psychological problems, such as anxiety [1], insomnia [2], and depression [3]. Mind-body training has also been shown to have positive effects as a complementary treatment for many physical disorders, including irritable bowel syndrome [4], chronic pain [5], and cardiovascular problems [6]. Using the mind to affect physical and mental health is a core concept of traditional Chinese medicine. Studies assessing the effect of *qigong*, a mind-body practice from ancient China, have demonstrated that *qigong* can elevate mood in elderly people with depression [7] and improve the psychological wellbeing and self-efficacy of patients with chronic physical illnesses [8]. *Tai Chi-*, one of the best known and widely studied mind-body exercises, originated in China and has been found to be effective in reducing anger, mood disturbances, somatic symptoms, and sleep problems in patients with chronic conditions [9, 10].

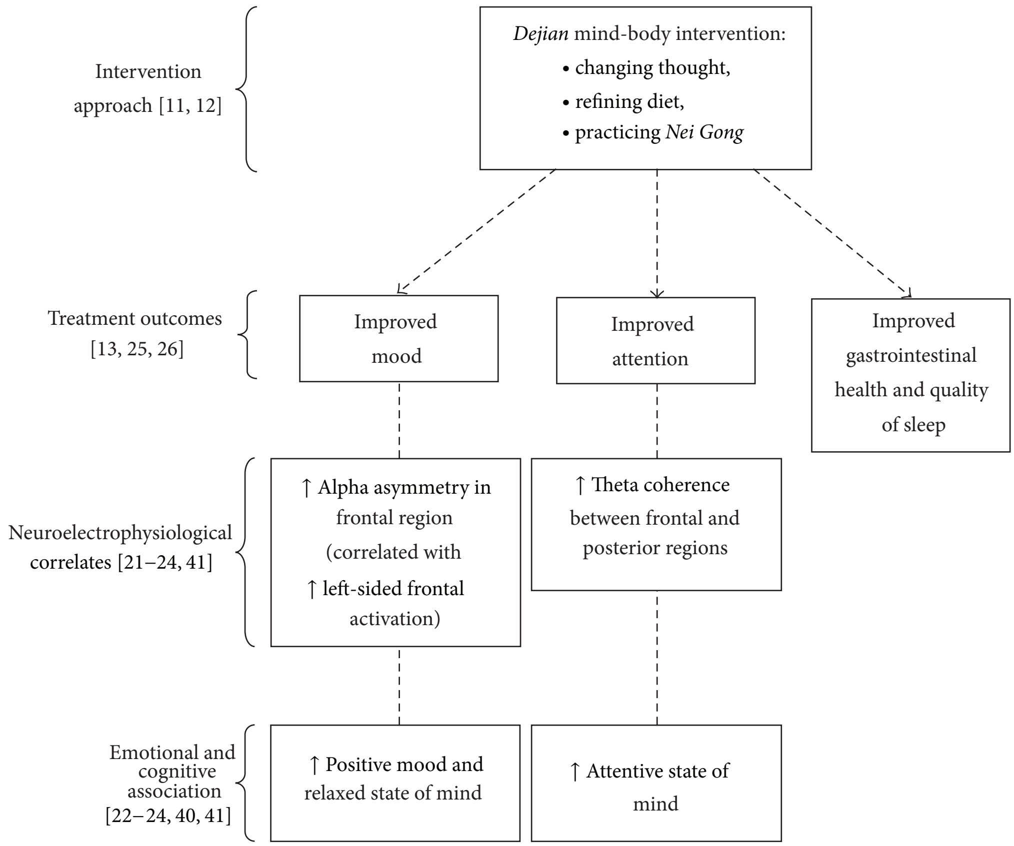


Figure 1: Summary of empirical evidence for the potential neural mechanism underlying the effects of *Dejian* mind-body intervention (DMBI). Dotted arrows represent empirically found treatment effects of DMBI, whereas dotted lines indicate hypothetical linkage between possible neuroelectrophysiological correlates and changes in mood and cognitive states.

Recently, a Chinese *Chan*-based mind-body intervention, termed "*Dejian* Mind-Body Intervention" (DMBI), has begun to be applied in clinical and educational settings as a complementary treatment for different psychological and cognitive disorders. This intervention is based on a medical principle that originated from the *Shaolin* Temple, is holistic in nature, and consists of three integrative treatment components: (i) psychological education, (ii) mind-body exercise, and (iii) diet modification [11, 12]. Empirical evidence has shown that the DMBI has beneficial effects on mood and cognitive problems related to brain disorders. Specifically, a randomized controlled study showed positive effects of one month of DMBI training on depressive mood in a group of community-dwelling adults [13]. Clinical studies of patients with developmental or acquired brain disorders who practice DMBI have also reported significant improvements in measures of cognitive function and substantial reductions of problem behaviors [14–19].

Some researchers attribute the reported therapeutic effects of mind-body interventions to the acute effects of complex mental processes that involve changes within the central nervous system (CNS) [20]. Indeed, the advent of brain imaging techniques has helped to address the fundamental question about the relationship between the mind and the brain. A recent electrophysiological study, that measured the electroneural activities associated with the DMBI mind-body exercise, which consists of the passive and active subtypes of *Dan Tian* breathing techniques [21], found that passive *Dan Tian* breathing induces a relaxed and calm state of mind as indicated by elevated EEG alpha asymmetry and that active *Dan Tian* breathing induces an attentive state of mind as indicated by elevated EEG theta coherence. These results are consistent with previous electrophysiological studies of affective processes that have shown that positive emotion is coupled with greater left-sided anterior activation as indexed by decreased alpha activity in the left hemisphere [22] and that enhanced attention and working memory are associated with elevated EEG theta coherence [23, 24]. The potential effects of DMBI on the CNS have been summarized in Figure 1.

The findings that the mind-body exercise of DMBI is able to elicit a specific state of consciousness in which relaxation and internalized attention coexist may provide an explanation of its therapeutic effects of reducing stress and improving cognitive function in patients with depression, group known to have attention problem and be more stress-prone; this brain state enables individuals to remain focused on a task, be free of distractions, and deal with life stressors in a relaxed and flexible manner. This idea is supported by one of our recent studies of patients with clinical depression

([25]; see Figure 1); in this study, 75 participants diagnosed with major depressive disorder were randomly assigned to receive 10 sessions of cognitive behavioral therapy (CBT) or 10 sessions of DMBI or placed on a waitlist. Pre-post measurements included the use of antidepressants, ratings from psychiatrists who were blinded to the experimental design, self-reported mood measures, and performance on an attentional task. The results showed that, although both the CBT and DMBI groups demonstrated significantly reduced overall depressive symptoms after the intervention with large effect size (0.93–1.10), only the DMBI group demonstrated a significant reduction in the intake of antidepressants and improvements in some common depression-related cognitive and physical symptoms, such as attention deficits and gastrointestinal problems. In addition to the reduction of depressive moods with DMBI, a related study of patients with depression practicing DMBI also reported substantial improvement in the patients' sleep patterns as measured by significant reductions in psychiatrists' ratings of overall sleep problems and total sleep time relative to waitlist or CBT controls ([26]; see Figure 1).

In sum, the results of our previous studies support the idea that DMBI is effective in improving mental and physical functioning. However, the neurophysiology of this mind-body intervention remains elusive. Thus, the purpose of the present study was to investigate how DMBI affects the function of the CNS of patients with depression, with a specific focus on the mental processes of positive emotion and attention. Given that positive emotion has been reported to be related to greater left-side anterior activation, as indexed by decreased EEG alpha activity in the left hemisphere, and attention has been linked to greater EEG theta coherence, we hypothesized that this *Chan*-based mind-body intervention would result in EEG changes involving increased left-sided anterior activation and increased theta coherence compared to controls. We also hypothesized that increased left-sided anterior activation would be associated with improved depressive symptoms and that increased theta coherence would be associated with improved attention in the patients practicing DMBI.

To further highlight DMBI's therapeutic effect of inducing a specific state of consciousness in which both relaxation and internalized attention coexist, we compared patients who received DMBI to CBT and waitlist controls. CBT has been empirically demonstrated to reduce depressive moods in people with depression by helping depressed individuals to reinterpret their environment and their interactions with others in a positive and realistic manner [27, 28]. We anticipated that both DMBI and CBT would induce increased left-sided anterior activation suggestive of reductions in depressive moods compared to the waitlist controls. However, we expected that only the DMBI would induce increased theta coherence, which is suggestive of focused internalized attention.

2. Materials and Methods

2.1. Participants. Seventy-five participants were recruited from the outpatient clinic at the West Kowloon Psychiatric Centre. All participants had received diagnoses of major depressive disorder from a clinical psychologist based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [29] and the Structural Clinical Interview for the DSM-IV (Chinese-bilingual SCID-I/P version) [30]. Exclusion criteria included positive history of head injury, seizure, stroke, other CNS diseases, other comorbid psychiatric illness, or reports of strong suicidal ideation. All participants were prescribed antidepressants and were continuously followed up by their psychiatrists, who were not coinvestigators and were blind to the group assignment and rationale of the present study. Randomization of the assignment of participants into the CBT, DMBI, or waitlist control groups was conducted by a medical professional who was blind to the experimental design. Participants in the two intervention groups were blind to the potential benefits of the two techniques.

Participants who dropped out of the study or attended less than 70% of the intervention sessions were excluded from analyses. After intervention, 16, 17, and 17 participants remained in the waitlist control, CBT, and DMBI groups, respectively. The average attrition rate (inclusive of dropouts and participants with <70% attendance rate) of the three groups is 33%, which is comparable to the average range of attrition rate of psychotherapy for patients with depression [31]. Reasons for the dropouts and low attendance rate included unexpected change in work schedule or other personal commitments that have clashed with the training or assessment sessions. Table 1 presents the demographic characteristics of each group of participants at baseline. The three groups were matched for age, $F(2, 47) = 0.198$, $P = 0.821$; education level, $F(2, 47) = 1.729$, $P = 0.189$; and gender, $\chi^2(2) = 1.103$, $P = 0.576$. Across groups, depression severity, as reflected by the SCID-based diagnoses, $\chi^2(4) = 3.133$, $P = 0.536$; illness duration, $F(2, 46) = 0.426$, $P = 0.656$; and total scores on the Chinese version of the Beck Depression Inventory (BDI-II) [32, 33], $F(2, 47) = 0.155$, $P = 0.857$, was similar.

2.2. Ethics. The study was conducted in accordance with the Helsinki Declaration of the World Medical Association Assembly. The research protocol was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster (Joint CUHK-NTEC) Clinical Research Ethics Committee (CREC) and the Kowloon West Cluster (KWC) CREC of the Hospital Authority in Hong Kong SAR.

2.3. Procedure. Written informed consent was obtained from each participant prior to the study. Each participant's state of depression was individually assessed by research assistants using a standardized questionnaire, attention abilities, and EEG activities at baseline and again after 10 weeks. The depression severity was measured with the 21-item BDI-II, which the participants themselves completed. The total maximum score of the BDI-II is 63, where higher score indicates more severe depressive symptoms. The total BDI-II scores can be classified into four severity levels: "Normal (0–13 points)," "Mild Depression (14–19 points)," "Moderate

Table 1: Demographic characteristics of each group of participants.

Characteristics	WL (n = 16)	CBT (n = 17)	DMBI (n = 17)	F or χ^2	P
Years of age					
Range	31–62	34–57	32–62	—	—
Mean (SD)	45.44 (8.25)	46.94 (6.54)	47.06 (9.54)	0.198	0.821
Years of education					
Range	3–11	6–16	3–16	—	—
Mean (SD)	8.06 (2.59)	9.82 (2.46)	9.18 (3.13)	1.729	0.189
Gender				1.103	0.576
Male	4	4	2		
Female	12	13	15		

Note. WL: waitlist control; CBT: cognitive behavioral therapy; DMBI: *Dejian* mind-body intervention.

Depression (20–28 points)," and "Severe Depression (29–63 points)." Attention abilities were assessed with the Digit Vigilance Test (DVT) [34], which requires participants to search for target digit "6" or "9" within an array of other distracting digits as quickly as possible. The total time taken to complete the task is the outcome measure, and shorter completion times suggest greater work efficiency and increased ability to maintain attention on the task. The EEG data were collected from each participant using the TruScan measuring set with 19 electrodes positioned across the scalp according to the International 10–20 System [35] in a sound- and light-attenuated room before and after intervention. During each measurement time point, the participants were required to follow through a brief video introducing the *Dan Tian* Breathing technique, after which they were required to perform the *Dan Tian* Breathing for five minutes. Then, they were asked to sit with their eyes closed for another five minutes, during which their resting state EEG data were captured for subsequent analyses. It should be noted that participants from all three groups have undergone the same experimental paradigm, and only participants from the DMBI group had continuous daily practice of the *Dan Tian* Breathing during the intervention period. The pre-post comparison on the EEG changes for each group will provide clue to the potential effects of regular practice of *Dan Tian* Breathing in DMBI and to minimize potential placebo effect. All electrode impedances were kept at 10 kΩ or below. The EEG signals were referenced to linked ears, digitally filtered at 0.5 and 100 Hz, and sampled at 256 samples per second with a high-frequency band pass limit of 30 Hz. Artifacts were removed off-line based on records of the bodily movements of the participants made by the experimenter throughout the EEG assessments. After the baseline assessment, the two treatment groups underwent 10 weekly 90-minute training sessions of either CBT or DMBI, and the waitlist control group did not receive any psychological intervention.

2.4. Intervention. The two intervention groups were designed to have similar structures and formats with respect of group size, the venue of intervention, the duration and frequency of the sessions, didactic teaching on the fundamental principles and corresponding techniques, in-session sharing, and home assignments. The CBT group was run by a clinical psychologist with over ten years of clinical experience conducting this type of group training regularly in a hospital. Another clinical psychologist who also has over ten years of clinical experience and developed DMBI ran the DMBI group. Participants in each intervention group were closely monitored in terms of their abilities to master the techniques by the respective therapists throughout the intervention period.

2.4.1. DMBI. This intervention was developed based on a Chinese *Chan* tradition called *Chanwuyi* (i.e., Zen, martial arts, and healing) that originated from the *Shaolin* Temple. This intervention was named after the Grand Master of *Chanwuyi—Shi Dejian* (a *Shaolin* monk). The principle of DMBI is to alleviate psychological distress by understanding the root of problems in accordance with Buddhism philosophy, enhance mental and physical health by practicing some of the *Shaolin* mind-body exercises (called *Nei Gong*), and uphold the concept of "food as medicine." The DMBI proposed to refine the diet to reduce the intake of high-fat and high-energy food that will generate excessive heat inside the body and cause blood and *Qi* stagnation, which in turn would have harmful effects on physical and mental health [17]. DMBI emphasizes integrative treatment for the mind and the body, which, on the one hand, changes the thought process and, on the other hand, improves mental and physical health via the practice of mind-body exercises and refining of the diet.

Details of the intervention regime have been elaborated in our previous studies [25, 26]. Briefly, the treatment has four components: (1) increase awareness of how greed, anger, and obsession affect our mental and physical health to guide changes that reduce psychosomatic problems; (2) consume seven categories of food (fresh vegetables, fruits, grain, beans, mushrooms, nuts, and root vegetables) that are healthy and reduce intake of some foods that generate internal heat (ginger, garlic, green onion, spicy foods, eggs, meat, and fish); (3) practice self-awareness and self-control; and (4) practice *Nei Gong* (the mind-body exercises) to reduce stress, increase flexibility in the four limbs, enhance strength of the legs, improve overall physical health, and improve the circulation of *Qi* and blood. A key of DMBI is that individuals are encouraged to execute their treatment regime naturally in adherence with their own lifestyles and plans and to feel the changes their minds and bodies undergo in response to changes in their thoughts, diet, and exercise habits. For instance, participants were not required to instantly abstain from all hot and spicy foods; rather, they were encouraged to gradually reduce their intake of these foods. Furthermore, there were no constraints regarding the time spent practicing *Nei Gong*. Participants were instructed to practice the exercises until they felt warm and relaxed and not to overexert themselves. The rationale behind this flexibility in the practice of DMBI was to facilitate increases in the participants' senses of self-control and self-awareness.

2.4.2. CBT. The present study adopted a CBT protocol that was developed based on three sources: *Cognitive Therapy for Depression* [36], *Mind Over Mood* [37], and *Cognitive Behavioural Therapy in Groups* [38]. This protocol covers the typical components of CBT, including progressive muscle relaxation (PMR), behavioral activation, self-monitoring, cognitive restructuring, rehearsal of coping skills, and relapse prevention. The intervention began with psychoeducation on the biopsychosocial model of depression and the triadic relationship between mood state, cognition, and behavior. Through the introduction of the triadic relationship, the participants were guided toward positively modifying their cognitive processes and behavior so as to trigger a positive change in mood. Furthermore, the participants were taught to practice PMR as a means to induce a relaxed state of mind. PMR is a stress management technique developed by Jacobson [39] and is a widely practiced relaxation method that has been reported to be effective in alleviating anxiety and mood problems [40]. Participants were taught to alternately tense and relax groups of muscles in a prescribed sequence from the head to the feet according to the standard procedure of the technique. Participants were also instructed to synchronize their breathing with the muscle-tensing/relaxing cycle and concurrently feel their bodily changes. Throughout the sessions, the therapist reviewed the experiences of participants during their daily practice of the techniques and closely monitored their progress.

2.5. EEG Indices

2.5.1. Frontal Alpha Asymmetry. The absolute power in the alpha frequency band (8–13 Hz) measured from the anterior scalp region (F7 and F8) was natural logarithm (ln)-transformed and used to calculate frontal alpha asymmetry. The asymmetry index was computed as $(\ln(F8) - \ln(F7))$, where F8 and F7 are the alpha powers in the right and left hemispheres, respectively. EEG alpha power has been reported to be negatively correlated with brain activation [41, 42]. Therefore, positive frontal alpha asymmetry values resulting from greater alpha power on the right and less alpha power on the left would represent greater activity in the left relative to the right brain (i.e., left-sided activation), whereas negative asymmetry values would suggest greater right side activation. The alpha asymmetry in the anterior frontal (F7 and F8) region was used given its reported association to emotions, of which greater left-sided activation was observed to be coupled with positive mood and relaxed mind [22].

2.5.2. Intra- and Interhemispheric Theta Coherence. Coherence values in the theta band (3–7 Hz) measured at the intra- and interhemispheric connections within and between the frontal (F3, F4, F7, and F8) and posterior (P3, P4, O1, and O2) scalp regions were obtained, and the square rooted values were normalized using Fisher's Z transformation. The mean values of six clusters of coherence pairs were computed. These means included intrahemispheric coherence in (i) frontal (F3-F7 and F4-F8), (ii) posterior (P3-O1 and P4-O2), and (iii) frontoposterior regions (F3-P3, F4-P4, F7-P3, F8-P4, F3-O1, F4-O2, F7-O1, and F8-O2) and interhemispheric coherence in (iv) frontal (F3-F4, F7-F8, F3-F8, and F4-F7), (v) posterior (P3-O2, P4-O1, P3-P4, and O1-O2), and (vi) frontoposterior regions (F3-P4, F4-P3, F7-P4, F8-P3, F3-O2, F4-O1, F7-O2, and F8-O1). The specific electrode sites were chosen and grouped based upon previous studies that reported that short- and long-range frontal and posterior theta coherence indices are sensitive to attentional processes [24, 43].

2.6. Data Analysis. All data were analyzed with SPSS (version 15.0) statistical software. Baseline group differences in demographic and clinical characteristics were explored with ANOVA and χ^2 tests. The main analyses of the effects of intervention on various EEG indices were performed using paired-sample one-tailed t statistics with planned comparisons. As specific hypotheses were tested, and the number of comparisons was large within a relatively small group of participants, Student's t-test was adopted without adjustments to the alpha level so as to avoid lowering the power of the tests. At the same time, effect sizes (Cohen's d statistic) were calculated to evaluate the degree of changes from baseline to after intervention. Any between-group differences were analyzed using ANOVA or independent-sample Student's t tests. Pearson's correlations and χ^2 tests were employed to explore possible associations between the variation in EEG indices and depression severity and attentional abilities.

3. Results

3.1. DMBI Enhanced Frontal Alpha Asymmetry. The ANOVA results revealed that the baseline levels of frontal alpha asymmetry were comparable across the three groups, $F(2, 46) = 0.894$, $P = 0.416$. Figure 2 shows the changes in alpha asymmetry in each group after intervention. Participants who received DMBI demonstrated significantly enhanced frontal alpha asymmetry after intervention, $t(15) = 1.866$, $P = 0.041$, and effect size = 0.466. Although participants who received CBT showed a trend toward enhancement, and their postintervention alpha asymmetry levels were intermediate to those of the waitlist control and DMBI groups, enhancement in this group did not reach statistical significance, $t(16) = 1.147$, $P = 0.134$, and effect size = 0.279. Participants in the waitlist group showed no significant changes in alpha asymmetry

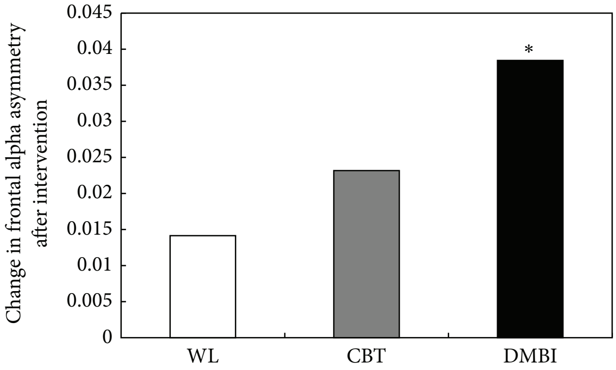


Figure 2: Comparison of the frontal alpha asymmetry after 10-week training between the waitlist, CBT, and DMBI groups. Each bar represents the difference in alpha asymmetry between baseline and postintervention values. Positive values indicate increased level of alpha asymmetry after intervention; negative values indicate a reduction in asymmetry. WL = waitlist group; CBT = cognitive behavioral therapy group; DMBI = *Dejian* mind-body intervention group. $^*P < 0.05$ (paired samples Student's t-test).

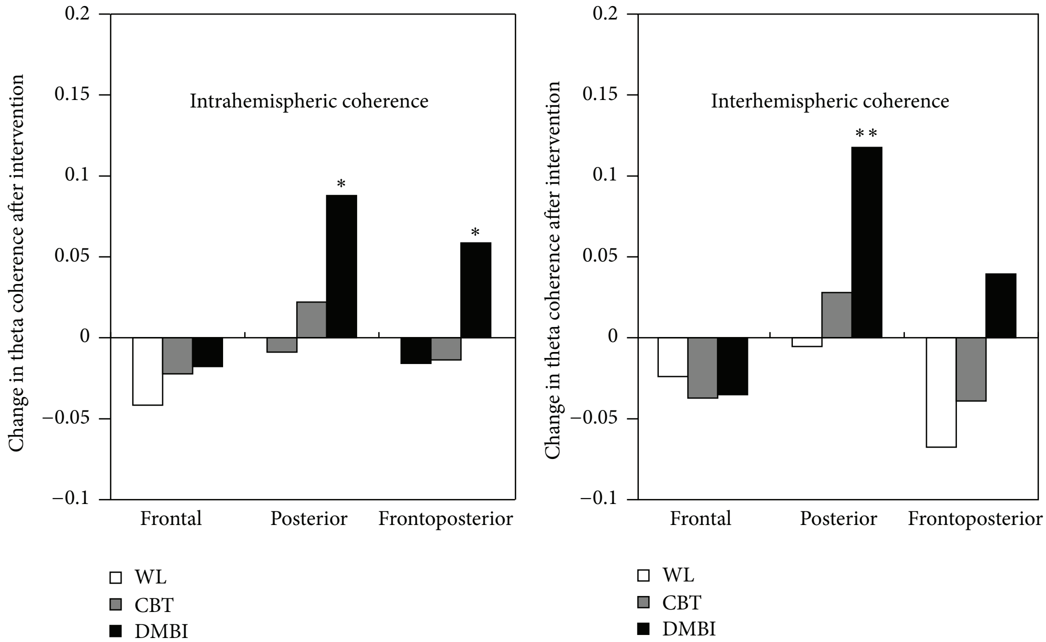
after 10 weeks, $t(15) = 0.422$, $P = 0.340$, and effect size = 0.106. The mean increment of asymmetry level in the DMBI group was 0.038 units (SD = 0.082), which was nearly double that of the CBT group (mean increment = 0.023 units; SD = 0.083) and nearly triple that of the waitlist group (mean increment = 0.014 units; SD = 0.134). Multiple sources of scientific evidence have suggested that greater frontal alpha asymmetry indicates positive mood and a state of relaxation [22, 23, 44, 45]. The significant elevation of frontal alpha asymmetry in the DMBI group implies that DMBI not only improves the mood states of patients with depression, as we have previously reported, but also fosters a more relaxed and "happier" brain state that is accompanied by left frontal activation.

3.2. DMBI Enhanced Inter- and Intrahemispheric Theta Coherence. At baseline, there were no significant differences between the DMBI, CBT, and waitlist groups in the six clusters of intra- and interhemispheric theta coherence; F values ranged from 0.025 to 1.522, $P > 0.05$. After intervention, as shown in Figure 3(a), the DMBI group demonstrated significantly enhanced intra- and interhemispheric theta coherence in posterior regions (intraposterior: $t = 2.116$, $P = 0.025$, and effect size = 0.513; interposterior: $t = 2.629$, $P = 0.009$, and effect size = 0.637) and intrahemispheric coherence in frontoposterior brain regions, $t = 2.039$, $P = 0.029$, and effect size = 0.494. In contrast, neither the CBT nor the waitlist group showed similar patterns of elevation of coherence extending through anterior and posterior brain regions: t values ranged from −1.664 to 0.675; effect sizes ranged from 0.033 to 0.416, $P > 0.05$. Regarding interhemispheric frontoposterior coherence, the DMBI group also showed a mean increment of 0.039 units, which was significantly greater than that of the CBT group (mean decrement of 0.039 units: $t(32) = 1.703$, $P = 0.049$, and effect size = 0.584) and the waitlist group (mean decrement of 0.068 units: $t(31) = 2.099$, $P = 0.022$, and effect size = 0.728). No significant changes in mean frontal intra- or interhemispheric coherence were observed in any group; t values ranged from −0.469 to −1.257; effect sizes ranged from 0.117 to 0.305, $P > 0.05$.

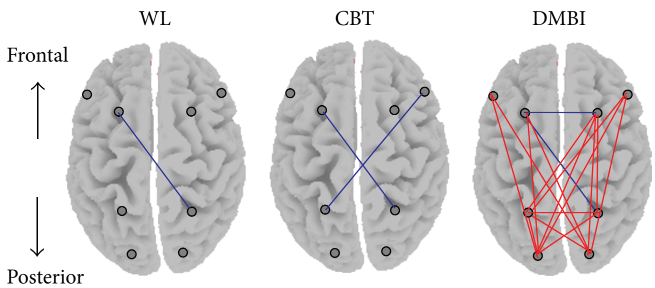
The topographic map in Figure 3(b) illustrates the individual electrode pairs that yielded significant changes in theta coherence after intervention. Consistent with the group mean differences in the clustered coherence indices, the DMBI group exhibited significant coherence elevation at long-range connections between hemispheres that involved anterior-posterior regions and intraposterior regions. Numerous neuroimaging and neuroelectrophysiological findings have suggested that the posterior association cortex and its functional connectivity with the frontal region have a salient role in mediating attention and effortful mental processing [46–49] and that these regions are involved in the pathology of people suffering from attention deficits [50, 51].

3.3. Enhanced Frontal Alpha Asymmetry Was Associated with Improvement of Depressive Symptoms. As frontal alpha asymmetry has repeatedly been found to be associated with positive mood, a relaxed state of mind, and depression, we anticipated that the elevated frontal alpha asymmetry that was specifically found in patients who received DMBI might be related to the reduction in their depressive states. Chi-squared tests were performed to explore changes in frontal alpha asymmetry and depression severity (as measured with the BDI-II). Depression severity was as the clinical classifications of the BDI-II. These classifications include "Normal (0–13 points)," "Mild Depression (14–19 points)," "Moderate Depression (20–28 points)," and "Severe Depression (29–63 points)." Participants who were in the normal range at baseline were excluded from analysis unless their condition deteriorated significantly after the intervention. After exclusion, there remained 13, 14, and 14 participants in the waitlist, CBT, and DMBI, respectively. Participants who were classified as having less severe depression after the intervention (e.g., participants who went from "Moderate Depression" at baseline to "Mild Depression" after the intervention) were clustered as "Improved"; all others were clustered as "Not Improved." Similarly, participants who showed increased alpha asymmetry after the intervention were clustered as "Increased", whereas those with reduced asymmetry were classified as "Decreased."

The results indicated that both DMBI, $\chi^2(1) = 5.250$, $P = 0.011$, and CBT, $\chi^2(1) = 3.590$, $P = 0.029$, groups reported significant improvement of depressive symptoms when compared to the waitlist control group (Figure 4(a)). However, the Chi-squared test showed that participants in the DMBI group with improved depressive symptoms were more likely to exhibit increased alpha asymmetry, $\chi^2(1) = 6.873$, $P = 0.009$ (Table 2). Among the 11 participants with reduced depressive symptoms, 9 (82%) exhibited increased alpha asymmetry after the intervention. Furthermore, all participants who did not exhibit reductions in depression severity exhibited decreases in alpha asymmetry after intervention. Although the CBT group also demonstrated significantly improved postintervention BDI-II scores, no significant association



(a)



(b)

FIGURE 3: Changes in intra- and interhemispheric theta coherence after intervention across three groups. (a) The bar chart shows the mean difference in theta coherence indices between baseline and postintervention of each group. Positive values indicate increased level of theta coherence after intervention; negative values indicate a reduction in coherence analyzed with paired samples Student's t-test; $^{**}P < 0.01$; $^{*}P < 0.05$. (b) The topographic map indicates the individual electrode pairs that yield significant changes in theta coherence of each group after intervention. Red lines linking the electrode pairs signify significant coherence increments, whereas blue lines indicate significant coherence decrements analyzed with paired samples Student's t-test, $P \leq 0.05$. WL = waitlist group; CBT = cognitive behavioral therapy group; DMBI = *Dejian* mind-body intervention group.

between reduction in depression severity and enhancement of alpha asymmetry was observed, $\chi^2(1) = 0.280$, $P = 0.597$. As expected, the waitlist group also failed to show any significant association between these two parameters, $\chi^2(1) = 1.040$, $P = 0.308$.

3.4. Enhanced Intra- and Interhemispheric Theta Coherence Was Associated with Attentional Ability. The increased long-range theta coherence in the DMBI group after the 10-session intervention may be suggestive of the possible neural mechanism underlying its improvements in attentional ability, which was revealed by the results of the DVT (Figure 4(b)). There was no significant difference in the total completion time at baseline among the waitlist, CBT, and DMBI groups, $F(2, 46) = 0.433$, $P = 0.651$. After 10-week training, the DMBI group demonstrated significantly improved performance on the DVT attentional task, $t(15) = 3.623$, $P = 0.002$, and effect size = 0.91, when compared to the CBT, $t(16) = 1.103$, $P = 0.143$, and waitlist, $t(16) = 0.432$, $P = 0.336$ groups. Therefore, the substantial improvement on the DVT attention task observed in the DMBI group after the 10-week training suggested that the DMBI had a significant effect on enhancing attentional ability in patients with depression.

To further explore the association between theta coherence and attentional ability, Pearson's correlations were calculated between DVT completion time and mean intra- and interhemispheric frontoposterior/posterior coherence indices after the intervention for each group. DVT completion times were negatively correlated with all four coherence indices in the DMBI group (Table 3); r values ranged

TABLE 2: Association between severity level of depression and frontal alpha asymmetry.

Subgroups of change in alpha asymmetry[a]	Subgroups of change in severity level of depression[b] Improved	Not improved	χ^2	E.S.
WL ($n = 13$)			1.040	0.28
Increased	1 (8%)	5 (39%)		
Decreased	3 (23%)	4 (31%)		
CBT ($n = 14$)			0.280	0.14
Increased	6 (43%)	3 (21%)		
Decreased	4 (29%)	1 (7%)		
DMBI ($n = 14$)			6.873**	0.70++
Increased	9 (64%)	0 (0%)		
Decreased	2 (14%)	3 (21%)		

Note. WL: waitlist control; CBT: cognitive behavioral therapy; DMBI: *Dejian* mind-body intervention; E.S.: effect size as measured by Phi value.
[a]Subgroups of change in alpha asymmetry are determined by the change in frontal alpha asymmetry from baseline to postintervention, where higher asymmetry level after intervention is considered as "Increased," and vice versa.
[b]Subgroups of change in severity level of depression are determined by the change in clinical classification based on the total score of Beck Depression Inventory from baseline to postintervention, where movement from more severe to less severe category after intervention is considered as "Improved"; otherwise, it is "Not Improved."
**$P < 0.01$; ++large effect size.

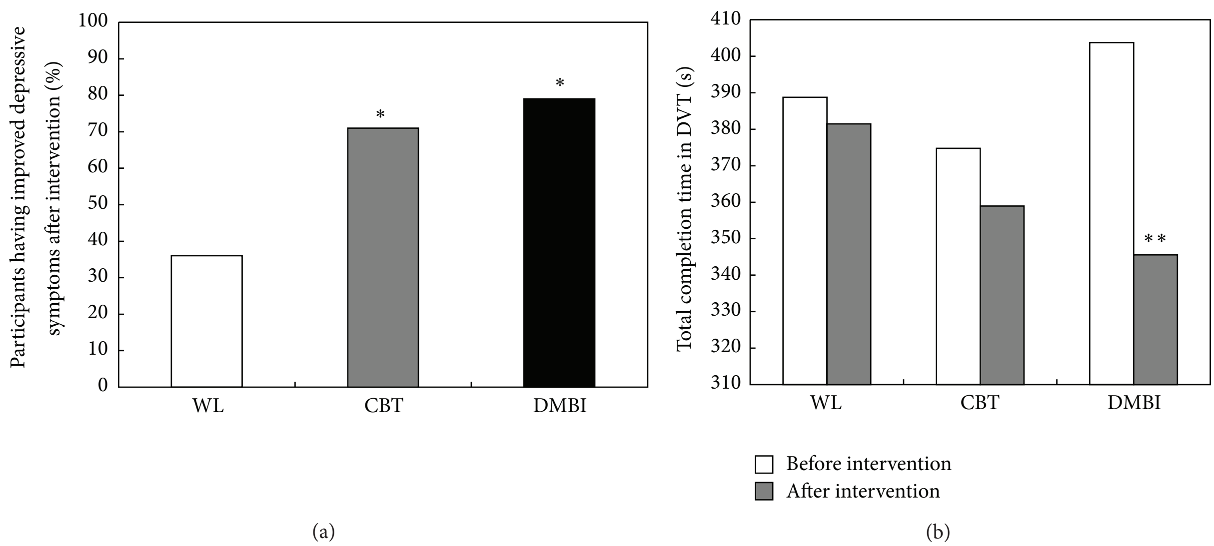


FIGURE 4: Difference in measures of depressive symptoms and attentional ability at baseline and after 10-week training for waitlist, CBT, and DMBI groups. (a) Each bar represents the percentage of participants in each group having reduced depressive symptoms as indicated by their shift to a less severe clinical classification as measured with the Beck Depression Inventory (BDI-II). (b) The ordinate represents the total completion time of the Digit Vigilance Test (DVT), where shorter completion time indicates greater work efficiency and increased ability to maintain attention on the task. *$P < 0.05$ (Chi-squared test or paired Student's samples t-test).

from −0.41 to −0.57, $P \leq 0.05$, suggesting that faster response times (which indicate increased attention) were associated with greater levels of coherence. This negative association is consistent with past empirical evidence for the involvement of frontoposterior functional connectivity and the significant contribution of the posterior brain regions in attention processing [46–49]. In contrast, no such associations were found in the CBT or waitlist groups (Table 3).

4. Discussion

The present study provides evidence that a Chinese *Chan*-based mind-body intervention can alter brain activity and connectivity patterns that are associated with positive mood and attentiveness in patients with major depressive disorders. It has been widely documented that positive emotions, feelings of well-being, and states of relaxation are associated with greater left-side anterior activation, which is indexed

Table 3: Correlation between digit vigilance test performance and theta coherence indices.

Coherence indices	Completion time of Digit Vigilance Test		
	WL ($n = 16$)	CBT ($n = 17$)	DMBI ($n = 17$)
Intrahemisphere			
Frontoposterior	−0.232	0.175	−0.568**
Posterior	−0.030	0.439*	−0.437*
Interhemisphere			
Frontoposterior	−0.231	0.133	−0.536*
Posterior	0.031	0.334	−0.412*

Note. WL: waitlist control; CBT: cognitive behavioral therapy; DMBI: *Dejian* mind-body intervention.
*$P \leq 0.05$; **$P < 0.01$.

by decreased alpha activity in the left hemisphere [23, 52] and that negative emotion is accompanied by greater right-side activation [44]. While insufficient left-anterior activation and/or excessive right-anterior activation have repeatedly been found in patients with depression [45], enhanced adaptive responses to stressful events have been noted in individuals with greater left-side anterior activation [44]. Our results showed that DMBI was associated with a significant elevation in left-side anterior activation and that the increased left-sided anterior activation was positively correlated with improvements in overall depressive symptoms, as measured by the BDI-II; these findings support our hypothesis that DMBI can elevate positive affect. These results are consistent with the findings of significant alleviations of depressive symptoms and reductions in the intake of antidepressants in patients with depression who practice DMBI [25]. Together, these results indicate that DMBI activates neural networks involved in positive affect and that the therapeutic, depression-reducing effects of DMBI are mediated by enhancement of frontal alpha asymmetry.

Interestingly, although patients who received CBT reported similar improvements in depressive symptoms after the intervention, their increment in frontal alpha asymmetry was not robust enough to reach statistical significance and was about half that of the DMBI group. This finding suggests that CBT has beneficial effects on the subjective feelings of the depressed patients but has relatively minimal effects on neural activity patterns. Although some recent studies have reported CBT-specific enhancements of frontal and/or subcortical region activity, the treatment protocols adopted in those studies typically required 15 to 20 individual sessions or small groups of, at most, 6 participants at a time [53–55]. Therefore, it is plausible that the 10-session CBT protocol and the inclusion of more than 10 persons in the CBT may have precluded results as robust as those reported in previous studies. In contrast, our 10-session DMBI was administered to a group of the same size and was able to foster frontal activation, suggesting that this Chinese *Chan*-based intervention may be a cost-effective complimentary intervention for patients with depression. DMBI's cost-effectiveness is also supported by another previous study that revealed improved depressive mood with increased frontal asymmetry in community-dwelling adults after 4 sessions of DMBI [13].

In addition to the alteration in mood and related neural responses elicited by DMBI, results from this study are also relevant to the electrophysiological changes associated with the attentional network. Our results indicated that DMBI was associated with significant elevations in intra- and interhemispheric frontoposterior and posterior theta coherences. EEG coherence is a correlate of functional connectivity [56, 57] and, in the theta frequency band, coupling between frontal and posterior cortical regions has been shown to underlie attentionally demanding processing [23, 24, 43]. Numerous empirical studies have also suggested the salient role of the posterior cortical regions (particularly the parietal cortex, which is located at the junction of multiple sensory regions and projects to several cortical and subcortical areas) in mediating sustained and selective attention [46, 47]. The robust enhancement in frontoposterior and posterior theta coherence within and between hemispheres in the DMBI group and its association with greater efficiency in a sustained attention task are coherent with the existing scientific findings regarding attention neural networks. The findings of the present study are also consistent with our previous research on the effects of one month of practice of the *Dan Tian* Breathing (a form of *Chan*-based mind-body exercise) in enhancing theta coherence [21]. The increase in theta coherence observed in the present study (maximal increment of 0.12 units) is much greater than that observed in the previous study (maximal increment of 0.04 units). One possible explanation of the more robust results of the present study may be related to the longer duration of intervention in the present study (10 versus 4 sessions). Another possible explanation could be that the present study applied the holistic DMBI model, while the previous study employed only one component of DMBI (i.e., the mind-body exercise). DMBI employs a holistic approach that incorporates integrative treatment of the mind and the body, which, on the one hand, changes the thought process and, on the other hand, improves mental and physical health by refining the diet and encouraging the practice of mind-body exercises for optimal treatment effects.

Collectively, our findings are consistent with the general understanding of the electrophysiological nature of mind-body interventions in which alpha and theta activations have been reported to be associated with changes in affective processes and attentional allocation [23, 58]. Interestingly, we observed both increased anterior left-side activation and increased theta coherence in the DMBI group, indicating that DMBI can produce positive changes in brain function. While the present study has provided some interesting observations on the potential effects of a 10-week DMBI training on improving the mood and cognitive function of patients with depression, yet its long-term effect remains unknown. In addition, it should also be noted that the generalization of the findings to the patient population with depression may be limited by the relatively small sample size. Future studies recruiting a larger sample, with a broader age range, and including longitudinal followup and different clinical populations would help extend current knowledge to a wider population. For example, it will be of interest to reduce stress in patients with anxiety depression or improve attention in children with attention-deficit hyperactivity disorder. In spite of this limitation, DMBI's potential to enhance the functioning of neural structures and the easy-to-practice and cost-effective characteristics of DMBI suggest that this Chinese *Chan*-based mind-body intervention is clinically applicable.

5. Conclusion

Our study showed that after 10 sessions of the Chinese *Chan*-based DMBI, patients with depression exhibited significantly increased EEG alpha asymmetry (which is an indication of left-side anterior activation) and intra- and interhemispheric theta coherences in frontoposterior and posterior brain regions. While the alpha asymmetry is an index associated with positive mood, the theta coherence is an index associated with attention. Furthermore, the asymmetry and coherence indices of the DMBI group were correlated with self-reported depression severity levels and performance on an attention test, respectively. In contrast, neither the CBT nor the waitlist group showed significant changes in EEG activity patterns. These findings support the idea that DMBI can promote positive emotional experience and induce a unique state of mind in which relaxation and internalized attention coexist.

Conflict of Interests

The authors declare that they have no conflict of interests.

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Research Article

Spatially Nonlinear Interdependence of Alpha-Oscillatory Neural Networks under Chan Meditation

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This paper reports the results of our investigation of the effects of Chan meditation on brain electrophysiological behaviors from the viewpoint of spatially nonlinear interdependence among regional neural networks. Particular emphasis is laid on the alpha-dominated EEG (electroencephalograph). Continuous-time wavelet transform was adopted to detect the epochs containing substantial alpha activities. Nonlinear interdependence quantified by similarity index $S(\mathbf{X}|\mathbf{Y})$, the influence of *source* signal $\mathbf{Y}$ on *sink* signal $\mathbf{X}$, was applied to the nonlinear dynamical model in phase space reconstructed from multichannel EEG. Experimental group involved ten experienced Chan-Meditation practitioners, while control group included ten healthy subjects within the same age range, yet, without any meditation experience. Nonlinear interdependence among various cortical regions was explored for five local neural-network regions, frontal, posterior, right-temporal, left-temporal, and central regions. In the experimental group, the inter-regional interaction was evaluated for the brain dynamics under three different stages, at rest (stage R, pre-meditation background recording), in Chan meditation (stage M), and the unique Chakra-focusing practice (stage C). Experimental group exhibits stronger interactions among various local neural networks at stages M and C compared with those at stage R. The intergroup comparison demonstrates that *Chan-meditation brain* possesses better cortical inter-regional interactions than the *resting brain* of control group.

1. Introduction

For several decades, scientific exploration has corroborated the effectiveness of meditation practice on health promotion. Particular evidence includes the improvement of cardiovascular functions, immunity, and hormone-level regulation. In addition, meditation makes positive changes in the brain and mind, including the positive emotional states, better stress manipulation, enhanced mindful attention, noticeable anxiety reduction, and depression relief, [1–7].

During the past decades, a number of meditation techniques have been developed and practiced all over the world. Although with somewhat different practicing scheme, almost all the practices are aimed to better manipulate the mind, brain function, and physical state of practitioners through mindfulness concentration and respiratory regulation. For many centuries, eastern religious and secular groups, such as the Buddhists, Taoist traditionalists, and the Indian Yogis, have been practicing meditation in order to achieve certain physical, mental, and spiritual realm. Meditation is a unique state of transcendental consciousness beyond the normal mind and mental process. Meditation may induce a series of integrated physiological changes. Among the diverse types of meditation, most practitioners are able to experience complete relaxation and the so-called tranquil awareness.

Although individuals in the East have been practicing various forms of meditation throughout history, scientific study of meditation did not begin until it became popular in the West. In recent years, meditation having been extended to complementary medical practices further motivated scientific studies with the focus of physiological alterations induced by the process [8, 9]. Increasing reports of meditation benefits further draw attention of researchers to the assessment of meditation in different indications. The research for physical and psychological correlation of meditation has been concentrated mostly on Yoga and transcendental meditation (TM) from India, Japanese Zen, and Tibetan Buddhism [10, 11]. Up to the present, little has yet been disclosed regarding the phenomena of Chan-Buddhist meditation (or simply "Chan meditation"). In the past decade, orthodox Chan meditation, as an unconventional therapy, has proved to be efficacious for many chronic diseases, infections, and even some malignant tumors. Consequently, more people began to practice orthodox Chan meditation in Taiwan. Accumulation of the effective evidences and health benefits of Chan meditation aroused our attention to the physiological investigation on the Chan-Buddhist disciples.

Since meditation process involves different states of mental activities and consciousness, EEG (electroencephalograph) thus became our major focus for exploring the human life system under Chan meditation. EEG applications in clinic and medical centers have become favorable since the 1970s because of its advantages of economy, safety, and convenience. Most of all, more scientific evidences of EEG variations have been disclosed in a number of different physiological, pathological, conscious and mental states in accordance with the various temporal, spectral, and spectral EEG characteristics. Although with the rapid progress in sophisticated medical imaging technologies, EEG still plays an important and irreplaceable role in long-term monitoring of brain functions exhibited as the lump variations of electrical activities. New findings have been continuously observed and reported [12–15]. As normally characterized by frequency, the EEG patterns are conveniently classified into five frequency ranges including delta (Δ, below 4 Hz), theta (θ, 4–8 Hz), alpha (α, 8–13 Hz), beta (β, 13–30 Hz), and gamma (γ, 30–70 Hz). Earlier paper [16], based on EEG spectral power and coherence estimates, reported the brain regions involved in meditative states as the selective associations of theta and alpha oscillating networks activity with states of internalized attention and positive emotional experience. According to our preliminary results, differentiation in frontal/occipital alpha activities plays a key role in comparing EEG between Chan-meditation practitioners (Appendix) and normal, healthy non-meditating subjects.

To explore the spatial interactions among brain local neural networks under alpha-rhythmic oscillation, methods developed in nonlinear dynamical theory become more versatile and favorable [17, 18]. The interactions among separate brain regions play a significant role in understanding the neurophysiological behavior of human brain. Accordingly, multivariate time series analysis based on nonlinear dynamical modeling becomes much appealing to investigate the important mechanism by which specialized cortical and subcortical regions integrate their activities into different functions and different spatial scales [19–23]. In recent studies, brain dynamics can be conceived as a large ensemble of coupled nonlinear dynamical subsystems. We have focused on investigating the nonlinear, chaotic characteristics of Chan-meditation EEG during the past decade, based on nonlinear deterministic modeling of brain dynamics [14, 24]. Significant nonlinear synchronization has been detected between the macroscopic scale of EEG channels. Thus, various types of synchronization based on the concepts of nonlinear dynamical systems theory have previously been proposed as a more powerful mechanism than narrow band frequency synchronization (e.g., coherence function) for achieving integrative neural processing. This type of "nonlinear coupling" allows studying nonlinear interdependence between multichannel recording sites and represents an alternative to the coherence function which addresses all of these limitations simultaneously [24–32]. As a consequence, this study aims to probe into the α-wave nonlinear interdependence behaviors among multichannel electroencephalograph (EEG) signals collected from the orthodox Chan-Buddhist practitioners (experimental group) and normal, healthy subjects (control group).

2. Material and Methods

2.1. Voluntary Subjects and Procedures. This study involved two groups of subjects, the experimental group including 10 volunteers with an average of 5.8-year Heart-Sealing Chan-meditation experience and the control group including 10 volunteers without any meditation experience. Seven men and three women were in either group. In the experimental group the average age was 28 years, while in the control group the average age was 23 years. Heart-Sealing Chan-meditation practitioners participated in one 90-minute group meditation session every week and practiced approximately 30-minute individual meditation on a daily basis. Heart-Sealing Chan meditation has been the only orthodox way of inheriting the lineage of Chan sect. The core essence of orthodox Chan-meditation practice is to transcend the physiological (fifth), mental (sixth), subconscious (seventh), and Alaya (eighth) states of consciousness and finally attain the realm of true self characterized by the pure golden light with eternal wisdom (Appendix). All the consciousness-transcending preprocesses inside can be completed for a well experienced orthodox Chan-meditation practitioner who has been able to spontaneously activate ten Chakras in our body [33]. These ten Chakras are important energy spots for altering states of consciousness by converting our physically and mentally dominant characteristics to a particular state of detachment. Accordingly, novice practitioners put lots of effort into the practice from Chakra focusing, Chakra perception, up to Chakra sealing. In the beginning stage of Chakra focusing, practitioners may practice the special *brain-drilling* technique to reduce all the wandering thoughts abiding in the brain. The *brain-drilling* technique involves, firstly, focusing alternately on frontal and posterior regions of the brain with mindfulness attention and, next, focusing alternately on left and right regions and perceiving the interconnections between two regions.

In the experiment, we conducted overall 50-minute recording of EEG signals for both groups. The EEG signals were recorded by the 30-channel, common-reference (linked-mastoid MS1-MS2) electrode montage based on the international 10–20 system. Figure 1 illustrates the EEG recording montage of the 30 electrode locations. The protocol designed

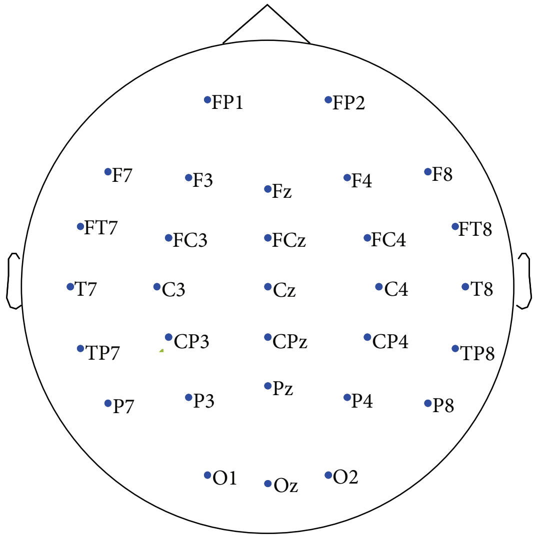


Figure 1: EEG electrode locations of the 30-channel recording montage.

for the experimental group involved three sessions: 5-minute premeditation relaxation (stage R), 40-minute Chan-meditation practice (stage M), and 5-minute Chakra focusing (stage C). In stage C, practitioners focused their mind and perception on a particular chakra named Chan Chakra (the third ventricle inside the brain, as illustrated in Appendix). No particular intervention was applied to the control group during the 50-minute EEG recording. The control subjects only sat in a relaxing position with eyes being closed, yet in the awake state.

2.2. Signal Acquisition and Preprocessing. The EEG signals were originally sampled at 1,000 Hz after being filtered by the analog, instrumentational band-pass filter with a passband of 0.5–50 Hz. The band-pass filter setting was selected to eliminate the 60 Hz interference by the power lines. A high sampling rate of 1,000 Hz was adopted to preserve the waveform quality of gamma rhythms (>25 Hz) often observed in Chan-meditation EEG that had been investigated in the other study of our research group. In this study, we downsampled the EEG with a sampling rate of 200 Hz since the major focus of this study is the alpha-dominated EEG epochs. The segments contaminated by such artifacts as eye blinking, eyeball movement, and muscle activities were prescreened in the preprocessing stage.

Wavelet decomposition provides an effective tool to extract the particular EEG rhythm of interest [34–36]. In addition, wavelet transform (WT) possesses such appealing properties as time-frequency localization and multirate filtering. Specific EEG rhythm may be extracted by dedicatedly designing the WT parameters. Wavelet transform can be implemented either in continuous configuration (CWT) or in discrete form (DWT). Due to the problem of extremely narrow-band EEG rhythmic pattern, CWT (continuous-time wavelet transform) was implemented in our study to reliably localize the correct spectral components of alpha rhythm.

In CWT, the signal to be analyzed is matched and convolved with the continuous wavelet basis function with the continuous time and frequency. The original signal is expressed as a weighted sum of the continuous basis wavelet function digitized by the sampling rate of the corresponding scale. The basis for wavelet transform is called the mother wavelet prototype. Wavelet functions are families of functions satisfying prescribed conditions, such as continuity, zero-mean amplitude, and finite or near finite duration. Some categories of wavelet functions may involve such properties like orthogonality and biorthogonality, regularity, and so forth [35–37].

Mother wavelet prototype needs to be appropriately selected according to the properties of the particular signal under investigation. Adeli et al. [38] successfully captured and localized the 3 Hz spike and wave complex in the epileptiform EEG by applying wavelet decomposition with Daubechies wavelets. Our previous study has corroborated the feasibility of adopting Daubechies 6 (DB6) wavelet as the mother wavelet in EEG rhythmic analysis [37].

The family of Daubechies wavelets is known for its orthogonal property and efficient implementation. The lower-order Daubechies wavelets are too coarse to properly represent EEG sharp transients. The higher-order ones with extra oscillations are beyond the requirements for analyzing the low-frequency EEG rhythms. Particularly, order 6 Daubechies wavelet becomes most appealing in our study because its waveform pattern appears to mimic the neuronal action potentials.

2.3. Nonlinear Interdependence Measure. The scheme for evaluating the nonlinear interdependence was based on the modified algorithm employed in computing the *similarity index* $S(\mathbf{X}|\mathbf{Y})$ [24]. Major tasks involved in the algorithm are reconstruction of the m-dimensional phase-space trajectory and computation of the average cloud radius centered at a given state point.

2.3.1. Reconstruction of m-Dimensional Trajectory. Consider the brain as a nonlinear dynamical system. The nonlinear interactions of the local neuronal networks can be assessed by the analysis of the collective dynamics underlying EEG time series simultaneously recorded from different brain regions. The first step is to reconstruct the multidimensional phase-space portrait of the system dynamics $\mathbf{X}$ and $\mathbf{Y}$, respectively, from EEG time series $x[i]$ and $y[i]$. According to the Takens embedding theory [39], a smooth map from the EEG time series $\{x[i] \mid i = 1, \ldots, N+(m-1)\tau\}$ to the phase-space trajectory $\mathbf{X} = \{X_i \mid X_i = (x[i], x[i+\tau], \ldots, x[i+(m-1)\tau])\}_{i=1}^{N}$ preserves some important topological invariants of the original system. The reconstruction assumes a total number of N system-state points in the m-dimensional phase-space trajectory, utilizing a rational time delay τ (in sample point) [40, 41]. The dimension m indicates the number of degrees of freedom of the nonlinear system and, accordingly, reflects the *complexity* of the system dynamics.

2.3.2. Computation of the Average Cloud Radius. Consider a state point X_i on the m-dimensional phase trajectory. As illustrated in Figure 2, a KNN hypersphere, formed by the K's nearest neighboring (KNN) points of $\mathbf{X}_i$, is a cloud composed of Km-dimensional neighboring points around X_i. Let $r_{i,j}$ and $s_{i,j}$, $j = 1, \ldots, K$, denote the time indices of the KNN points of X_i and Y_i, respectively. Then, the set of state points in the KNN hypersphere centered at X_i is $\{X_{r_{i,j}} \mid j = 1, \ldots, K\}$. The average square Euclidean distance from X_i to its KNN neighbors (or the average square radius of the cloud centered at X_i) is defined as

$$R_i^{(K)}(X) = \frac{1}{K}\sum_{j=1}^{K}\left\|X_i - X_{r_{i,j}}\right\|^2, \tag{1}$$

where $\|\cdot\|$ indicates the operator for calculating the Euclidean distance. Another point cloud around X_i is formed with respect to its *mutual* neighbors $X_{s_{i,j}}$, which share the same temporal indexes of the KNN of Y_i. In this sense, the $\mathbf{Y}$-conditioned average square Euclidean distance is defined by replacing the true nearest neighbors of X_i by the *mutual* neighbors [37]:

$$R_i^{(K)}(X \mid Y) = \frac{1}{K}\sum_{j=1}^{K}\left\|X_i - X_{s_{i,j}}\right\|^2. \tag{2}$$

In the extreme case of $K = N$, the average square radius of the trajectory centered at X_i is given by

$$R_i(\mathrm{X}) = \frac{1}{N-1}\sum_{j=1, j\neq i}^{N}\left\|X_i - X_j\right\|^2. \tag{3}$$

Then, for two strongly synchronized systems, both self and mutual neighbors mostly coincide so that $R_i^{(K)}(X) \approx R_i^{(K)}(X \mid Y) \ll R_i(X)$; whereas for independent systems, mutual neighbors are more scattered that leads to $R_i^{(K)}(\mathrm{X}) \ll R_i^{(K)}(\mathrm{X} \mid Y) \approx R_i(X)$. Accordingly, the degree of interdependence of these two systems is reflected by the similarities (or dissimilarities) between these two cloud patterns formed by self and mutual neighbors. The strength of similarity between these two point clouds is termed as similarity index S [24, 37] and is defined as follows:

$$S^{(K)}(X \mid Y) = \frac{1}{N}\sum_{i=1}^{N}\frac{R_i^{(K)}(X)}{R_i^{(K)}(X \mid Y)}. \tag{4}$$

$S^{(K)}(X \mid Y)$ assesses the statistical dependence of the state-space structure of $\mathbf{X}$ on that of $\mathbf{Y}$ in the sense of testifying whether closeness in $\mathbf{X}$ implies closeness in $\mathbf{Y}$ and vice versa. Two identical systems with the same sets of self and mutual neighbors result in the maximum similarity index ($S = 1$), whereas the index is close to zero ($S \approx 0$) for completely independent systems. The opposite interdependence ($S^{(K)}(Y \mid X)$) can be computed analogically. Notice that similarity indexes are in general asymmetric; that is, $S^{(K)}(Y \mid X) \neq S^{(K)}(X \mid Y)$. $S^{(K)}(X \mid Y)$ evaluates the effect of system $\mathbf{Y}$ on system $\mathbf{X}$. From the point of view of the system theory, signal $\mathbf{Y}$ is regarded as the *source* or the active role in the interaction, while signal $\mathbf{X}$ plays a passive role (a *sink*). On the other hand, $S^{(K)}(Y \mid X)$ analysis considers $\mathbf{Y}$ as the *sink* that plays the passive role [24, 37].

The asymmetry of S is one of the main advantages over the other nonlinear measures such as the mutual information and the phase synchronizations. The fact that S is asymmetric allows us to study not only topographic patterns but also functional properties. By considering each EEG electrode either as a sink or as a source in the nonlinear-interdependence interaction, we may thereby further explore the brain functional topological profile and the direction of interaction among local neuronal networks [19]. For example, the condition of $S(Y \mid X) > S(X \mid Y)$ indicates that $\mathbf{Y}$ depends more on $\mathbf{X}$ than vice versa. In other words, $\mathbf{X}$ has a greater influence on $\mathbf{Y}$ than vice versa. In such a case, $\mathbf{X}$ is said to be more *active* and $\mathbf{Y}$ is more *passive*. By considering each electrode either as a sink or as a source in the nonlinear dynamical interaction, we may thereby explore the spatial direction of the interaction and the dominance of local neuronal networks under Chan meditation [42].

In order to maximize the sensitivity to the underlying synchronization and gain the robustness against noise, we proposed a modified version of S measure with an adjustable range of KNN. Following our previous study of dimensional complexity index [27, 28], a reliable estimate of dimensional complexity of a system was obtained by averaging the complexity indexes over a moderate range of K's. A small K causes superimposed noise, while a large K results in a measurement involving multimodal effects [27]. To determine a robust measure against noise, it follows that the final estimate of nonlinear interdependence is the average $S^{(K)}(X \mid Y)$ over an appropriate range of K's and is denoted by $S(X \mid Y)$.

In the practical implementation, previous studies of dimensional complexity for meditation EEG have established a moderate choice of parameters. The time delay τ can be determined by the first zero-crossing of the corresponding autocorrelation function. Embedding dimension m can be determined by the convergent estimate of dimensionality. The window length N is selected to encompass the stabilization of dynamical behavior in the phase space in the sense of the convergent estimate of quantitative nonlinear dynamical property of reconstructed EEG trajectory, for example, correlation dimension. As a consequence, the implementing parameters were selected to be $\tau = 5$ (sample points), $m = 10$, and window length $N = 1,000$ sample points (5 seconds) that ensure convergent and reliable estimates [24, 27, 28]. The final estimate, $S(X \mid Y)$, was obtained by averaging the $S^{(K)}(X \mid Y)$ for K ranging from 20 to 35.

2.3.3. Outline of the Scheme. The entire scheme employed in this study is illustrated in Figure 3 that integrates different theories and methods to evaluate the nonlinear interdependence for multichannel EEG.

To investigate the nonlinear-interdependent behaviors of alpha activities, CWT is employed to identify alpha-dominated epochs in the entire EEG record. An EEG segment

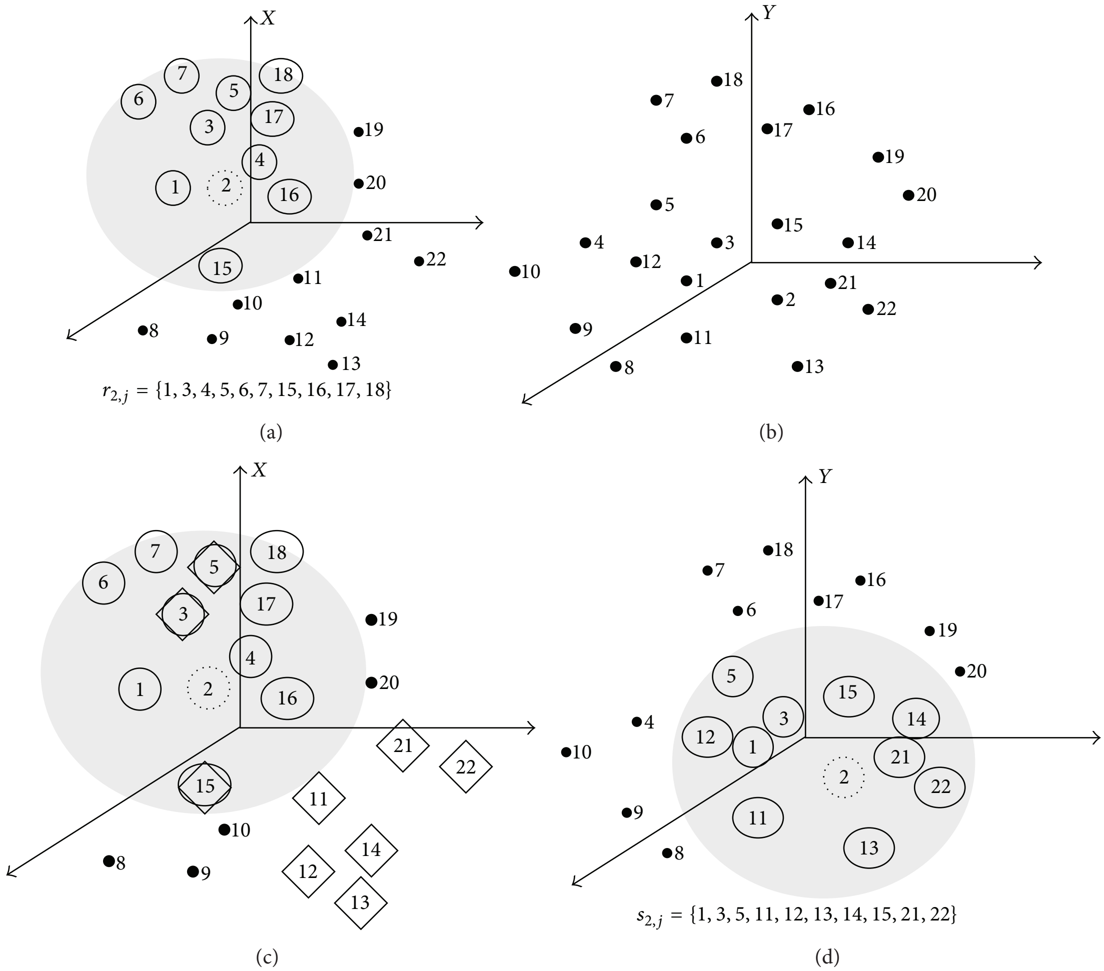


Figure 2: Illustration for (a) self neighbors $X_{r_{2,j}}$ (◯), (b) state points in Y, and (c) mutual neighbors $X_{s_{2,j}}$ (◇) where the indexes $s_{2,j}$ are determined from the indexes of (d) KNN of Y_2 ($K = 10$), assuming $m = 3$, $K = 10$, $i = 2$, and $N = 22$.

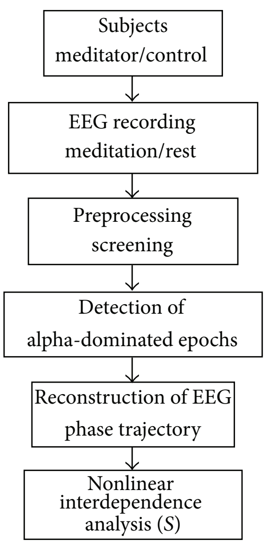


Figure 3: Scheme for evaluating nonlinear interdependence of multichannel EEG.

is identified to be alpha dominant if the percentage of α power to the total power is at least 50% in more than 15 channels (one half of the total channels). Figure 4 displays the results of interpreting the 5-second EEG recorded from channels Oz, Cz, and Fz. The alpha-power percentage (denoted as ρ) for each one-second epoch is listed beneath the EEG tracing. The 5-second EEG tracing is plotted with the amplitude ranging from $-50\,\mu$V to $50\,\mu$V. Parameter ρ evaluated for different channels may reflect the focalized behavior of alpha activity.

To extend the capacity of assessing the neural-network interaction, the *source* X_j can be generalized as an integrated local network involving L *active* electrode sites so that $S_p(X_i)$ becomes the average of L's $S(X_i \mid X_j)$, assuming $X_j \neq X_i$:

$$S_p(X_i) = \frac{1}{L}\sum_j S(X_i \mid X_j). \tag{5}$$

Equation (5) then evaluates the integrative effects of L *active* electrodes on X_i. On the other hand, the influence of an *active*

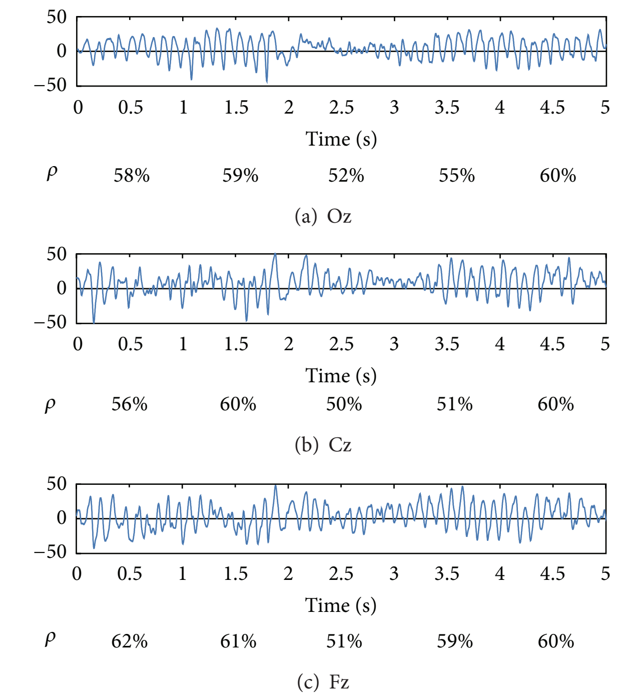


Figure 4: Percentage of alpha power to total power for each one-second epoch of the five-second EEG segments (amplitude in μV) recorded from (a) Oz, (b) Cz, and (c) Fz.

electrode X_j on the integrative neural network encompassed by L *passive* electrodes (X_i) can be evaluated by

$$S_a\left(X_j\right) = \frac{1}{L}\sum_i S\left(X_i \mid X_j\right) \quad (6)$$

assuming $X_i \neq X_j$. Both $S_p(X_i)$ and $S_a(X_j)$ are called *regional interdependence index* (*RII*).

In Chan-meditation practice, practitioners often focus on five regions alternately, frontal, posterior, left, right, and central regions, after activating the *Chan Chakra* inside the third ventricle. The purpose is to eliminate the stream of jumbled thoughts and produce a tranquil mind. To investigate the effect of such regional focusing, we accordingly divided 30 EEG recording sites into five regions:

frontal (F): Fp1, Fp2, F7, F3, Fz, F4, and F8;

posterior (P, Parietal + Occipital): O1, Oz, O2, P7, P3, Pz, P4, and P8;

central (C): FCz, Cz, and CPz;

left Temporal (LT): FC3, FT7, T7, C3, TP7, and CP3;

right Temporal (RT): FC4, FT8, T8, C4, TP8, and CP4.

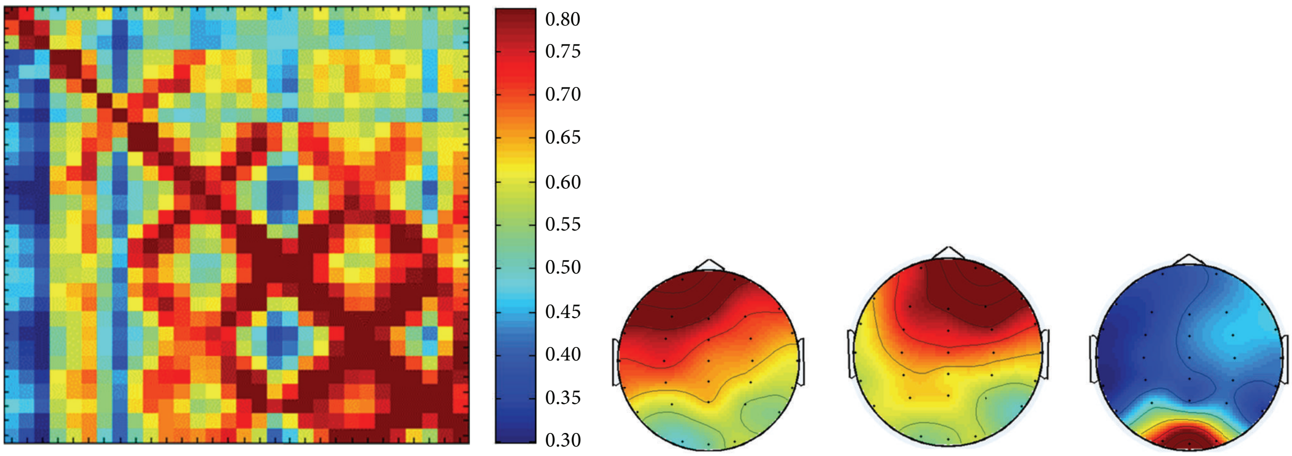
3. Results and Discussion

3.1. Interdependence Matrix of Chan-Meditation EEG. Consider a given *source* signal $\mathbf{Y}$. The influence of *source* signal $\mathbf{Y}$ on *sink* signal $\mathbf{X}$, $S(\mathbf{X} \mid \mathbf{Y})$, can be expressed as a 30 × 30 interdependence matrix with the element $S_{ij} = S(X_i \mid Y_j)$ denoting the coupling strength of interaction of the source Y_j affecting the sink X_i. The similarity index (S.I.) was calculated for 870 (30 × 29) electrode pairs. As displayed in Figure 5(a), the color image encoded the quantities in the 30 × 30 interdependence matrix $\mathbf{S}$. The right-side color chart encodes the strength level of S_{ij}, from blue to red indicating the range of S from the smallest to the largest value. EEG channels are in the order of (from top/left): O2, Oz, O1, P7, P3, Pz, P4, P8, TP8, CP4, CPz, CP3, TP7, T7, C3, Cz, C4, T8, FT8, FC4, FCz, FC3, FT7, F7, F3, Fz, F4, F8, Fp2, and Fp1. For example, the box at the lower-left corner characterizes the effect of O2 channel on Fp1 channel, as denoted by S(Fp1 | O2). Accordingly, the first row reveals the effect of *source* O2, Oz, . . ., and Fp1, respectively, on *sink* O2. On the other hand, the first column indicates how *source* O2 affects *sink* O2, Oz, . . ., and Fp1, respectively. The dark red along the diagonal line indicates the highest similarity index $S = 1$ when the *source* and *sink* signals are identical.

This figure exhibits some typical behavior in the S matrix; that is, stronger interdependence occurs in the pairs of nearby EEG channels. On the other hand, weaker interaction is measured as two channels are much apart. Moreover, box (i, j) does not equal its transposed partner box (j, i), indicating the asymmetry of S matrix. Figures 5(b)–5(d) display the top view of brain topographic mapping of S_a(FP1), S_a(FP2), and S_a(Oz) extracted, respectively, from the 30th, 29th, and 2nd columns of Figure 5(a). The topographic mapping was plotted by the function *topoplot.m* provided by EEGLab. The mappings exhibit the efficacy of the given channel acting as the *source* role. The results in Figures 5(b) to 5(d) reveal the right-frontal dominance. The occipital channels are comparably less active with respect to the frontal neuronal networks. Such weaker influence of occipital and posterior regions on the other regions can be clearly observed from the blue color dominating in the left three columns of $\mathbf{S}$ matrix (Figure 5(a)), corresponding to the *source* at O2, Oz, and O1.

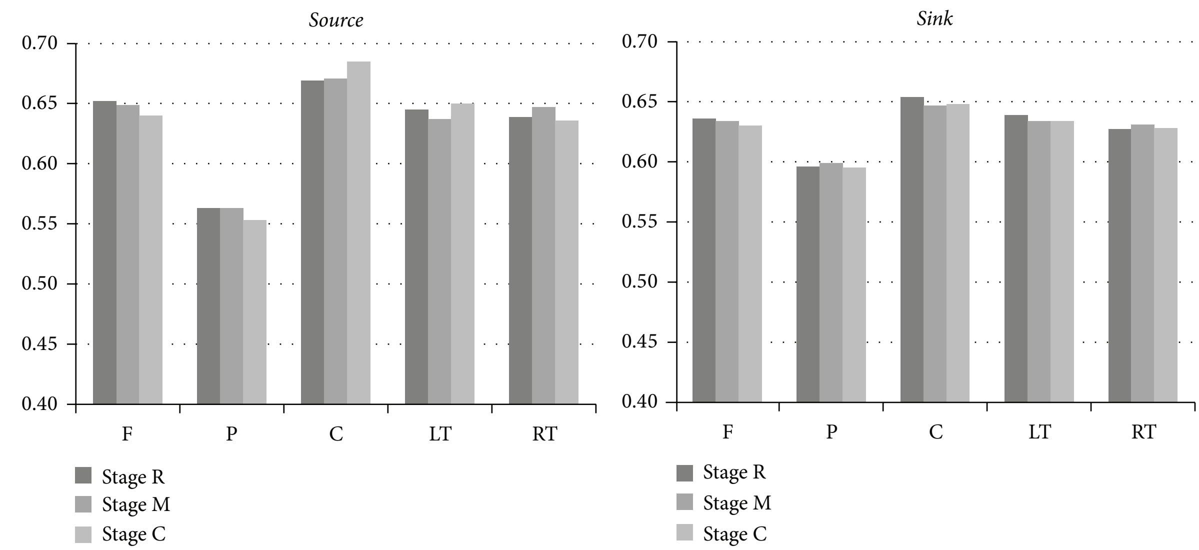
3.2. Inter-Region Interdependence Analysis—Experimental Group. Inter-regional nonlinear interdependence was analyzed for EEG recorded in three different sessions (stage R, M, and C). Due to the premeditation *brain-drilling* practice described in previous section, we particularly focused on the left-right temporal (LT-RT) and frontal-posterior (F-P) neural-network interactions. For example, $S(\mathrm{F} \rightarrow \mathrm{P})$ is computed by averaging all $S_a(X_j)$ in (6) for all $X_j \in \mathrm{F}$ and $X_i \in \mathrm{P}$ to assess the integrative *source* effect of all electrodes in frontal region driving the posterior region. On the other hand, $S(\mathrm{P} \rightarrow \mathrm{F})$ is computed by averaging all $S_a(X_j)$ in (6) for all $X_j \in \mathrm{P}$ and $X_i \in \mathrm{F}$ when all the electrodes in the posterior region play the *source* role to drive the frontal region.

Table 1 lists the group averages and standard deviations of $S(\mathrm{F} \rightarrow \mathrm{P})$, $S(\mathrm{P} \rightarrow \mathrm{F})$, $S(\mathrm{LT} \rightarrow \mathrm{RT})$, and $S(\mathrm{RT} \rightarrow \mathrm{LT})$ at three experimental stages (R, M, and C). Evidently, $S(\mathrm{F} \rightarrow \mathrm{P})$ is consistently greater than $S(\mathrm{P} \rightarrow \mathrm{F})$ for all three stages. The P values (0.0055, 0.0031, and 0.0302) of paired sample t-test are all smaller than 0.05, that demonstrates the



(a) (b) S_a(FP1) (c) S_a(FP2) (d) S_a(Oz)

FIGURE 5: S.I. analysis for experienced practitioner during Chan meditation (Stage M) (a) 30×30 **S** matrix, and brain topographical mappings (top view) of (b) S_a(FP1), (c) S_a(FP2), and (d) S_a(Oz), indicating the average driving strength of the EEG sites FP1, FP2, and Oz.



(a) (b)

FIGURE 6: Average effectiveness of each region playing the role of a *source* (a) and *sink* (b). Three bars in each *RII* cluster correspond to three experimental stages.

statistical significance of frontal-alpha dominance at all three stages. On the other hand, results of the left-right temporal analysis of nonlinear interdependence reveal no distinctly dominant role of the laterally neural-network operation, that is, $S(\mathrm{LT} \rightarrow \mathrm{RT}) \approx S(\mathrm{RT} \rightarrow \mathrm{LT})$. The higher P values for the $S(\mathrm{LT} \rightarrow \mathrm{RT})$-$S(\mathrm{RT} \rightarrow \mathrm{LT})$ paired t-test indicate no statistically significant difference between two sets of results. We may further infer the balancing operations between the left-brain and right-brain hemispheres.

Our results demonstrate that interactions between left and right hemispheres are much more intensive than the interactions between frontal and posterior regions, with $P = 0.0016$, considering all the experimental subjects at all three stages.

Figure 6 provides an alternative viewpoint for exploring how a given region of interest ROI (F, P, C, LT or RT) influences or is influenced by the other regions. In Figure 6, left (right) group of five 3-bar clusters corresponds to the average effectiveness of each region playing the active (passive) role at three stages. For example, the leftmost bar indicates the average of $S(\mathrm{F} \rightarrow \mathrm{P})$, $S(\mathrm{F} \rightarrow \mathrm{LT})$, $S(\mathrm{F} \rightarrow \mathrm{RT})$, and $S(\mathrm{F} \rightarrow \mathrm{C})$ for stage R, while the rightmost bar indicates the average of $S(\mathrm{F} \rightarrow \mathrm{RT})$, $S(\mathrm{P} \rightarrow \mathrm{RT})$, $S(\mathrm{C} \rightarrow \mathrm{RT})$, and $S(\mathrm{LT} \rightarrow \mathrm{RT})$ for stage C. Among all five regions, posterior region, as either the *source* or *sink*, apparently exhibits the weakest link to the other regions. In addition, the effectiveness of *active* role of posterior region is weaker than that of *passive* role. The results strongly

Table 1: Group averages and standard deviations of $S(\mathrm{F} \rightarrow \mathrm{P})$, $S(\mathrm{P} \rightarrow \mathrm{F})$, $S(\mathrm{LT} \rightarrow \mathrm{RT})$, and $S(\mathrm{RT} \rightarrow \mathrm{LT})$ at three experimental stages (R, M, and C), including the P values of student t-test for $S(\mathrm{F} \rightarrow \mathrm{P})$-$S(\mathrm{P} \rightarrow \mathrm{F})$ and $S(\mathrm{LT} \rightarrow \mathrm{RT})$-$S(\mathrm{RT} \rightarrow \mathrm{LT})$ pairs.

Stage	$S(\mathrm{F} \rightarrow \mathrm{P})$		$S(\mathrm{P} \rightarrow \mathrm{F})$	$S(\mathrm{LT} \rightarrow \mathrm{RT})$		$S(\mathrm{RT} \rightarrow \mathrm{LT})$
R						
Group average	0.56		0.51	0.60		0.61
Group std	0.05		0.05	0.07		0.05
P value		0.0055			0.3476	
M						
Group average	0.56		0.50	0.60		0.61
Group std	0.03		0.06	0.06		0.04
P value		0.0031			0.1987	
C						
Group average	0.55		0.49	0.61		0.61
Group std	0.07		0.06	0.06		0.06
P value		0.0302			0.3953	

suggest the inactive behaviors of parietal-occipital lobes since region P encompasses the EEG-electrode sites of parietal and occipital lobes. The parietal lobe is responsible for integrating sensory information from various parts of the body, with the particular functions of determining spatial sense and navigation. Functions of occipital lobe mainly include visual reception, visual-spatial processing, and color recognition. As described previously, the core essence of orthodox Chan-meditation practice is to transcend physiological, mental, and all states of consciousness to prove the existence of true being. The inactive posterior regions may provide the evidence of brain rewiring in preparation for such transcendence.

Region C encompasses three midline electrodes locating from precentral to postcentral cortex. Region C, as the *source*, apparently dominates over the other four regions regardless of the stages. On the other hand, region C as the *passive* role is affected mostly among the five regions. Region C constantly exhibits the largest *RII* at all stages.

We may draw a tentative hypothesis from the mechanism of Chan-meditation practice. Practitioners are required to keep Chan Chakra active at any moment, that results in the formation of an energy pathway between Chan Chakra and Qian-Ding acupoint on scalp (Figure 10(b)). Does such physiological reformation correlate to the significant effectiveness of region C? It leaves an open question for future investigation.

RII characterizing the regional interdependence behaves differently for each region when the experimental subjects switch their mental states from R (resting) to M (meditation) or from R to C (Chakra focusing). To investigate the effect of different experimental sessions, the *RII* percentage increase/decrease from stage R to M and from stage R to C were computed for each of the five regions (F, P, C, LT, and RT) acting as either the *active* or the *passive* role. In comparison of *RII* between stage M and stage R, the percentage larger than 1% was observed in the regions of $\mathrm{LT}_{\mathrm{active}}$(−1.24%), $\mathrm{RT}_{\mathrm{active}}$ (1.25%), and $\mathrm{C}_{\mathrm{passive}}$ (−1.07%). On the other hand, the regions of significant change in *RII*, when comparing stage C with R, include $\mathrm{F}_{\mathrm{active}}$ (−1.84%), $\mathrm{P}_{\mathrm{active}}$ (−1.78%), and $\mathrm{C}_{\mathrm{active}}$ (2.39%). On the basis of *RII* of stage R for each individual region, we summarize the changes of *RII* at stages M and C as follows.

(1) In the *active*-role analysis, region LT becomes more deactivated at stage M, while region RT becomes more activated. When meditation subjects focused on Chan Chakra, the active driving strength of region C increases significantly (2.39%). On the other hand, suppression of the source activity occurs to both regions F and P (the regions anterior to and posterior to region C).

(2) In the *passive*-role analysis, only region C becomes notably deactivated at stage M (free meditation). In general, differences are trivial in comparison of RII_{passive} between stages M and R.

(3) Chan meditation deactivates the left brain hemisphere, whereas it inactivates the right brain hemisphere.

Except for region P, the *active*-role effectiveness of a given region is better than its *passive*-role effectiveness.

3.3. Inter-Region Interdependence Analysis—Control Group. In control group, the group average and standard deviation of $S(\mathrm{F} \rightarrow \mathrm{P})$, $S(\mathrm{P} \rightarrow \mathrm{F})$, $S(\mathrm{LT} \rightarrow \mathrm{RT})$, and $S(\mathrm{RT} \rightarrow \mathrm{LT})$ at stage R are, respectively, 0.55 ± 0.04, 0.51 ± 0.04, 0.59 ± 0.03, and 0.58 ± 0.04. The P values of student t-test for $S(\mathrm{F} \rightarrow \mathrm{P})$-$S(\mathrm{P} \rightarrow \mathrm{F})$ and $S(\mathrm{LT} \rightarrow \mathrm{RT})$-$S(\mathrm{RT} \rightarrow \mathrm{LT})$ pairs are 0.002 and 0.457. The results also reveal the frontal dominance and left-right lateral balance for the control group at rest. Yet, compared with the Chan-meditation practitioners, control group exhibits weaker strength of effectiveness no matter if the region plays an *active* or a *passive* role.

To explore the average effectiveness of a given ROI, we averaged the *RII*s for the region in connection with the other four regions. Figure 7 displays how a given ROI (F, P, C, LT, or RT) influences (*active*) or is influenced (*passive*) by the other regions. Similar to the results of experimental group, region P as either the *active* or *passive* role exhibits the weakest links to the other regions.

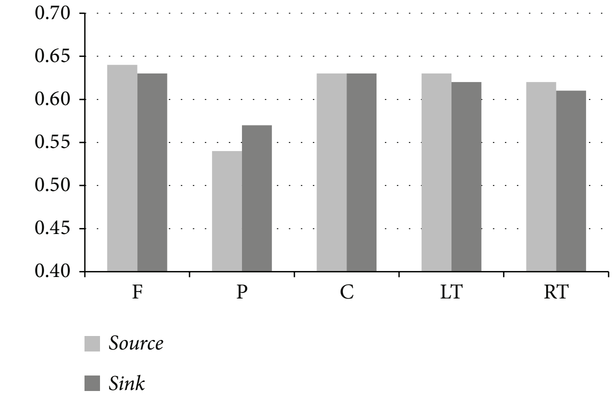


Figure 7: Average effectiveness of each region playing either the *active* or *passive* role.

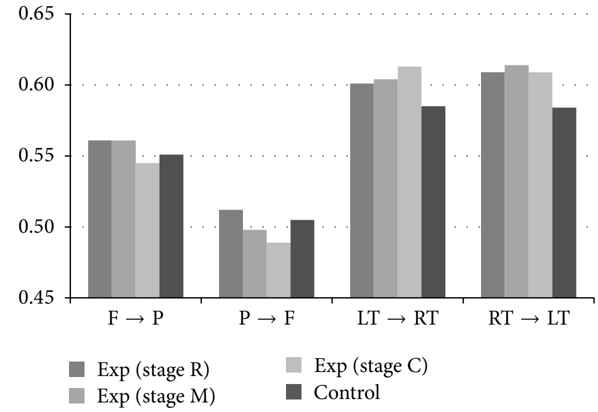


Figure 8: Group averages of *RIIs* (S(F → P), S(P → F), S(LT → RT), and S(RT → LT)) for experimental group at three stages and for control group at rest.

Comparing the efficacy of two counteractive roles played by the same region, we observe that the *source*-role effectiveness of a given ROI is higher than its *sink*-role effectiveness except region P.

3.4. Comparison between Experimental and Control Groups. Figure 8 illustrates the group averages of *RIIs*, including S(F → P), S(P → F), S(LT → RT), and S(RT → LT), for the experimental group at three stages (R, M, and C) and for the control group at rest. Experimental group reveals much more intensive lateral (LT ⟷ RT) interactions than control group. The differences are statistically significant for experimental group at stage M ($P = 0.0336$) and at stage C ($P = 0.0411$). On the other hand, region P responsible for spatial sense and navigation becomes comparatively inactive for Chan-meditation practitioners at stage C.

The assembling illustration in Figure 9 is used to compare the average effectiveness of each region between two groups. Experimental group, playing either a *source* role or a *sink* role, apparently exhibits higher average effectiveness in all five regions. The extraordinarily large *RIIs* for region C, particularly acting the *source* role, may be assumed to be correlated with the strengthening of neural networks of region C dominating over the other regions through the spiritual focusing on Chan Chakra. According to the post-experimental interview with Chan-meditation practitioners, such central (FCz-Cz-CPz) dominating behavior could be linked to the Chan-Chakra activation that further induces the perception of grand, solemn energy flow in and out through the cortical regions defined by acupoints DU20 (Baihui), DU21 (Qianding), and DU22 (Xinhui) in TCM (traditional Chinese Medicine). Figure 10(b) (Appendix) illustrates the locations of these three acupoints.

4. Conclusion

The time-transcending, nonmaterial sacred spiritual experiences of Chan-meditation practitioners bring our attention to the study of the unique interactions among regional neural networks in the brain. Scientific approach to the scope of Chan meditation provides insight into the mechanism in addition to the vague sketch of meditation sensation and its multiform benefits to human beings. This paper presents our preliminary results, based on nonlinear dynamical theory, of exploring the spatial interactions among brain local neural networks under alpha-rhythmic oscillation. Quantification of nonlinear interdependence based on similarity index reveals significant intergroup difference. Significant higher lateral interactions between left and right temporal regions were observed in Chan-meditation practitioners at the stages of Chan meditation and Chakra-focusing practice. In Chan practice, practitioners follow the doctrine that the mind can be enlightened only if it surrenders its leadership power to the "heart" (Bodhi, the true self with eternal wisdom). They accordingly can experience better balance and integration of the brain hemispheres through years of Chan-meditation practice.

Chan-Chakra spiritual focusing (at stage C) remarkably strengthens the central neural-network dominance over the other regions. On the other hand, suppression of the *source* activity in regions F and P at stage C appears to reveal the meditation state of transcending the realm of physical body and mind. The particular central (FCz-Cz-CPz) dominating phenomenon is reflected in long-term Chan practitioners as one of the metamorphosing processes that opens the energy pathway between Chan Chakra and the central-line scalp from acupoint DU20 to DU22 (Figure 10(b) in Appendix). In the case, practitioners experience tranquil brain and calm mind in every moment. Chan-meditation practice is to realize a Chan-style brain and Chan-style physical body, instead of merely sitting still for one hour to pursue temporary peace of mind and relief of body.

Appendix

Chan meditation originating more than 2,500 years ago has been proved to benefit the health while on the way toward the ultimate Buddhahood state. Buddha Shakyamuni disclosed the eternal truth, the supreme wisdom, the noumenal energy,

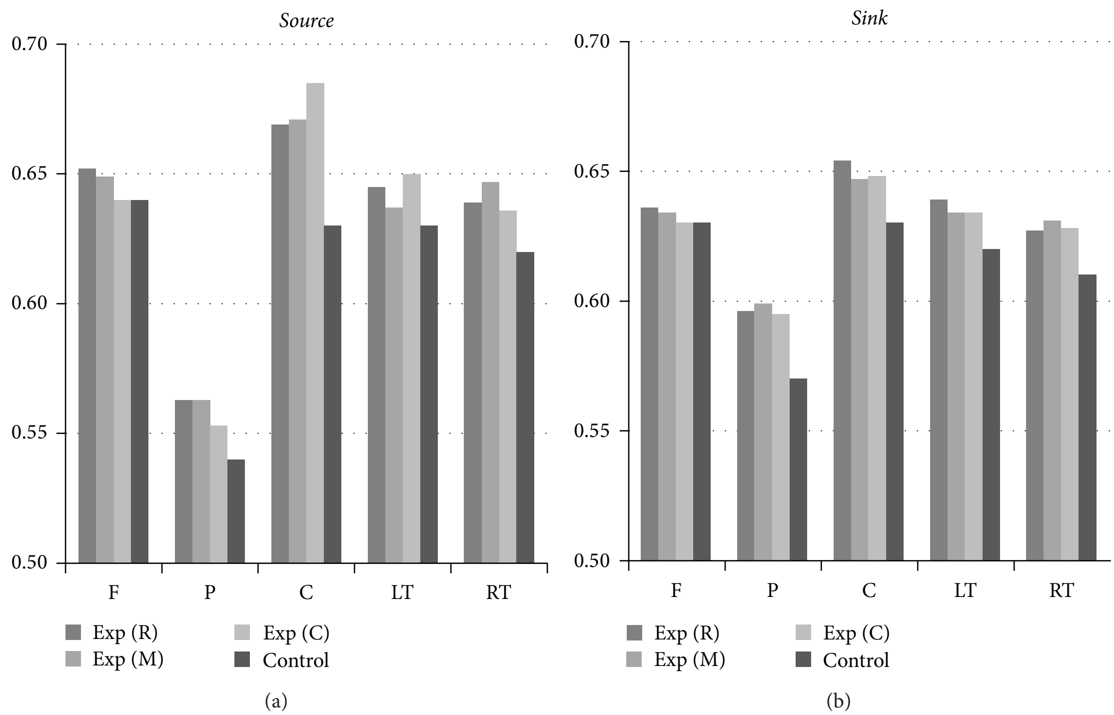


Figure 9: Comparison of average effectiveness of each region, as a *source* (a) or a *sink* (b), between experimental and control groups.

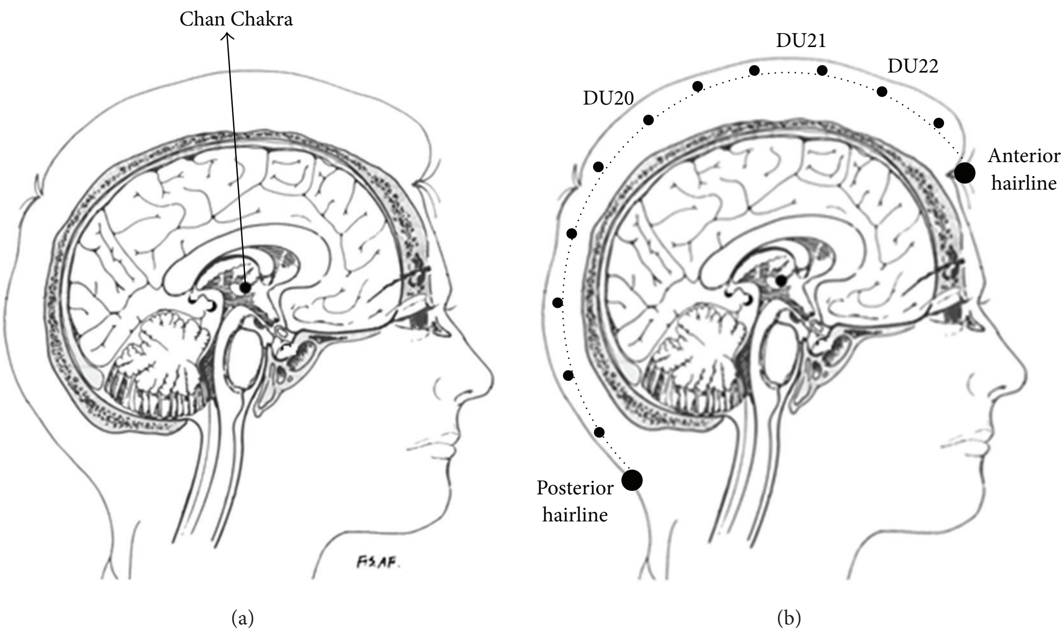


Figure 10: (a) Location of the Chan Chakra (inside the third ventricle). (b) Illustration of acupoints DU20 (Baihui), DU21 (Qianding), and DU22 (Xinhui) on DU meridian.

and the natural powers of the universe in Chan meditation under a linden tree. The orthodox Chan Buddhism was originated by such an exceptional affair that Buddha Shakyamuni transmitted this light of supreme wisdom to the Great Kashiyapa. The same path towards perfect enlightenment (Buddhahood) was promulgated in mainland China in 527 by Bodhidharma, the 28th patriarch. The current patriarch is Chan master Wu Jue Miao Tian, the 85th patriarch of the orthodox Chan-Buddhism Sect since the Great Kashiyapa. In orthodox Chan-Buddhist practice, very few disciples were able to catch the quintessence since it cannot be taught in any form of lectures. Written material and spoken words cannot promulgate the true wisdom of Chan, which can only be conveyed by the *Buddhist Heart-seal Imprint* from a true master.

In Chan meditation, practitioners aim to attain the *true self* (*Buddha nature*) with eternal wisdom (Bodhi) through body-mind-soul purification. Substantially speaking, such purification procedure involves the journal of transcending the physiological state (five sensory organs), the mental activities and normal consciousness, the subliminal (the manas) consciousness, and the Alaya state at which practitioners are able to perceive the sacred light emitted from *Buddha nature*. *Buddhist Heart-seal Imprint* from the Chan Patriarch is a must to assist in the purification and accomplishment. To prepare for attaining such realm, practitioners meditate with full-lotus, half-lotus, or leg-crossing posture and sit still to cultivate spiritual *Reiki* for penetrating into the ten important Chakras. In the course of Chan meditation, practitioners must switch their normal, chest breathing to the *Navel-Chakra* breathing (also called "fetal breathing") that is the breathing scheme for entering into deep meditation. Among the ten Chakras, Chan Chakra locating inside the third ventricle is the Buddhist paradise implemented in our body. Figure 10(a) illustrates the location of Chan Chakra.

The *cun*-measurand system is normally used to measure and locate the acupoints. To determine the locations of acupoints DU20, DU21, and DU22 on Governor Vessel meridian (DU meridian), we first measure the scalp-midline length between anterior hairline and posterior hairline, that is divided into 12 *cuns*. The locations are defined as follows:

DU20: 7 *cuns* above the posterior hairline and 5 *cuns* above the anterior hairline;

DU21: 3.5 *cuns* directly above the anterior hairline or 1.5 *cuns* anterior to DU20;

DU22: 2 *cuns* posterior to the anterior hairline or 3 *cuns* anterior to DU20.

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Research Article

The Effect of Live Spontaneous Harp Music on Patients in the Intensive Care Unit

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This study was performed to investigate the effect of live, spontaneous harp music on individual patients in an intensive care unit (ICU), either pre- or postoperatively. The purpose was to determine whether this intervention would serve as a relaxation or healing modality, as evidenced by the effect on patient's pain, heart rate, respiratory rate, blood pressure, oxygen saturation, and heart rate variability. Each consenting patient was randomly assigned to receive either a live 10-minute concert of spontaneous music played by an expert harpist or a 10-minute rest period. Spontaneous harp music significantly decreased patient perception of pain by 27% but did not significantly affect heart rate, respiratory rate, oxygen saturation, blood pressure, or heart rate variability. Trends emerged, although being not statistically significant, that systolic blood pressure increased while heart rate variability decreased. These findings may invoke patient engagement, as opposed to relaxation, as the underlying mechanism of the decrease in the patients' pain and of the healing benefit that arises from the relationship between healer, healing modality, and patient.

1. Introduction

Use of complimentary and alternative medicine (CAM) as an adjunct to healing has been studied in postoperative cardiac patients in a few settings. Kshettry et al. [1] found that using CAM as an adjunct treatment in a pre- and postoperative setting is both feasible and useful for decreasing patient pain and tension. They studied the effects of guided imagery and gentle massage before operation, music for two days after surgery, and gentle massage after leaving intensive care, versus patient standard care. The authors found that, of these CAM therapies, music therapy was associated with reduced pain and tension in early recovery from cardiac surgery.

Music has been used as a CAM adjuvant for healing and symptom management. Research on this topic has increased over the last decade including four published reviews in the Cochrane database in the past 5 years. The data published to date suggest that listening to music affects multiple physiological parameters, especially those related to the autonomic nervous system (ANS). Bradt et al. reviewed the evidence for music therapy with cancer patients and concluded that music therapy may have beneficial effects on anxiety, pain, quality of life, heart rate (HR), respiration rate (RR), and blood pressure (BP) in cancer patients [2]. Another study by Huang et al. revealed that cancer patients who listened to sedative music reported less pain than those receiving analgesic alone [3]. Listening to music also appears to benefit patients receiving mechanical ventilation by influencing their HR, RR, and anxiety [4, 5]. In addition, Bradt et al. [2], in their review on the effects of listening to music by patients with coronary artery disease, concluded that listening to music "may have a beneficial effect on their BP and HR." Music can also be effective in reducing anxiety in patients with myocardial infarction (MI) and there may be a slight benefit in reducing pain [6]. In another Cochrane review by Cepeda et al., it was concluded that music reduced pain, and in those patients who experienced reduced pain, the required dose of opioid analgesics was also decreased [7].

One possible mechanism by which listening to music can exert beneficial effects is through increased relaxation. White [8] studied the effects of relaxing music on the cardiac ANS after an acute MI. They compared music in a restful environment, rest alone, and normal therapy with no intervention. No difference in BP was found between the three groups, but heart rate variability (HRV) increased in the rest group and the music group, while anxiety decreased in the music group. These results support listening to music as a way of preventing the deleterious effects of the stress response.

Acute stress can activate the immune system and cause inflammation through the complement cascade [9]. On the other hand, chronic stress can impair immune function and delay wound healing [10]. It is important that when people are in a state of healing their immune systems are functioning optimally, that is, neither overreacting nor underreacting. Therefore environmental stress should be kept to a minimum. Unfortunately, in hospitals, due to the high level of personnel activity and noise from monitors, this is not always possible. For this reason, the concept of whether music increases relaxation in the hospital environment is of interest. For this study, spontaneous, live harp music was specifically chosen because live harp music has been previously investigated with positive findings in the hospital setting [11–13].

One small study ($N = 17$) addressed live harp music in a postoperative thoracic unit and found that live harp music decreased BP and HR and increased oxygen saturation (O_2SAT) [12]. In addition, Sand-Jecklin and Emerson [14] researched the impact of live relaxing harp music intervention on patients' experience of pain, anxiety and muscle tension after admission to the hospital with an emergent medical or traumatic illness. Thirty-one patients reported significant reductions in pain, anxiety and muscle tension and significant reductions in RR and systolic BP, while no significant difference in HR or diastolic BP. So far, no effects of harp music on patients' HRV have been reported except for a study on premature infants by Kemper and Hamilton [11]. In this study harp music did not significantly alter HRV. However, only 8 infants were monitored and they were divided among 3 groups only one of which experienced harp music.

The purpose of this study was to investigate the effect of live, spontaneous harp music on individual patients in an intensive care unit (ICU), either pre- or postoperatively to determine whether it would serve as a relaxation modality, decreasing HR, BP and respiration rate and increasing HRV and whether, based on previous results, it would reduce self-reported pain. Each consenting patient was randomly assigned to receive either a live 10-minute concert of spontaneous music played by an expert harpist or a 10-minute rest period. The type and severity of the diseases were similar between the two groups.

2. Materials and Methods

2.1. Experimental Design. This study used a case control design with pre- and postmeasurements on a convenience sample of all patients admitted to an academic ICU. The University of Arizona Institution Review Board approved the study design prior to its commencement. Before starting the study, a power analysis was performed to determine a statistically appropriate group size. Using previous data comparing HRV before and during self-administration of another alternative therapy, a group size of 25 was calculated. Power was estimated assuming standard α values (95% confidence limits or $\alpha = 0.05$). The calculated power was 0.87 and was above the sufficient statistical power of 0.8.

All patients in the ICU who were able to consent, or who had a family member who could consent, were invited to participate, regardless of diagnosis or pre- or postoperative status. Patients who agreed was consented and the study performed. Measurements were made on patients between the hours of 10 am and 3 pm. The intervention was a 10-minute live, spontaneous harp session in the patients' rooms. The same harpist, a professional harpist and harp teacher, was used for all patients in the experimental group. She played spontaneous improvised music with the intention of helping the patients heal. For the control group, the patients were left in their rooms for 10 minutes and advised to relax during that time period. Each participant (cases and control group) was given CD of the harpist at the end of the session as a thank you and as incentive for participation in the study.

2.2. Experimental Measures. Heart rate variability is a noninvasive measure of the complementary relationship between the sympathetic and parasympathetic branches of the ANS [15]. Instruments used for recording HRV analyze the signal by means of time domain or frequency domain (spectral analysis) to quantify the variability in HR that exists in a given recording. Time domain parameters include the standard deviation of the interbeat interval (IBI), SDRR, which provides a gross measure of HRV, and the root mean square of successive differences in IBI (RMSSD), which reflects the parasympathetic activity of the ANS.

Prior to the harp or control session, a plethysmograph (pulse sensor) was clipped to the subject's ear lobe for HRV measurements. When HRV was recorded, the patients were resting, either lying in bed or sitting on a reclining chair, and they were asked not to speak during the measurement to prevent movement artifacts from confounding the data. The sensor was attached to a computer via an emWave PC (HeartMath LLC) device that output inter-beat interval (HR) data to a text file that was analyzed in greater detail using a freeware HRV program, http://kubios.uef.fi/. Algorithms within the software program provide interactive interpretation of waveforms for the raw interbeat interval data collected. During analysis any abnormal beats were manually removed from the data. Artifacts due to slight movements of the patients were also eliminated. In cases in which too much data are eliminated, some HRV indices cannot be properly estimated. We therefore introduced an artifact percentage threshold of 10% to our analysis [16]. Data files from which

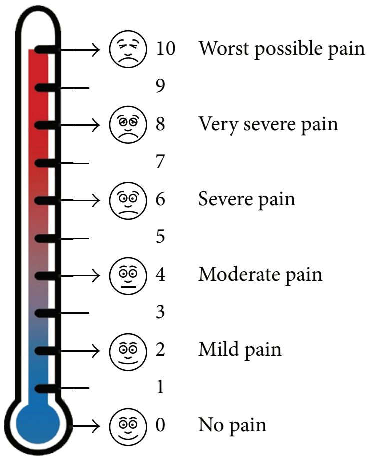

Figure 1: The enclosed material was prepared by Northeast Health Care Quality Foundation (NHCQF), the Medicare Quality Improvement Organization (QIO) for Maine, and New Hampshire and Vermont, under contract with the Centers for Medicare & Medicaid Services (CMS), an agency of the U.S. Department of Health and Human Services. The contents presented do not necessarily reflect CMS policy.

more than 10% of the data had to be eliminated were excluded from the analysis.

During the 5-minute period while HRV was being recorded, systolic and diastolic BP, O_2 SAT, RR, and HR were collected from the monitors or from the patient, directly. Patient pain report, as per the thermometer visual pain scale, (Figure 1) was also reported. All measurements were repeated after the patients in the experimental group had heard 10 minutes of harp music, and after the patients in the control group had rested for another 10 minutes. No medications were given to patients in either group during the interval between initial and final measurements. In a given week, data were collected from either the music group or the control group in order to prevent the live harp music from affecting the control patients in adjacent rooms. The data were analyzed by a member of the research team blinded as to the identity of the data groups.

2.3. Statistical Analysis. For gender comparison between groups, a 2 × 2 chi square test was used for P value <0.05. Student t-tests were run to test for significant differences between the two groups for baseline values of all physiological parameters. For data sets that failed the normality test, the Mann-Whitney rank sum test was used. Paired Student t-tests were run for control and for music groups to determine the treatment effect, pre versus post, for all parameters. For data sets that failed the normality test, the Wilcoxon signed rank test was used. If the P value were less than 0.05, the statistical comparison would be considered significant.

3. Results and Discussion

Statistical analysis demonstrated no significant difference between control and music groups for patient age or gender.

Table 1: Music and control group comparison.

Parameter	Music gr.	Control gr.	P value
N	50	50	
Average age (years)	65.29 (13.8)[1]	59.05 (19.3)	NS
Percent male[2]	58%	72%	NS

[1](Standard deviation) of age.
[2]Chi square = 2.9 with 1 df, $P = 0.1$.

These results are presented in Table 1. In addition, there was no significant difference between baseline values of control and those of music groups for any of the measured physiological parameters. With regards to pain, there was a 27% reduction in patient-reported pain after the music (a decrease of 0.8 on a pain scale of 0–10 ($P = 0.005$)). There was no significant difference in pain for the control group pre- and postrest session. Seven of the 50 patients in the control group and 11 out of the 50 patients in the music group were asleep during the experiment and so no pain scores could be obtained from those patients. Our statistical analysis showed that there were no significant differences regarding age or gender between the two groups from whom we obtained pain scores.

The other physiological parameters (HR, O_2 SAT, BP, RR, and HRV) did not show any significant differences pre and postmusic or rest period. These data are presented in Tables 2 and 3. Values of N for HRV are less than fifty as some data could not be analyzed due to arrhythmias and anomalies. Although there was no significant difference regarding age between the control and music group patients from whom HRV data were obtained, there was a significant gender difference ($P = 0.002$, chi square = 9.62). It is unlikely that this difference affects the HRV data because gender differences in HRV disappear after age 50 [17]. The average ages of the two groups from whom HRV data were obtained were 58.8 and 56.6.

Most of the patients were at a fairly low level of pain before the harpist played, the average being 3 on a scale from 0 to 10. The finding of a 0.8 decrease in the pain scale may seem low, yet it actually represents a 27% reduction in pain. The fact that a significant reduction in pain was experienced despite the initial low level of pain speaks to the effectiveness of the music. A significant reduction in pain in this environment is a valuable finding; the perception of pain by the patients is an important aspect of patient care and healing. Patients' pain is often not adequately addressed in clinical settings and this study has shown that a simple noninvasive intervention such as a live harp session can have a positive impact on pain and outcome. Pain medications used in ICU setting have been associated with significant side effects. These include nausea, vomiting, respiratory depression, constipation, hallucinations, and disorientation. This supports the recommendation of use of safe adjunctive therapies for pain control that do not have these side effects.

While our study reveals that spontaneous live harp music significantly decreased patient perception of pain, the music did not significantly affect RR, HR, HRV, BP, or O_2 SAT when values were averaged over all patients in a given group.

Table 2: Experimental parameters for music group pre- and postharp session.

Parameter	N^1	Preharp session (SD)	Postharp session (SD)	P value
Respiration rate (br/min)	48	19.8 (6.0)	19.4 (5.9)	NS
Oxygen saturation (%)	49	95.8 (4.7)	96.20 (4.3)	NS
Systolic BP (mmHg)	50	112.0 (23.3)	113.3 (22.8)	NS
Diastolic BP (mmHg)	50	62.1 (16.0)	61.2 (13.7)	NS
Heart rate (bpm)	50	84.4 (16.6)	83.0 (16.1)	NS
SDRR2[2] (ms)	23	37.4 (28.3)	33.7 (28.5)	NS
RMSSD[3] (ms)	23	48.3 (43.7)	42.2 (40.4)	NS
Pain (0–10)	39	3.0 (3.3)	2.2 (2.7)	0.005

[1]Values of N for HRV (SDRR and RMSSD) are less than 50 as some data could not be analyzed due to arrhythmias and anomalies. Values of N for pain are reduced due to inability for some patients to self-report pain.
[2]SDRR: standard deviation of the RR interval in the HRV monitoring.
[3]RMSSD: the root means square of successive differences of the RR interval.

Table 3: Experimental parameters for control group pre- and postrest period.

Parameter	N^1	Prerest period (SD)	Postrest period (SD)	P value
Respiration rate (br/min)	48	19.3 (4.8)	18.8 (4.6)	NS
Oxygen saturation (%)	49	96.2 (3.2)	96.3 (3.0)	NS
Systolic BP (mmHg)	48	116.7 (21.0)	115.7 (20.5)	NS
Diastolic BP (mmHg)	48	62.6 (11.4)	61.2 (12.0)	NS
Heart rate (bpm)	48	76.7 (9.6)	76.7 (9.8)	NS
SDRR[2] (ms)	27	34.3 (29.2)	32.7 (29.1)	NS
RMSSD[3] (ms)	27	45.5 (44.5)	43.2 (42.9)	NS
Pain (0–10)	43	2.5 (3.0)	2.5 (3.0)	NS

[1]Values of N for HRV (SDRR and RMSSD) are less than 50 as some data could not be analyzed due to arrhythmias and anomalies. Values of N for pain are reduced due to inability for some patients to self-report pain.
[2]SDRR: standard deviation of the RR interval in the HRV monitoring.
[3]RMSSD: the root means square of successive differences of the RR interval.

Since the study took place in the ICU, most of the patients were taking medications that would affect HR and BP (such as cardiac medications including beta-blockers) and RR and pain (such as opiates). In an effort to reduce the impact of this study as much as possible on nursing care in the ICU, patient medication data were not collected from the electronic medical records of the participants. That element would have added an entirely different aspect to our study, because it would have compelled nurses to stop their work and check their patient's chart with us, thus disrupting the flow of work in the ICU. For this reason the data analysis could not be adjusted to account for medications that impact HR, BP, and RR. Had patient data been stratified into cardiac and pain medications this may have led to different findings. Since pharmacological interventions were already in place to keep the patients' outcome measures as low and stable as possible this also means that the effects of the harp music on outcome measures were probably underestimated. Although it would be interesting to repeat this study on patients not taking medications that affect the ANS, this is not clinically or ethically feasible for patients in pain.

Notably, the HRV measures in our music group trended toward a decrease after intervention, although these findings were not statistically significant. The small size of the effect was probably due to the fact that many of the outcome variables were most likely modified or dampened from the pharmacological interventions the patients were receiving. That being said, these trends are potentially an interesting finding. A larger study would likely illuminate this result, especially if the data were stratified by pharmacologic interventions.

Another trend was that systolic BP increased slightly in the music group after intervention despite pharmacologic control. This finding contrasts with another result [14] in which a slight but significant decrease in BP was observed in patients who listened to slow tempo, relaxing harp selections on the Celtic harp. However, in our study each patient may have been affected differently on an autonomic level, with differing degrees of arousal and relaxation. A large variation in patient response is likely, because the harpist played music for each person consisting of the combination of tempos that she perceived was most appropriate for them. Previous studies [18, 19] have shown that the underlying tempo of music may have an effect on HR and BP. In those experiments an arousal effect was observed proportional to the speed of the music, with slower rhythms inducing relaxation and faster rhythms promoting sympathetic stimulation.

The idea that varying tempos of music may have different effects on the ANS highlights the concept that the decreased pain experienced by some of the patients in our study may not be from relaxation, but from engagement with the music. This idea is consistent with the observed slight reduction in HRV. This response may be evidence of the impact of a healing dynamic within the healer-patient relationship. Our harpist played directly to whatever she was sensing within the patient in order to enable healing through the music and through her presence with the patient. One aspect of this study that is unique is the participation of a master harpist and composer who is able to play spontaneous compositions directed specifically towards each patient's needs. This type of playing may have captured the effect not of relaxation by the patient but of engagement in a healing relationship. Patients reported they felt better and more energized. This may be reflected in the decreased pain and also slight rise in BP. It would be interesting to complete another study with taped harp music and see how this in would be compared to the live sessions and controls.

These findings, if sustained and amplified in a larger study, could lead to an interesting discussion about what other measures could be introduced into the ICU to engage patients, that is, an increase in volunteers, reading to patients or having other health related practitioners visit patients in the ICU. In fact, perhaps focusing on the patient's attention is a significant factor in pain control. It seems that the human aspect of this focus is important, as many of the patients were already watching television when they were asked to prepare for the intervention. The control patients continued to watch television, an engaged focus with no relationship. The harpist's intention was to fully engage the patient, not to make them relax. The intervention engaged the patients visually (for those awake), auditorially and socially. Perhaps engaging patients in a multisensorial way will reduce pain and decrease the use of pain medication in an ICU-like setting.

There were limitations to the study. Firstly, the patients were all in the ICU, some preoperatively, some postoperatively, and some were in the ICU for the only reason of needing a monitored ICU bed when there was ICU overflow. Therefore not all the patients had a cardiac diagnosis. This is the practical reality of how the ICU unit runs in the hospital in which this study was performed. The decision was made to include all patients as potential candidates for the music or control groups to mimic reality in the event that this intervention was to be adopted by this hospital.

Another confounding variable was that other family members or acquaintances often joined the participants. In order to mimic reality as much as possible, all individuals in the music or the control group were taken as they were without asking anyone to leave the room. However, the effect of other people in the room could have altered the patient's relaxation state and healing response. Since the intervention needs to be feasible for routine usage, the presence of patient visitors remains a confounding variable that cannot be assessed. A third limitation to the study was that the 2-group design did separate out the effects of the actual music from those of the nonverbal interaction between the harp player and the patients. Inclusion of a third group of patients listening to recorded harp music would show which of these two factors is of primary importance in reducing patient pain perception.

Lastly, since participation in the experiment was voluntary, patients who did not like harp music could decline. There are data indicating that the individual taste of patients affects how effective music is as an intervention [20]. Our study showed that live harp music decreased pain by 27% in a volunteer sample of people who liked harp music. If live harp music is offered to patients as a standard therapy, music preference would not matter as only those who liked the harp would agree. However, if these results were extrapolated to live music in other settings, such as the waiting area for the operating room, the impact of the music would be influenced by personal preferences of those listening.

Despite the limitations, the impact of this study on the environment of the ICU is important. One of the clinical nurse specialists who oversaw the ICU wrote this comment to us. "As so many of us, I truly believe in the healing properties of music and would love nothing more than to share this with others. This harp study has been a wonderful experience for both our patients and staff," (personal communication).

4. Conclusion

This study reveals that spontaneous live harp music significantly decreased patient perception of pain by 27% in a ICU setting, but on average RR, HR, HRV, and O_2 SAT were not significantly affected. Possibly each patient was affected differently on an autonomic level, with differing degrees of arousal and relaxation, because the harp piece for each individual containing a different combination of tempos that the harpist perceived was most appropriate for them. The reduction in patient's perception of pain supports the introduction of live harp music into the ICU as a non-invasive means to reduce patient pain.

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Research Article

Comparison of Physical Therapy with Energy Healing for Improving Range of Motion in Subjects with Restricted Shoulder Mobility

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Two forms of energy healing, Reconnective Healing (RH) and Reiki, which involve light or no touch, were tested for efficacy against physical therapy (PT) for increasing limited range of motion (ROM) of arm elevation in the scapular plane. Participants were assigned to one of 5 groups: PT, Reiki, RH, Sham Healing, or no treatment. Except for no treatment, participants were blinded as to grouping. Range of Motion, self-reported pain, and heart rate variability (HRV) were assessed before and after a 10-minute session. On average, for PT, Reiki, RH, Sham Healing, and no treatment, respectively, ROM increased by 12°, 20°, 26°, 0.6°, and 3° and pain score decreased by 11.5%, 10.1%, 23.9%, 15.4%, and 0%. Physical therapy, Reiki, and RH were more effective than Sham Healing for increasing ROM (PT: $F = 8.05$, $P = 0.008$; Reiki: $F = 10.48$, $P = 0.003$; RH: $F = 30.19$, $P < 0.001$). It is possible that this improvement was not mediated by myofascial release because the subjects' HRV did not change, suggesting no significant increase in vagal activity. Sham treatment significantly reduced pain compared to no treatment ($F = 8.4$, $P = 0.007$) and was just as effective as PT, Reiki, and RH. It is the authors' opinion that the accompanying pain relief is a placebo effect.

1. Introduction

Shoulder pain is a common musculoskeletal symptom, accounting for 16% of all musculoskeletal complaints [1]. Lifetime prevalence of shoulder pain has been reported to range from 7% to 36% of the population [2]. The precise causes of shoulder pain within the joint are unknown, but the nongenetic variants are thought to result from joint intra-articular degeneration (osteoarthritis), structural damage (torn rotator cuff and/or ligaments), infection or inflammation (bursitis and tendinitis), or arthritis [3–6]. Rotator cuff pathology and subacromial impingement are among the most common diagnoses pertaining to shoulders [2, 7].

Apart from pain, shoulder damage or degeneration often leads to limited ROM of the shoulder. Chronic soft tissue disorders, such as tendinitis, bursitis, rotator cuff tears, and impingement syndrome, may result in secondary adhesive capsulitis. It is the adhesions that limit ROM [8]. Physical therapy is usually the first choice of treatment for these problems [9]. Physical therapy encompasses many types of interventions including manual manipulation, therapeutic exercise, functional training, and electrotherapeutic modalities. However, it is the manual manipulation that requires the most sustained physical effort by the therapist. In a study addressing job strain in physical therapists [10], 58% of the 882 physical therapists interviewed experienced a work-related ache or pain during the year prior to the follow-up survey. The most common region was the low back, followed by the wrist and hand. In another investigation [11], 83% of 344 physical therapists who returned completed questionnaires indicated that they were treating or handling a patient when they first experienced lower back pain on the job. When asked to select the mechanism of injury, 24% of the respondents selected "lifting with sudden maximal effort" and 24% chose "bending and twisting." Over half of these therapists reported recurrent episodes. Since manual manipulation may cause recurrent pain for the therapists it would be advantageous to limit its use to cases in which it is strictly necessary in order to promote a patient's recovery.

The purpose of this research was to determine whether manual manipulation is necessary for success in short-term treatment of limited ROM of arm elevation in the scapular plane. Other therapies, such as Reiki and Reconnective Healing, that do not involve physical effort were compared with PT for effectiveness in improving ROM. The 2007 National Health Interview Survey, compiled by Barnes et al., [12] indicated that 1.2 million adults and 161,000 children in the United States received one or more sessions of energy healing, such as Reiki, during the previous year. According to the American Hospital Association, [13] 15% of American hospitals (more than 800 facilities) offered Reiki as a hospital service in 2007. A joint publication by the American Holistic Nurses Association and American Nurses Association [14] lists Reiki as an accepted form of treatment.

Reiki is administered by the hands, placed lightly on or near the body of the recipient. The Reiki practitioner focuses his attention on the recipient and then allows the energy to flow passively through their body and hands where it is passed to the recipient. These procedures are described by various Usui Reiki training manuals and Reiki websites, such as http://www.reiki.org/FAQ/Questions&Answers.html; http://www.reiki.org/reikipractice/practicehomepage.html #Intention.

Practitioners who learn Usui Reiki receive similar training and specific objectives are laid out for each one of the three levels (e.g., see http://www.reiki.org/Download/FreeDownloads.html).

Peer-reviewed research demonstrates that recipients of Reiki experience feelings of relaxation, mental clarity, pain relief, decreased anxiety, and a sense of wellbeing. These studies are described in several reviews [15–17]. Physiological signs of relaxation in recipients include increases in their parasympathetic autonomic nervous system activity [15, 18–20]. There are currently no studies published in peer-reviewed journals addressing the effects of Reiki on ROM.

Reconnective healers work with their hands to sense and manipulate what they term as biofields, which are energy fields that surround living beings [21]. Reconnective Healing is said to involve tuning into the healing energy frequencies needed by each recipient and receiving and sensing the energy. Unlike Reiki, there is no specific "centering" or "grounding" process involved in which practitioners focus on the present moment through concentrating on their breathing. All Reconnective healers receive training from instructors who have followed a prescribed syllabus which is the same worldwide, and so the procedure is reproducible among healers (see http://www.thereconnection.com/programs/reconnective-healing-level -i-ii/).

People receiving Reconnective Healing anecdotally report a range of sensations including warmth, tingling, cold, and throbbing and physiological responses such as rapid eye movements, deepening breath, stomach gurgling, and muscle twitching. However, there are no published studies addressing the effectiveness of RH in reducing pain. Overall, none of the energy healing modalities have been tested for efficacy on people with limited ROM.

In this study, manual manipulation (joint mobilization, long axis distraction, and gentle rebounding) was tested against RH and Reiki in patients with limited ROM. These energy healing therapies only involve light touch or no touch and so if they are as effective as manual manipulation in improving ROM, this would imply that manual manipulation, per se, is not necessary for alleviating this particular impairment.

Another objective was to assess self-reported pain and heart rate variability (HRV) as secondary outcome variables, before and after each type of treatment; HRV is a measure of sympathovagal balance which may provide some insight into possible mechanisms of pain relief because it is known that stimulation of the vagus nerve can reduce pain [22]. Such stimulation can occur directly through myofascial release [23] and there is some evidence that it can be mediated indirectly by application of Reiki [20, 24].

2. Methods

2.1. Recruitment and Consenting of Participants. This investigation was approved by the University Institutional Human Subjects Protection Committee. People with limited range of motion of one or both shoulders were recruited for the study by providing fliers to local chiropractors, physical therapists, masseurs, and fitness coaches, by posting the flier at various locations of the university campus such as Campus Health Service, Family and Community Medicine, Student Recreation Center, Libraries, Arthritis Center, Athletics Departments, and Center for Integrative Medicine and by running a radio advertisement on National Public Radio. The fliers were deliberately posted in a wide variety of locations in order to attract potential participants who were representative of the population at large rather than just individuals looking for nontraditional therapies. Investigators' conversations with the potential participants during the enrollment process confirmed that most potential participants were fairly traditional in their medical choices.

Potential participants were first screened by telephone to determine whether they met the following inclusion and exclusion criteria:

(1) at least 18 years of age;

(2) self-ambulatory (no assistive devices);

(3) having had a nongenetic ROM limitation for at least one year and having some form of medical documentation of the problem;

(4) ROM limitation being the result of injury (sports related or otherwise), surgery, arthritis, or adhesive capsulitis;

(5) having had no experience of energy healing (Reiki or Reconnective Healing), including sessions, seminars, or reading "The Reconnection" by Dr. Pearl [25];

(6) if female, must not be pregnant.

Table 1: Medical diagnoses of experimental participants.

Number of patients	SLAP tear	Torn RC	Arthritis	Impingement	Bone spur	Injury	Capsulitis	Bursitis	Unknown	X-ray/MRI
78	1	22	18	4	2*	14	2**	2	16	55

*One case was in combination with torn rotator cuff.
**Both cases were in combination with torn rotator cuff.
SLAP: superior labrum, anterior to posterior.

Those who met all the criteria were interviewed at the university and tested to determine whether the ROM of at least one of their arms was limited to somewhere between 30° below the horizontal plane and 60° above the horizontal plane. People who were qualified were consented for the study after the experimental protocols; risks and benefits had been explained. During the consenting process, participants filled out a demographics questionnaire, consisting of birthplace, ethnicity, age, height, and weight. They also provided the following information regarding their specific shoulder problem:

(1) reason for ROM limitation and whether diagnosed by a physician;

(2) length of time they have had limited ROM;

(3) whether left, right, or both arms are affected;

(4) types of health-based practitioners the person had previously visited for this problem, such as medical doctor (MD), chiropractor (DC), osteopath (DO), physical therapist (PT), naturopath (ND), acupuncturist (LAc), and massage therapist;

(5) whether or not the problem was diagnosed as a result of MRI scanning or radiographs;

(6) whether the subject had surgery to attempt to alleviate the problem, and if so, the type of surgery. Was internal fixation inserted? Did surgery make the problem better/worse/or cause no change?

(7) Whether a prior surgery caused the problem.

2.2. Group Assignment. A power analysis at 80% power was performed to find the number of subjects necessary to detect a significant difference between groups of 20° for arm elevation in the scapular plane, based on the previously observed variance. From this test, a group size of 15 was chosen for the study. The value of 20° was chosen because the focus of this study was to determine whether energy healing produced large improvements in ROM. The study was conducted in the following way: six experimental sessions, involving 12–17 participants, were held at a local hotel, easily accessible by participants and therapists. The six sessions were carried out in the following order: (i) Reconnective Healing, (ii) Reiki, (iii) Sham Healing, (iv) physical therapy, (v) control, and (vi) RH plus PT. Due to logistics, recruitment was performed in two phases. In the first phase subjects were recruited for the RH, Reiki, and Sham Healing groups, and in the second phase they were recruited for the RH, PT, and control groups. In both cases participants were assigned to one of three groups on a rotating basis according to order of recruitment.

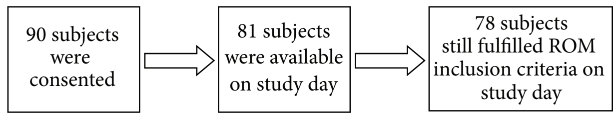

Figure 1: Flow chart of subject participation.

2.3. Demographics of Experimental Participants. A flow chart of the retention of 90 recruited subjects is shown in Figure 1.

Of the 78 participating subjects, 37 were males and 41 were females. All subjects were Caucasian, except for seven Hispanic, two Asian, and one "other." The participants' ages ranged from 20 to 89 and the mean age for each group was 61.3 ± 53.2 (SD) (control), 58.5 ± 59.4 (Sham), 64.4 ± 56.6 (PT), 66.4 ± 58.3 (Reiki), and 59.8 ± 52.2 (RH). The difference in mean age between groups was not statistically significant (ANOVA analysis of variance). The corresponding gender ratios for each group (male to female) were 1.14, 0.50, 0.60, 1.50, and 1.12.

2.4. Medical History and Diagnosis of Experimental Participants. The diagnoses of the participants relevant to restricted shoulder mobility are shown in Table 1. In most cases (55/78) the diagnoses were made using radiographs and/or magnetic resonance imaging. The frequency of the different diagnoses was fairly uniform between groups (see Table 2). Nineteen of the participants had experienced their condition for less than two years, 30 for between two and five years, and 29 for more than five years. Sixteen of the participants had experienced shoulder surgery, between one and 20 years previously, in an attempt to improve their range of motion and/or reduce pain. The surgery had been partially successful for a short time in five cases and unsuccessful in the others. Each experimental group included some participants who had had surgery (Table 2).

2.5. Selection of Therapists. Three therapists were selected for each arm of the study, except for the no-treatment control group. Each therapist would work on one-third of the participants in their group. The Reconnective healers (2 males, 1 female) were experienced instructors from The Reconnection LLC Teaching Team, who train students worldwide. The Reiki practitioners (1 male, 2 females) were local, had been practicing Usui Reiki professionally for a minimum of 4 years, were 6 generations removed from the founder, Mikao

Table 2: Group distributions of medical diagnoses and surgeries.

Diagnosis/surgery	Number of Control groups	Number of Sham groups	Number of PT groups	Number of Reiki groups	Number of RH groups
SLAP	0	0	0	0	1
Torn RC	4	4	5	5	4
Arthritis	3	5	3	3	4
Impingement	1	1	0	1	1
Bone spur	0	0	1	1	0
Injury	3	3	3	3	2
Capsulitis	1	0	0	1	0
Bursitis	1	1	0	0	0
Unknown	3	1	4	2	6
Shoulder surgery	3	3	2	5	3

Usui, and had received the highest level of Reiki training. The licensed physical therapists (3 females) were local and did not include energy work in their repertoire. All had practiced PT for over 10 years, had their own practices, and were experienced in treating complex medical and physical conditions in a range of traditional PT settings. Three people (1 male, 2 females) who had absolutely no experience with any form of energy healing were chosen to be sham healers.

2.6. Instructions to Therapists. All practitioners were instructed not to disclose what type of therapy they would provide because the participants did not know what kind of treatment they were getting.

Reconnective healers used mainly hands-off treatment. Reiki practitioners focused their healing intention on increasing the participant's ROM and used mainly hands-on treatment for each participant. Physical therapists were asked to give their normal basic manipulation of the shoulder joints and surrounding deep tissue. The physical therapists chose to provide gentle passive ROM and simple glenohumeral joint mobilizations (inferior glides) in attempt to increase shoulder abduction and flexion. Long axis distraction was applied to the glenohumeral joint, as was gentle rebounding. Sham healers were asked to wave their hands slowly over the participant's shoulder area and upper body, 6–12 inches away from their body, and to occasionally draw their hands back away from them, similar to the actions of Reconnective Healers.

All therapists were told that the participants had ROM limitations resulting from shoulder injuries or arthritis but were not told any details about the specific problems of individual participants or which shoulder was most affected. Each practitioner worked with 2 participants, one after the other, and then had a 20-minute rest before working with the next 2 participants. During the practitioner rest breaks, the participants went to another room for pre-or post measurement of their ROM and HRV.

2.7. Experimental Procedure. On arrival, participants were informed by a student that they would be receiving a treatment, which may be energy healing, Sham Healing, or PT, or no treatment at all, to assess how this affects their range of motion. The student was blinded as to the type of therapy each participant would receive except for those in the no-treatment control group. The participants were similarly blinded. Each participant filled out a visual analog scale (VAS) expectancy survey, asking whether they expected the treatment to work. They were then shown a video explaining how their ROM would be measured before and after treatment. Briefly, they would be asked to stand close in front of a wall, without touching it, with their arms at their sides. They would then be video-recorded as they moved their arms out to the sides and then up towards their head, in a scapular plane (i.e., not bringing their arms forward) as far as they could go, while keeping their arms straight, so as not to involve the elbow joint in the exercise, once with palms facing up and once with palms facing down. One reason ROM was measured by video analysis rather than using a goniometer is that it is noninvasive. A goniometer is positioned on the subjects, scapular spine as they hold their full ROM, which can be painful. In addition, since we were looking for large improvements in ROM, there was no need for the 0.1° accuracy of the goniometer.

After watching the video, each participant performed the exercise and then filled out a VAS pain assessment reflecting the maximum pain they felt when moving their arms. Next, each participant was seated for measurement of HRV. It is generally recognized that respiration has an important effect on HRV and so respiration was also measured in this study. A strap was snugly placed around their chest to measure respiration rate, and a pulse sensor was connected to the middle finger of their left hand to measure pulse rate (interbeat interval) for calculation of HRV. The strap and sensor were connected to a computer via a BioGraph Infiniti ProComp module (Thought Technology Ltd., Montreal, Canada) to enable data recording. Each participant was asked to relax, keep still, and not speak for five minutes while data were recorded.

Next, each participant was taken to the treatment room to meet the therapist or to lie supine on a massage table for 10 minutes if they were in the no-treatment control group. In this case, since no therapist was present, a student sat quietly in the same room as the participant and then told them when the 10 minutes was up and directed them back to the measurement room. If a therapist was present, he asked the participants to show how high they could raise their arms in a scapular plane out to the sides and towards their head, keeping their arms straight and palms down, and took a photo of them showing their maximal ROM with a camera that was provided in the treatment room. Then he asked the subjects to lie supine on the massage table for the treatment. After the therapist had completed the treatment he asked the participants to stand and demonstrate their ROM, palms down as before, and took another photo. These photos were later compared with the videos taken in the measurement room to check for reproducibility of pre-and postmeasures. The participant was then guided to the measurement room to reassess his ROM, pain evaluation, and HRV.

2.8. Outcome Measures. The primary outcome variable was pre-and postmeasurement of ROM of arm elevation in the scapular plane. The video measure of ROM was highly reproducible. Corresponding measures for a given person taken in the measurement and treatment rooms only differed by an average of 2°. Secondary outcome variables were (i) expectancy, pretreatment, that the treatment would work, (ii) self-reported pain level during elevation, and (iii) HRV. Pain and HRV were evaluated pre- and posttreatment or no treatment. All data were coded to conceal the identity of each subject and their experimental group from the data analyzer, thus minimizing, and hopefully preventing, effects of possible researcher bias.

2.8.1. Range of Motion. The video recordings were used to obtain an image of each participant's maximal ROM pre- and posttreatment. From each image the angle of elevation of each arm (as depicted by the straight line connecting the wrist to the mid-point of attachment of the shoulder to the trunk) could be measured above or below the horizontal (humeral angle). A depiction of this measurement is shown in Figure 2. Angles above the horizontal were positive from 0° to 90°, and those below the horizontal were negative. Four angles were obtained for each pre- and postmeasure: left arm palms up, left arm palms down, right arm palms up, and right arm palms down.

2.8.2. Secondary Outcomes

(i) Expectancy that the treatment would work was assessed with a 100 mm VAS before the subject entered the treatment room. Each subject was asked to mark a vertical line on the VAS to indicate expectancy. No expectancy at all was represented by 0 mm and definite expectancy by 100 mm.

(ii) Pain severity was assessed with a 100 mm VAS. Each subject was asked to mark a vertical line on the VAS to indicate perceived level of pain. No pain was represented by 0 mm and extreme pain by 100 mm. A previous study [26] performed on patients treated for rotator cuff disease indicated that the minimal clinically important difference (MCID) for VAS measuring pain is 14 mm.

(iii) Interbeat interval (heart rate) data, measured over a period of 5 minutes pre- and posttreatment, were exported as a text file from the BioGraph Infiniti Physiology Suite software into a freeware HRV program, http://kubios.uef.fi/. This program analyzes the data to quantify the variability in heart rate that exists in a given recording in terms of established measures. Time domain parameters include the standard deviation of the interbeat interval (IBI), SDRR, which provides a gross measure of HRV, and the root mean square of successive differences in IBI (RMSSD), which reflects the parasympathetic activity of the autonomic nervous system.

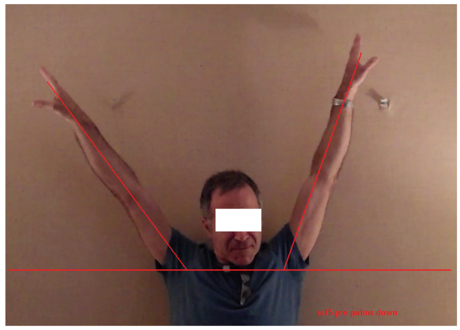

Figure 2: Depiction of humeral angle as a measure of range of motion. Angles above the horizontal are positive from 0° to 90°, and those below are negative.

2.9. Statistics. Four-way Repeated Measures Analysis of Variance (ANOVA) was run for ROM to test for significant differences among the 5 groups for the treatment effect, pre versus post, palms down or up and left arm or right arm. If the difference was significant, ANOVA was then repeated pairwise. Similar tests were run for pain scores, HR, and HRV. STATISTICA for Windows software was used for the analysis.

3. Results

3.1. Expectation. There was no significant difference between the average self-reported expectation levels of the 5 groups ($F = 0.25$, $P = 0.9$). The mean expectation values were as follows: control: 54.5; Sham: 64.1; PT: 56.5; Reiki: 57.8; and RH: 55.1.

3.2. Range of Motion. Most of the patients who received PT, Reiki, or Reconnective Healing showed improved ROM. Relative numbers of subjects in each group showing improvement were as follows: PT: 15/16; Reiki: 12/15; and RH: 16/17. Although it appears that the Reiki group started the study with a lower range of motion than the other groups, this difference was not statistically significant. There was no significant difference between the pretreatment ROM measures of the 5 groups (ANOVA analysis of variance, $F =$

Table 3: Mean pre- and post-ROM averaged over palms up and down and left and right arms.

Group	Mean ROM Pre ± SD (degrees)	Mean ROM Post ± SD (degrees)	Difference (Post − pre)	N
Control	44.96 ± 28.46	47.97 ± 30.78	3.01	15
Sham	48.13 ± 31.63	48.75 ± 31.56	0.62	15
PT	51.47 ± 35.49	63.63 ± 46.99	12.16	16
Reiki	24.85 ± 8.35	44.58 ± 27.39	19.73	15
RH	47.81 ± 32.31	74.17 ± 58.02	26.36	17

Table 4: Mean pre- and postpain scores.

Group	Mean pain Pre ± SD	Mean pain Post ± SD	Difference (Post − pre)	N
Control	46.4 ± 5.7	46.6 ± 5.4	0.2	15
Sham	53.2 ± 5.8	37.8 ± 5.4	−15.4	15
PT	52.1 ± 5.6	40.6 ± 5.2	−11.5	16
Reiki	41.3 ± 5.7	31.2 ± 5.4	−10.1	15
RH	46.1 ± 5.4	22.2 ± 5.1	−23.9	17

1.4, $P = 0.24$). The average pretreatment ROM values for all 5 groups were positive, although some individuals showed negative values. Comparing postmeasures to premeasures there was a highly significant difference between the 5 groups (averaged over palms up and down and left and right arms, $F = 10.3$, $P < 0.001$). These results are shown in Figure 3 and Table 3.

On average ROM increased by 3°, 0.6°, 12°, 20°, and 26° for control, sham, PT, Reiki, and RH groups, respectively. Pairwise analysis showed that Sham treatment was no better than the no-treatment control and that PT, Reiki, and RH were all significantly more effective than Sham (PT: $F = 8.05$, $P = 0.008$; Reiki: $F = 10.48$, $P = 0.003$; RH: $F = 30.19$, $P < 0.001$). Reconnective Healing was significantly more effective than PT ($F = 9.61$, $P = 0.004$), but there was no significant difference between Reiki and PT ($F = 1.73$, $P = 0.20$).

3.3. Self-Reported Pain. There was no significant difference between the pretreatment pain scores of the 5 groups (ANOVA analysis of variance, $F = 0.73$, $P = 0.57$). Comparing postmeasures to premeasures there was a highly significant difference between the 5 groups, ($F = 4.75$, $P < 0.002$). These results are shown in Figure 4 and Table 4.

On average the pain score decreased by 0%, 15.4%, 11.5%, 10.1%, and 23.9% for control, sham, PT, Reiki, and RH groups, respectively. However, the average pain reduction in the PT and Reiki groups did not reach the MCID. Pairwise analysis showed that unlike the ROM results, the sham treatment was significantly more effective in reducing pain than the no-treatment control ($F = 8.4$, $P = 0.007$); in fact, none of the other treatments were anymore effective than the sham treatment (PT: $F = 0.42$, $P = 0.52$; Reiki: $F = 0.57$, $P = 0.46$; RH: $F = 1.9$, $P = 0.18$). Although RH was no more

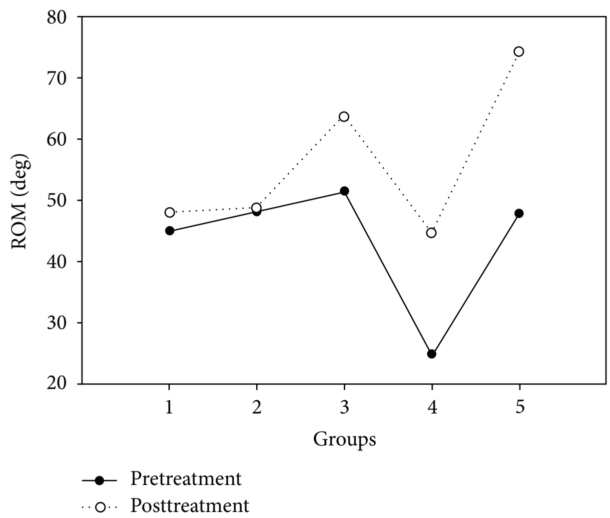

Figure 3: Average range of motion, in degrees above the horizontal, for all 5 treatment groups.

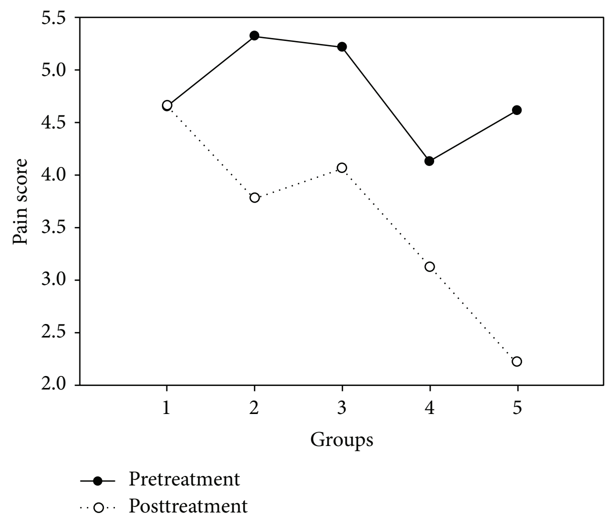

Figure 4: Average pain score (VAS) for all 5 treatment groups.

effective than the sham treatment in reducing pain, pairwise comparisons indicated that RH was more effective than Reiki ($F = 4.77$, $P = 0.037$) or PT ($F = 5.48$, $P = 0.026$).

3.4. Heart Rate. Although heart rate significantly decreased posttreatment when all 5 groups were considered ($F = 6.55$, $P = 0.01$), there was no difference in this reduction in HR between the groups, including the no-treatment control group. The results are shown in Figure 5.

3.5. Heart Rate Variability. The mean respiration rate of participants did not vary between groups. Therefore, the HRV results of the study were not influenced by alterations in respiration. Neither SDRR nor RMSSD significantly changed posttreatment compared to pretreatment when all 5 groups were considered (SDRR: $F = 2.3$, $P = 0.134$; RMSSD: $F = 1.46$, $P = 0.23$).

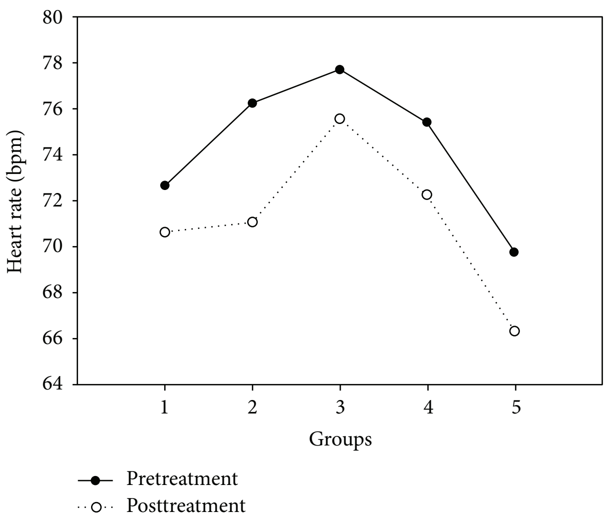

Figure 5: Average heart rate (beats/minute) for all 5 treatment groups.

4. Discussion

This study showed that a 10-minute session of RH or Reiki was as effective as PT in improving ROM in people with restricted shoulder mobility; in fact RH, but not Reiki, was significantly more effective than PT when performed for this short time period. These results cannot be explained by a placebo effect because sham treatment did not significantly improve ROM. On the other hand, although PT, RH, and Reiki all significantly reduced the pain scores reported by participants compared to no treatment, the sham treatment was just as effective as the 3 healing modalities. The reduction in pain experienced by participants apart from those in the no-treatment group can be attributed to the placebo effect.

It is interesting that Sham Healing significantly reduced pain but did not improve ROM. These results suggest that the beneficial effects of Reiki and RH (but not Sham) on ROM may arise from alterations in local joint or muscle structures rather than the pain system. The success of the Sham Healing in reducing pain was probably triggered by the expectation of healing arising from the appearance and actions of the sham healer that may have then stimulated a release of endogenous opiates or activated the dopaminergic system [27].

Previous experiments evaluating the immediate effectiveness of PT (manual manipulation only) in improving ROM and reducing pain in subjects with shoulder problems report mixed results and small sample sizes. Surenkok et al. [28] showed that scapular mobilization of the affected shoulder of 13 people with painful shoulder restriction significantly improved ROM by an average of 4°. The mobilization included superior and inferior gliding, rotations, and distraction to the scapular. A control group was included. However, there was no significant reduction of pain as measured by a VAS when participants raised their arms before and after treatment. Teys et al. [29] tested a Mulligan's mobilization with movement technique, in which the physical therapist applies a sustained glide to the glenohumeral joint while the patient concurrently actively moves the joint, on 8 patients with painful shoulder constriction. Sets of 10 repetitions were applied with a 30 s rest interval between sets. A control group was included. This type of therapy had an immediate positive effect on both ROM and pressure pain threshold. Range of motion increased on average by 15.3°. Pressure pain threshold, or the degree of pressure sufficient to cause the patient pain when applied to the most sensitive point on the anterior aspect of the shoulder, was significantly decreased by 20%. However, the change in ROM was not related to the reduction in pain pressure threshold, consistent with our finding that Sham Healing significantly reduced pain but did not affect ROM.

Five other studies investigated the effects of PT manual manipulation on patients with painful shoulder restriction, but these experiments extended over weeks and no measurements were reported after the first session. Three of the 5 investigations showed improvement in average ROM after treatment [30–32]. Two studies did not show improvement [33, 34] but only mid-range rather than endrange manipulations were applied to the shoulders.

The mechanisms by which PT, Reiki, and RH improved ROM are not known. A theoretical basis for the action of manual manipulation PT and its effect in the body has been advanced based on autonomic activation causing concomitant vasodilatation, smooth muscle relaxation, and increased blood flow, resulting in improved ROM, decrease in pain perception, and/or change in tissue. In support of this theory it was shown that cervical myofascial release, such as that used by physical therapists, shifts sympathovagal balance from sympathetic to parasympathetic [23]. However, the improvement in ROM seen in the PT group in the current study may not have been mediated by this mechanism because no significant increase in HRV was observed after PT. For the same reason the beneficial effects of RH and Reiki in this case did not seem to operate through rebalancing of the autonomic nervous system.

One limitation of this study is that inferences drawn from the results should be confined to those seen in a single 10-minute treatment session with no follow-up. Another possible limitation is that the physical therapists chose to only include manual therapy performed at the glenohumeral joint rather than the entire shoulder complex and this may have limited their effectiveness. Further studies to evaluate such issues as the timecourse of the effect of PT, Reiki, and RH and the outcome on disability and function are warranted. There is a clear clinical need for nonsurgical treatments that are safe and effective for chronic, painful shoulder.

5. Conclusion

This pilot study is a proof of the concept that the use of RH or Reiki is as effective as manual manipulation PT in improving ROM in patients with painful shoulder limitation when evaluated immediately after a 10-minute treatment. The results suggest that it would be beneficial for physical therapists to be trained in RH or Reiki as well as PT so that they could reduce the need for manual work on patients, at least in cases of shoulder limitations. However, further research is required in which patients are reevaluated over longer time periods to determine whether the healing effect of a 10-minute RH or Reiki session is sustained at least as long as for a 10-minute PT session. The degree of increased effectiveness of longer or repeated treatments of RH, Reiki, or PT would also need to be compared.

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Research Article

Randomized Controlled Trial of Mindfulness Meditation and Exercise for the Prevention of Acute Respiratory Infection: Possible Mechanisms of Action

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Background. A randomized trial suggests that meditation and exercise may prevent acute respiratory infection (ARI). This paper explores potential mediating mechanisms. *Methods*. Community-recruited adults were randomly assigned to three nonblinded arms: 8-week mindfulness-based stress reduction ($N = 51$), moderate-intensity exercise ($N = 51$), or wait-list control ($N = 52$). Primary outcomes were ARI illness burden (validated Wisconsin Upper Respiratory Symptom Survey). Potential mediators included self-reported psychophysical health and exercise intensity (baseline, 9 weeks, and 3 months). A Baron and Kenny approach-based mediational analysis model, adjusted for group status, age, and gender, evaluated the relationship between the primary outcome and a potential mediator using zero-inflated modeling and Sobel testing. *Results*. Of 154 randomized, 149 completed the trial (51, 47, and 51 in meditation, exercise, and control groups) and were analyzed (82% female, 94% Caucasian, $59.3 \pm$ SD 6.6 years old). Mediational analyses suggested that improved mindfulness (Mindful Attention Awareness Scale) at 3 months may mediate intervention effects on ARI severity and duration ($P < 0.05$); 1 point increase in the mindfulness score corresponded to a shortened ARI duration by 7.2–9.6 hours. *Conclusions*. Meditation and exercise may decrease the ARI illness burden through increased mindfulness. These preliminary findings need confirmation, if confirmed, they would have important policy and clinical implications. This trial registration was Clinicaltrials.gov: NCT01057771.

1. Introduction

Acute respiratory infection (ARI), also known as a "common cold" or "cold," is extremely common, often debilitating, and easily transmittable. It is one of the top 10 most expensive illnesses [1] and one of the leading causes for health care utilization and school and work absenteeism [2–4]. Despite its high prevalence and impact, available treatments for ARI are not very effective and usually limited to symptomatic care [5, 6]. Development of new therapies for ARI prevention and/or treatment could tremendously benefit both individuals and society at large.

It is common wisdom that being in a state of "good health" is one of the few measures one can do in order to prevent "a bad cold." Research corroborates this belief by documenting links between poor psychophysical health and worse ARI-related outcomes [7–9]. Recently, two health behaviors, exercise and mindfulness meditation ("meditation"), have been gaining support as both "healthy lifestyle" modalities and medically-recommended therapies for a variety of conditions. Regular exercise may not only protect from ARI, but also decrease the duration and severity of ARI illness [10–12]. Evidence shows that meditation training can modulate immune response, including an enhanced response to the flu vaccine [13], and it can be effective for a variety of mental health problems, such as stress and depression [13, 14] that are known correlates of ARI illness severity [7–9].

With scientific evidence and public interest aligned in the search for effective therapies for the common cold, especially using "holistic" healthy approaches, we designed and conducted a three-arm randomized controlled trial (RCT) evaluating efficacy of meditation and exercise interventions for ARI illness prevention and treatment during a single cold/flu season ($N = 154$) [14]. Findings of this trial have been consistent with the existing literature and suggested that 8 weeks of training in meditation (Mindfulness Based Stress Reduction) [15] or moderate-intensity exercise can improve ARI-related outcomes. In this RCT, during the 3 month follow-up period, 149 participants provided outcome data and were included in analysis. Among them, 44% experienced an ARI illness and reported 27 ARI episodes in the meditation, 26 episodes in the exercise, and 40 episodes in the waitlist observational control group. Both meditation and exercise groups reported shorter ARI duration than controls (257 and 241 versus 453 days, resp.; one-sided $P = 0.03$). Compared to control, the meditation group also reported a statistically significant reduction in the global severity of ARI illness ($P = 0.004$), while the exercise group did not ($P = 0.16$). Similarly, the ARI-related absenteeism was lower in meditation (16 days, $P < 0.001$) and only marginally so in exercise (32 days, one-sided $P = 0.04$) group compared to controls (67 days) [14]. Interestingly, an evaluation of the individual ARI symptoms showed that the potential advantage of training in meditation over exercise for reducing cold and flu illness was explained as much or more by reduced functional and quality of life impact rather than by lower severity of individual ARI symptoms [16].

The current study, based on a mediational analysis from the above RCT ($N = 149$), was focused on exploration of possible mechanisms underlying efficacy of meditation and exercise interventions on primary outcomes: ARI illness duration and global severity, with an *a priori* hypothesis that reduction in perceived stress and/or increase in mindfulness scores mediated intervention effects.

2. Materials and Methods

Details of the rationale and methods of the primary study are described elsewhere [14]. What follows is a brief description of methods relevant to this paper.

2.1. Design. Participants were randomly allocated into one of the 3 parallel equal groups: (1) meditation, (2) exercise, or (3) waitlist observational control. The primary RCT aim was to determine whether training in either intervention could reduce ARI illness burden, as compared to control (findings are published elsewhere [14]). Secondary aims were to test whether the training in meditation or exercise could improve psychosocial and physical health indices, and explore whether changes in these health indicators could explain or "mediate" intervention effects on primary, ARI-related outcomes; the current paper focuses on these secondary aims.

2.2. Study Arms. The mindfulness meditation intervention, Mindfulness Based Stress Reduction (MBSR), was led by trained, experienced instructors through the University of Wisconsin (UW) MBSR program [17]. The standardized 8 week MBSR training included weekly 2.5 hour group sessions, 45 minutes of daily at-home practice, and a one day retreat, and promoted continued lifelong meditation practice [17]. The conceptual premise of mindfulness training, corroborated by evidence, is rooted in the idea that increased awareness of present-moment experiences can lead to a healthier or "mindful" response to challenges as opposed to reactive or habitual response.

The exercise program was designed and led by experienced Exercise Physiology staff from the UW Health Sports Medicine Center. It was matched to the meditation program in meeting location, contact duration, time and type, and home practice requirements. The goal was to achieve moderate intensity sustained exercise (target exertion rating of 12–16 points on the 6–20 point Borg's Exertion scale [18]). Group sessions were divided into didactic instruction and exercise practice. For most participants, home exercise consisted of brisk walking or jogging.

Waitlist observational control group participants were eligible to receive meditation training or monetary equivalent at trial's end and were monitored and evaluated using the same methods as the intervention groups.

2.3. Participants/Setting. Community-based participants were recruited from Madison, WI and vicinity. The protocol was approved by the UW Health Sciences Institutional Review Board (protocol no. 2009-0075). The trial was monitored by a Data and Safety Monitoring Committee. The American Heart Association guidelines [19] for safety of exercising were followed.

Inclusion criteria included: age ≥50 years, reported ≥2 colds in the last 12 months, or ≥1 cold on average per year, and a successful completion of a 2 week long run-in trial. Exclusion criteria included: previous training in or current practice of meditation; moderate exercising ≥ twice/week or vigorous exercising ≥ once/week; score <24 points on the Folstein minimental exam [20]; score >14 points on the Patient Health Questionnaire-9 depression screen [21]; and self-reported immunodeficiency, autoimmune or malignant disease, or allergic response to flu vaccine or eggs.

2.4. Recruitment and Monitoring. Potential participants, recruited primarily via media ads during the single cold/flu season (September 2009 and January 2010) were screened by phone ($N = 833$). Interested eligible adults then met with the study coordinator for enrollment procedures and entry into the 2 week long run-in trial ($N = 204$) whose completers were consented, enrolled, and randomized into the main trial ($N = 154$): 51 in the exercise, 51 in the meditation, and 52 in the waitlist control group. Participants were followed until study exit (May 2010); 149 participants provided outcome data (96.7% retention rate) and were included in analysis (Figure 1).

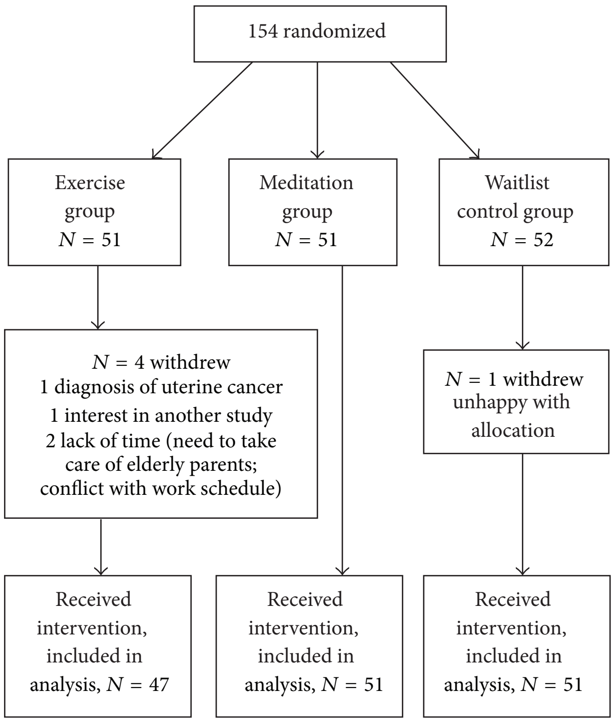


Figure 1: Participant Flow Diagram.

2.5. Outcome Measures. All outcome measures were collected at baseline, 9 weeks (postintervention) and 3 months postentry. Starting at postintervention, participants were also monitored for ARI onset biweekly by telephone. Those who developed a cold were additionally asked to report their ARI symptoms daily.

The primary outcomes evaluated the ARI illness burden: severity and duration (no. days). The ARI illness presence was determined using the Jackson cold severity scale [22] and a 24-item version of the Wisconsin Upper Respiratory Symptom Survey (WURSS-24) [23–25] which adds items assessing headache, body aches, and fever to the well-validated WURSS-21 [26]. The WURSS-24 was filled out daily during the duration of each ARI episode. The illness severity during each ARI episode was assessed daily using the WURSS-24-scale [23–25]. For each subject, based on each ARI illness episode, global severity score (area under the curve, AUC) for all ARI illness days throughout the study was calculated, with the global score being the sum of scores for items 2 through 23 of the WURSS-24 questionnaire (first and last items were analyzed separately). ARI illness duration was assessed in minutes then converted to decimalized days.

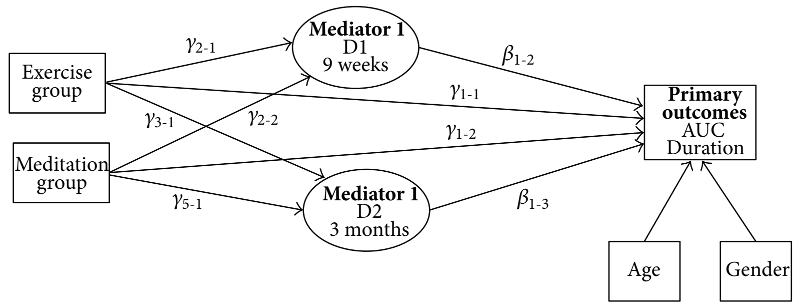
Health indicator outcomes included validated questionnaires inquiring about self-reported health. The 12-item Medical Outcomes Study Short Form (SF-12) measured overall health in physical and mental health domains [27]. The 10-item Perceived Stress Scale (PSS-10) evaluated severity of perceived stress; its score has been linked to ARI outcomes, including in influenza [8]. The Positive and Negative Affect Schedule (PANAS) [28] assessed positive and negative emotion levels, also known to be linked to ARI outcomes [29]. The six-item Life Orientation Test (LOT) assessed cognitive aspects of optimism [30]. The nine-item Positive Relationships with Others (PR) scale assessed perceived social support [31]. The 15-item one-factor Mindful Attention Awareness Scale (MAAS) measured the so-called degree of mindfulness [32]. The International Physical Activity Questionnaire (IPAQ) [33] measured the number of minutes and intensity of exercising. Spielberger's State Trait Anxiety Inventory (STAI) assessed severity of anxiety symptoms [34]. The Pittsburgh Sleep Quality Index (PSQI) [35] served as a measure of sleep quality. Details of other methods, not relevant to this analysis, can be found elsewhere [14, 36].

2.6. Randomization/Blinding. Using SAS software [37], 165 unique identification numbers were generated (balanced blocks of 3) and then concealed in sealed envelopes. The research coordinator opened consecutively-numbered envelopes after consent to determine allocation. Participants and assessors were not, but statistician was blinded.

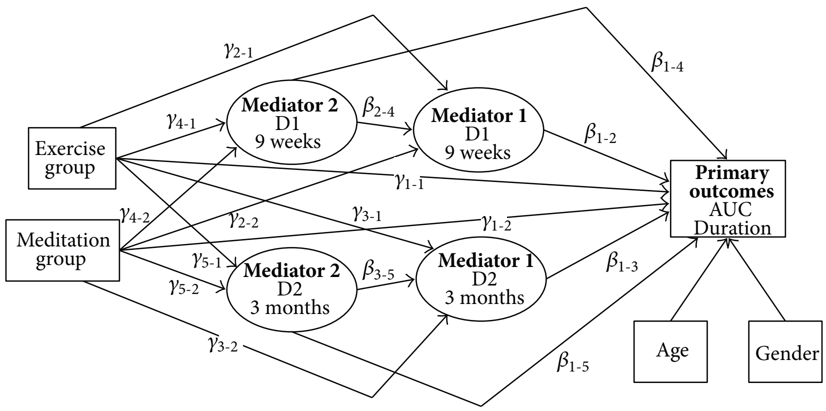
2.7. Statistical Methods. SAS statistical program (version 9.2) was used for data analysis [37]; to evaluate possible mechanisms of intervention action, a complete data set was required ("per protocol" analysis). The sample size was determined *a priori* [14]. Two-sided P value ≤ 0.05 was considered statistically significant. Distributional data characteristics were assessed. Descriptive statistics were conducted with results presented as mean value ± standard deviation (SD) and 95% Confidence Intervals (CIs), unless otherwise specified.

The current paper is focused on evaluation of potential mechanisms that may underlie effects of the two interventions [14]. Based on the hypothesis that the score change in health indicators ("mediators") may have mediated intervention effects on the ARI global severity (AUC) or illness duration (no. days) outcomes, mediational analyses examined the potential explanatory pathways using the statistical framework derived from the Baron and Kenny model [38], and modified by Krull and MacKinnon [39] and coauthor Brown [40]. Inclusion of a given health indicator into the mediational analysis model was based on (a) theoretical considerations, with the literature suggesting that improved health indicators, primarily the reduction in perceived stress (PSS scores) and/or increase in the degree of mindfulness (MAAS scores) could be "active ingredients" ("mediators") underlying treatment efficacy and (b) results of prior analyses [14] showing that some, but not all, health indicators changed their scores over time within the group or when comparing active groups versus the control group. Scores of 7 health indicators, including the PSS and MAAS, that exhibited a statistically significant change [14], were included in modeling as potential mediators; four health indicators (PANAS-Negative, STAI, PSQI and SF-12 physical health) did not change and were, therefore, not included [14].

Two types of mediational models, Stage 1 and Stage 2, were developed, differing in how the MAAS score was approached (Figure 2). The literature supports using the MAAS as either an outcome measure or health indicator (Stage 1 modeling) or as a "surrogate measure" that can reflect



(a) Stage 1 modeling



(b) Stage 2 modeling

Figure 2: Mediational analysis models: the relationship between the "dependent variable" (primary outcomes: acute respiratory infection (ARI) severity and duration), "independent variables" (group status) and possible "mediators" (health indicators); separate models were created for each health indicator. Stage 1 models illustrate single-mediation, while Stage 2 models illustrate compound-mediation (change in the mindfulness score as Mediator 1, and change in the health indicator score as Mediator 2). *Abbreviations/Explanations*: AUC: area under the curve global ARI severity; "Mediator" is a proposed mediating variable; D1 refers to the "mediator" score change at 9 week, and D2 to the "mediator" score change at 3 month followup; $\gamma 1$ pathways represent a direct relationship between group status and the primary outcome; $\gamma 2$ through $\gamma 5$ pathways represent relationships between group status and the potential mediator; $\beta 1$ pathways represent relationships between the potential mediator and the primary outcome; and $\beta 2$ and $\beta 3$ pathways represent relationships between the two potential mediators.

the intensity of mindfulness practice with the premise being that the more intense practice the larger increase in the MAAS scores (Stage 2 modeling) [41]. Each model evaluated a relationship between the ARI illness global severity or duration "dependent variable" and a health indicator that could mediate the intervention effects. Stage 1 models (Figure 2(a)) included the following: (i) the proposed mediating variable (its score change at 9 week [D1] or 3 month [D2] followup), (ii) group status ("independent variable," expressed as two "dummy variables": exercise versus control as Group 1, and meditation versus control as Group 2), (iii) age, and (iv) gender (Male = 1, Female = 0). Stage 2 models (Figure 2(b)) contained all Stage 1 variables and, in addition, included the change in MAAS scores at D1 and D2 (compound mediation structure).

Because most participants did not report any ARI illness, the mediational analyses used a zero-inflated model (ZIM) approach [42, 43] to control for potential confounders and "adjust" for those who did not report any cold ("no-cold" participants, $N = 83$). Modeling data with a high number of "zeroes," while ignoring such zero-inflation, could result in biased parameter estimates. The most common approach to modeling such distributions is to assume a logistic regression model for the "zero/nonzero" values of the outcome (i.e., "at least one cold episode" versus "no cold" participants) and a censored distribution for the model [44]. Because the zeros are accounted for in the logistic portion of the model, the variable portion can reflect, more accurately, the nonzero distribution. We used a censored-inflated regression model that estimated two equations: one for the continuous measures of ARI illness severity or duration and one binary (logistic regression). The continuous model was for participants who were above the censoring point (those who reported at least one cold); data distribution of the global ARI illness severity (AUC) was skewed and the Box Cox transformation normalized it. The binary model was contrasting participants who were above versus below the censoring point. As an outcome, each of Stage 1 and 2 models evaluated both (i) predictors of the ARI severity or duration among those who reported at least 1 cold and (ii) predictors of getting a cold. Mplus Version 6.12 [45] was used to construct the zero-inflated censored models.

Once relationships between individual variables are established, the next step is to interpret these relationships in light of whether other variables may either influence or explain it; this latter case, of how other variables could explain the various relationships found in the studied causal pathways has been termed “mediation” [38] which was the focus of the current study. In general, mediation can be assessed by evaluating the products of the sequential pathways (Figure 2). Stage 1 or single-variable mediation models (Figure 2(a)) considered three separate relationships between (A) group status and primary outcomes ($\gamma 1$ direct pathways); (B) group status and the potential mediator ($\gamma 2$ and $\gamma 3$ pathways), and (C) the potential mediator and primary outcomes ($\beta 1$ pathways). To consider the presence of mediation, all three relationships, when considered individually, need to be statistically significant. Stage 2 or compound-variable mediation models (Figure 2(b)) accounted for the possible influence of two mediators: change in the MAAS score and change in the health indicator score. These models evaluated the relationships between (A) the group status and primary outcomes ($\gamma 1$ direct pathways), (B) group status and the potential mediators ($\gamma 2$ through $\gamma 5$ pathways), (C) the potential mediators and primary outcomes ($\beta 1$ pathways), and, in addition, (D) the two potential mediators ($\beta 2$ and $\beta 3$ pathways). The model suggests complete mediation when a direct $\gamma 1$ pathway “loses” statistical significance after adjustment for the influence of a potential mediator or mediators (product of the γ2-5 pathways and β pathways). When the presence of significant direct influence of a given variable on the primary outcomes was suggested by Stage 1 and Stage 2 models ($P < 0.05$), the Sobel testing [46, 47] was used to further assess mediation. Health indicator could be considered a “true” mediator only if the results of Stage 1 or 2 modeling were corroborated by the statistically significant results of the Sobel test. The Sobel test involves computing the ratio of the product of the mediated effects along with an estimate of its standard error. A significant P value ($P < 0.05$) for the product ratio is used to support the hypothesis of mediation.

3. Results

Details on participant study flow, baseline characteristics, and primary outcome analysis findings were published elsewhere [14]. Briefly, participants ($N = 149$; Figure 1) were on average 59 (±6.6) years old, with 82% women, 94% Caucasian, 93% nonsmokers, 60% reporting college or postgraduate degrees, and 55% reporting annual household income ≥$50,000. Baseline measures were similar across the three groups.

Stage 1 modeling (Table 1) evaluated effects of individual health indicators (their change over time) on ARI-related outcomes when adjusted for age, gender, and group status (single mediation). It showed that change in the mindfulness score at 3 months (MAAS-D2) emerged as a potential mediator of beneficial intervention effects on both ARI illness global severity and duration ($P < 0.05$ for both β and γ pathways). Change in the optimism score was also identified as a possible mediator of intervention effects on ARI illness severity, suggesting that those with larger increases in optimism at 9 weeks reported more severe symptoms of ARI illness (LOT-D1, $P < 0.05$ for both β and γ pathways). However, this relationship trended in the opposite direction at 3 months, when those who endorsed more optimism were less likely to report severe ARI illness (LOT-D2, $P = 0.06$ for β pathway). Although changes in perceived stress (PSS-D2) and mental health (SF-12M-D2) scores also correlated to the ARI duration ($P < 0.05$ for β pathways), they did not appear to mediate intervention effects ($P \geq 0.05$ for $\gamma 2$ pathways).

Stage 2 models (Table 2) assessed for the presence of compound mediation, by evaluating effects of individual health indicators on ARI-related outcomes when adjusted for age, gender, group status (as in Stage 1 modeling), and, additionally, for the change in MAAS scores. Stage 2 modeling indicated that change in the mindfulness score at 3 months (MAAS-D2) could be a potential mediator of intervention effects ($P < 0.05$ for both β and γ pathways) on the ARI illness severity (optimism, positive emotion, social support, and mental health models) as well as duration (exercise intensity, optimism, and social support models; and marginal significance in the mental health model, $P = 0.056$ for $\beta 13$ pathway). In addition to mindfulness, change in exercise intensity also emerged as a possible mediator in the Stage 2 modeling for ARI illness severity, with increasing exercising at 9 weeks (IPAQ-D1) positively related to the increased cold severity (parameter estimate 0.3, $P < 0.05$ for $\beta 14$ pathway). Although change in mindfulness score at 9 weeks (MAAS-D1, exercise model for ARI illness severity) and mental health score at 3 months (mental health model for ARI duration) correlated to the ARI illness severity and duration ($P < 0.05$ for β pathways), they were not likely mediators ($P \geq 0.05$ for γ pathways).

Overall, Stages 1 and 2 modeling indicated that an increase in the mindfulness score at 3 months (MAAS-D2) correlated to the decrease in ARI illness severity ($P < 0.05$; coefficient range from 333.1 to 484.5) and the reduction in ARI duration ($P < 0.05$). Across the models where MAAS-D2 appeared to be a potential mediator, each 1 point increase in the MAAS score corresponded, on average, to a shortened ARI illness duration by 7.2–9.6 hours (coefficient 0.3–0.4). Mediational analysis also showed a positive association between age and cold duration (but not severity) in several models ($P < 0.05$ for $\gamma 13$ pathway): Stage 1 model for perceived stress (Table 1), and Stage 2 models for optimism, social support (Table 2), and perceived stress (details not presented), with estimated coefficient, on average, of 0.03 suggesting that with increase in age by 1 year, the cold duration lengthens by approximately 0.6 hours. Only one model showed a significant gender influence: in the Stage 2 exercise model for ARI illness severity, men were less likely than women to report severe ARI illness ($P < 0.05$ for $\gamma 14$ pathway).

In addition to the investigation of potential predictors of the ARI illness severity and duration, the logistic portion of mediational analysis evaluated predictors of “catching a cold” versus not. Compared to those who reported at least one ARI episode ($N = 66$, “cold group”), the “no-cold” participants tended to be older ($P < 0.05$ in Stage 1 exercise and mindfulness models for ARI severity, and the perceived stress model for ARI duration; and in Stage 2 optimism, social support, and mental health models for ARI severity), with coefficient 0.2 in all but one model (Stage 1 exercise

Table 1: Stage 1 mediational analysis models for ARI illness global severity and duration: main findings ($N = 149$).

Health indicator	Graphic symbol	Variables	Estimated coefficient	S.E.	P value	Sobel test single mediation coefficient (95% CI)
		Stage 1 models for ARI illness severity (AUC): potential mediators				
Optimism (LOT) score	$\beta 12$	(A) LOT-D1*[1]	120.8	50.5	0.017*	
	$\beta 13$	LOT-D2	−110.6	58.8	0.060	
	$\gamma 11$	Group1	−232.4	377.3	0.538	
	$\gamma 12$	Group2*	−471.7	192.4	0.014*	
		Age	12.8	55.4	0.818	
		Sex	11.1	347.6	0.975	
		(B) LOT-D1[1] ON:				
	$\gamma 21$	Group1*	1.6	0.5	0.001*	$\gamma 21$-$\beta 12$ = 193.2 (−2.0, 388.4)
	$\gamma 22$	Group2	0.5	0.4	0.246	N/A
Mindfulness (MAAS) score	$\beta 12$	(A) MAAS-D1	−269.4	230.0	0.241	
	$\beta 13$	MAAS-D2*[1]	−368.4	151.9	0.015*	
	$\gamma 11$	Group1	365.7	300.2	0.223	
	$\gamma 12$	Group2	−266.4	162.9	0.102	
		Age	12.1	16.8	0.473	
		Sex	47.3	203.9	0.817	
		(B) MAAS-D2[1] ON:				
	$\gamma 21$	Group1*	0.3	0.1	0.024*	$\gamma 21$-$\beta 13$ = −99.5 (−217.7, 18.7)
	$\gamma 22$	Group2*	0.3	0.1	0.009*	$\gamma 22$-$\beta 13$ = −117.9 (−246.7, 10.9)
		Stage 1 models for ARI illness duration (no. days): potential mediators				
Perceived stress (PSS) score	$\beta 12$	(A) PSS-D1	0.01	0.02	0.778	
	$\beta 13$	PSS-D2*	0.06	0.03	0.023*	
	$\gamma 11$	Group1	0.1	0.2	0.524	
	$\gamma 12$	Group2	−0.3	0.2	0.141	
		Age*	0.03	0.01	0.033*	
		Sex	0.06	0.2	0.793	
		(B) PSS-D2 ON:				
	$\gamma 21$	Group1	−1.6	0.9	0.081	N/A
	$\gamma 22$	Group2	−1.7	1.0	0.093	N/A
Mental health (SF12M) score	$\beta 12$	(A) SF12M-D1	−0.01	0.006	0.085	
	$\beta 13$	SF12M-D2*	−0.01	0.002	<0.001*	
	$\gamma 11$	Group1	0.03	0.2	0.864	
	$\gamma 12$	Group2	−0.4	0.2	0.072	
		Age	0.02	0.01	0.134	
		Sex	0.006	0.2	0.972	
		(B) SF12M-D2 ON:				
	$\gamma 21$	Group1	−1.3	6.5	0.842	N/A
	$\gamma 22$	Group2	4.4	5.5	0.425	N/A
Mindfulness (MAAS) score	$\beta 12$	(A) MAAS-D1	0.02	0.2	0.945	
	$\beta 13$	MAAS-D2*[1]	−0.4	0.2	0.037*	
	$\gamma 11$	Group1	0.1	0.2	0.553	
	$\gamma 12$	Group2	−0.3	0.3	0.172	
		Age	0.03	0.01	0.052	
		Sex	0.2	0.2	0.374	

Table 1: Continued.

Health indicator	Graphic symbol	Variables	Estimated coefficient	S.E.	P value	Sobel test single mediation coefficient (95% CI)
		(B) MAAS-D2[1] ON:				
	$\gamma 21$	Group1*	0.3	0.1	0.024*	$\gamma 21$-$\beta 13 = -0.1\ (-0.2, 0.02)$
	$\gamma 22$	Group2*	0.1	0.1	0.009*	$\gamma 22$-$\beta 13 = -0.1\ (-0.3, 0.02)$

Variables included: health indicator score change at D1 (9 weeks), and D2 (3 months), group status, age, and gender. Results presented only for the models that suggested presence of potential mediation. Sobel testing of indirect effects was conducted only for the identified potential mediators.
[1]Potential mediator ($P < 0.05$ for both β and γ pathways).
*$P < 0.05$.

for ARI duration model estimated coefficient = 0.05). In addition, the no-cold participants were more likely to be in the exercise rather than the meditation group ($P < 0.05$; Stages 1 and 2 optimism models for the ARI duration; Stage 2 perceived stress model for the ARI severity; and Stage 2 positive emotion and mental health models for the ARI duration), with β estimate for exercise group of 0.9–2.6. When assessing the potential effects of health indicators, the no-cold versus cold participants only marginally differed in one of the health indicators: optimism score changed at 9 weeks (Stage 2 model for ARI duration, $P = 0.046$, β estimate 0.07) suggesting that the no-cold participants had a tendency to be more optimistic at the 9 week followup. Gender status reached significance in one model (Stage 2 perceived stress model for ARI severity; $P < 0.05$, β estimate −3.1) suggesting that women were more likely than men to report a cold.

Health indicators that, as based on Stages 1 and 2 modeling, appeared to be potential mediators, were then additionally examined using the Sobel analysis. The Sobel test, evaluating indirect mediational pathways, confirmed that change in the mindfulness score at 3 months can potentially explain intervention effects on the ARI illness severity (Table 2, $P < 0.05$ for MAAS-D2 in Stage 2 positive emotion and social support models). Change in exercising at 9 (IPAQ-D1) weeks was not corroborated by the Sobel testing to be a potential mediator of intervention effects on cold severity (Table 2).

4. Discussion

The primary goal of this mediational analysis was to explore potential mechanisms of action underlying efficacy of mindfulness meditation and moderate intensity exercise interventions, as compared to waitlist observational control, on ARI illness outcomes. Overall, Stage 1 and Stage 2 mediational analyses consistently indicated that improved mindfulness score, especially at the 3 month followup (MAAS-D2), may mediate intervention effects on ARI severity and duration ($P < 0.05$; direct mediational effects) and may, at least partially, mediate the relationship between ARI illness burden and the change in optimism, social support, mental health, and positive emotion scores. On average, each 1 point increase in the MAAS-D2 score corresponded to a shortened cold duration by 7.2–9.6 hours. In two Stage 2 models, the Sobel testing confirmed that mindfulness score change may mediate the beneficial intervention effects on ARI illness burden ($P < 0.05$). Although in several other models (both Stage 1 and Stage 2) the Sobel testing did not corroborate the presence of statistically significant indirect mediational effects of mindfulness ($P \geq 0.05$), this may represent a "sensitivity issue" related to the small sample size since only 44% of participants reported having a cold during the study. Such interpretation is supported by the consistency of findings across the models, and the values of 95% confidence intervals for the Sobel test coefficient trending toward "zero" in multiple models.

The literature supports the hypothesis that improved mindfulness may be "the active ingredient" underlying intervention effects. An uncontrolled trial of MBSR ($N = 121$) found that self-reported time spent on meditation practice positively correlated to the improved mindfulness score (the Five Facet Mindfulness Questionnaire, FFMQ) which, in turn, mediated the relationship between meditation practice and improvements in psychological wellbeing and perceived stress at 8 weeks [48]. Participants in that study who meditated 31–35 minutes per day on average also reported a decrease (large effect size, Cohen's $d = 0.9$) in the medical symptom severity, consistent with our findings that increased mindfulness scores may mediate decreased ARI illness burden. An 8 week long RCT ($N = 57$) of community adults with increased distress, noted that the MBSR group, compared to waitlist controls, increased their mindfulness MAAS score which was identified as a potential mediator of intervention effects on perceived stress and quality of life outcomes [49]. Another RCT ($N = 76$), comparing effects of MBSR against a waitlist control for anxiety disorders, noted that change in the mindfulness score (FFMQ) was a potential mediator of improved anxiety outcomes [50]. Cross-sectional studies of chronic pain patients also suggested a strong link between mindfulness and health-related quality of life outcomes [51, 52].

Although change in the score of several other health indicators, such as optimism, perceived stress, and mental health status also emerged as possible mediators, these findings lacked the kind of consistent pattern that was apparent for mindfulness. Interestingly, exercise intensity did not seem to play a substantial role in Stage 1 modeling, but appeared to correlate to cold severity when adjusted for mindfulness ($P < 0.05$, Stage 2 modeling), with improvement in the MAAS score at least partially explaining effects of exercise

Table 2: Stage 2 mediational analysis models for Acute Respiratory Infection (ARI) illness global severity and duration: main findings ($N = 149$).

Health indicator	Graphic symbol	Variables	Estimated coefficient	S.E.	P value	Sobel test single mediation coefficient (95% CI)	Sobel test compound mediation coefficient (95% CI)
Stage 2 models for ARI illness severity (AUC): potential mediators							
Exercise (IPAQ) METS	$\beta 12$	(A) MAAS-D1*	−580.0	201.6	0.004*		
	$\beta 13$	MAAS-D2	−132.2	162.5	0.416		
	$\beta 14$	IPAQ-D1*[1]	0.3	0.1	0.021*		
	$\beta 15$	IPAQ-D2	−0.005	0.07	0.942		
	$\gamma 11$	Group1	−174.4	237.6	0.463		
	$\gamma 12$	Group2*	−344.6	164.0	0.036*		
		Age	29.2	23.0	0.204		
		Sex	−6.11	0.001	0.001		
		(B) MAAS-D1 ON:					
	$\beta 24$	IPAQ-D1	<0.001	<0.001	0.259	N/A	N/A
	$\gamma 21$	Group1	−0.009	0.101	0.928	N/A	N/A
	$\gamma 22$	Group2	0.141	0.106	0.181	N/A	N/A
		IPAQ-D1[1] ON:					
	$\gamma 41$	Group1*	997.2	286.5	0.001*	$\gamma 41$-$\beta 14$ = 259.2 (−5.48, 524.04)	$\gamma 41$-$\beta 24$-$\beta 12$ = −578.2 (−1813, 657.1)
	$\gamma 42$	Group2	−186.4	266.0	0.483	N/A	N/A
Optimism (LOT) score	$\beta 12$	(A) MAAS-D1	−305.9	207.9	0.141		
	$\beta 13$	MAAS-D2*[1]	−333.1	157.7	0.035*		
	$\beta 14$	LOT-D1	51.4	49.2	0.296		
	$\beta 15$	LOT-D2	−32.7	35.1	0.352		
	$\gamma 11$	Group1	291.0	267.2	0.276		
	$\gamma 12$	Group2	−304.7	165.7	0.066		
		Age	12.5	14.3	0.381		
		Sex	39.4	209.2	0.851		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	LOT-D2*	0.1	0.02	0.013*	$\beta 35$-$\beta 13$ = −18.0 (−39.2, 3.2)	N/A
	$\gamma 31$	Group1*	0.2	0.1	0.045*	$\gamma 31$-$\beta 13$ = −76.6 (−180.0, 26.8)	N/A
	$\gamma 32$	Group2*	0.3	0.1	0.008*	$\gamma 32$-$\beta 13$ = −102.9 (−224.8, 19.0)	N/A
Positive emotion (PANAS-P) score	$\beta 12$	(A) MAAS-D1	−183.0	195.2	0.349		
	$\beta 13$	MAAS-D2*[1]	−484.5	163.0	0.003*		
	$\beta 14$	PANAS-P-D1	−18.1	33.7	0.590		
	$\beta 15$	PANAS-P-D2	246.6	39.5	0.238		
	$\gamma 11$	Group1	482.8	278.6	0.083		
	$\gamma 12$	Group2	−236.0	165.5	0.154		
		Age	3.4	22.2	0.878		
		Sex	127.0	202.7	0.531		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	PANAS-P-D2*	0.03	0.009	0.001*	$\beta 35$-$\beta 13$ = −14.3 (−27.4, −1.7)*	N/A
	$\gamma 42$	Group1*	0.24	0.12	0.038*	$\gamma 31$-$\beta 13$ = −115.8 (−249.0, 17.5)	N/A
	$\gamma 52$	Group2*	0.27	0.12	0.022*	$\gamma 32$-$\beta 13$ = −130.3 (−271.5, 10.9)	N/A

Table 2: Continued.

Health indicator	Graphic symbol	Variables	Estimated coefficient	S.E.	P value	Sobel test single mediation coefficient (95% CI)	Sobel test compound mediation coefficient (95% CI)
Social support (PR) score	$\beta 12$	(A) MAAS-D1	−320.8	207.8	0.122		
	$\beta 13$	MAAS-D2*[1]	−437.4	169.8	0.010*		
	$\beta 14$	PR-D1	−0.89	8.8	0.920		
	$\beta 15$	PR-D2	28.8	17.5	0.1		
	$\gamma 11$	Group1	387.0	278.0	0.164		
	$\gamma 12$	Group2	−246.3	165.4	0.137		
		Age	11.3	13.6	0.405		
		Sex	34.1	203.5	0.867		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	Ryff-D2*	0.04	0.01	<0.001*	$\beta 35$-$\beta 13$ = −18.8 (−36.4, −1.2)*	N/A
	$\gamma 31$	Group1*	0.2	0.1	0.028*	$\gamma 31$-$\beta 13$ = −104.9 (−227.9, 18.0)	N/A
	$\gamma 32$	Group2*	0.3	0.1	0.017*	$\gamma 32$-$\beta 13$ = −118.9 (−252.1, 14.2)	N/A
Mental health (SF12M) score	$\beta 12$	(A) MAAS-D1	−259.5	230.6	0.260		
	$\beta 13$	MAAS-D2*[1]	−355.2	153.5	0.021*		
	$\beta 14$	SF12M-D1	0.9	8.8	0.919		
	$\beta 15$	SF12M-D2	−2.08	2.7	0.446		
	$\gamma 11$	Group1	396.6	316.4	0.210		
	$\gamma 12$	Group2	−253.3	174.6	0.147		
		Age	9.4	230.6	0.658		
		Sex	27.3	153.4	0.896		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	SF12M-D2*	0.005	0.002	0.012*	$\beta 35$-$\beta 13$ = −1.8 (−3.8, 0.3)	N/A
	$\gamma 31$	Group1*	0.3	0.1	0.016*	$\gamma 31$-$\beta 13$ = −96.6 (−201.0, 16.8)	N/A
	$\gamma 32$	Group2*	0.3	0.1	0.015*	$\gamma 32$-$\beta 13$ = −105.8 (−229.2, 17.5)	N/A
Stage 2 models for ARI Illness Duration (no. days): potential mediators							
Exercise (IPAQ) METS	$\beta 12$	(A) MAAS-D1	0.07	0.3	0.788		
	$\beta 13$	MAAS-D2*[1]	−0.4	0.2	0.046*		
	$\beta 14$	IPAQ-D1	<0.001	<0.001	0.591		
	$\beta 15$	IPAQ-D2	<0.001	<0.001	0.127		
	$\gamma 11$	Group1	0.2	0.2	0.311		
	$\gamma 12$	Group2	−0.3	0.2	0.164		
		Age	0.02	0.01	0.207		
		Sex	0.2	0.2	0.451		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	IPAQ-D2	<0.001	<0.001	0.17	N/A	N/A
	$\gamma 31$	Group1*	0.2	0.2	0.044*	$\gamma 31$-$\beta 13$ = −0.1 (−0.2, 0.03)	N/A
	$\gamma 32$	Group2	0.3	0.1	0.01*	$\gamma 32$-$\beta 13$ = −0.2 (−0.3, 0.03)	N/A

Table 2: Continued.

Health indicator	Graphic symbol	Variables	Estimated coefficient	S.E.	P value	Sobel test single mediation coefficient (95% CI)	Sobel test compound mediation coefficient (95% CI)
Optimism (LOT) score	$\beta 12$	(A) MAAS-D1	0.01	0.2	0.964		
	$\beta 13$	MAAS-D2*1	−0.4	0.2	0.047*		
	$\beta 14$	LOT-D1	−0.01	0.04	0.893		
	$\beta 15$	LOT-D2	−0.01	0.05	0.807		
	$\gamma 11$	Group1	0.1	0.2	0.522		
	$\gamma 12$	Group2	−0.3	0.3	0.186		
		Age*	−0.4	0.01	0.047*		
		Sex	0.2	0.2	0.376		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	LOT-D2*	0.05	0.02	0.013*	$\beta 35$-$\beta 13 = -0.02$ (−0.04, 0.005)	N/A
	$\gamma 31$	Group1*	0.2	0.1	0.045*	$\gamma 31$-$\beta 13 = -0.08$ (−0.2, 0.03)	N/A
	$\gamma 32$	Group2*	0.3	0.1	0.008*	$\gamma 32$-$\beta 13 = -0.1$ (−0.2, 0.03)	N/A
Social support (PR) score	$\beta 12$	(A) MAAS-D1	−0.005	0.2	0.894		
	$\beta 13$	MAAS-D2*1	−0.4	0.2	0.041*		
	$\beta 14$	PR-D1	−0.002	0.02	0.908		
	$\beta 15$	PR-D2	0.01	0.02	0.495		
	$\gamma 11$	Group1	0.1	0.2	0.523		
	$\gamma 12$	Group2	−0.4	0.2	0.15		
		Age*	0.03	0.01	0.044*		
		Sex	0.02	0.2	0.371		
		(B) MAAS-D2[1] ON:					
	$\beta 35$	PR-D2*	0.04	0.01	<0.001*	$\beta 35$-$\beta 13 = -0.02$ (−0.04, 0.001)	N/A
	$\gamma 31$	Group1*	0.2	0.1	0.028*	$\gamma 31$-$\beta 13 = -0.1$ (−0.2, 0.03)	N/A
	$\gamma 32$	Group2*	0.3	0.1	0.017*	$\gamma 32$-$\beta 13 = -0.1$ (−0.2, 0.03)	N/A
Mental health (SF12M) score	$\beta 12$	(A) MAAS-D1	0.1	0.3	0.677		
	$\beta 13$	MAAS-D2[2]	−0.3	0.2	0.056[2]		
	$\beta 14$	SF12M-D1	−0.009	0.007	0.183		
	$\beta 15$	SF12M-D2*	−0.006	0.002	0.007*		
	$\gamma 11$	Group1	0.2	0.2	0.391		
	$\gamma 12$	Group2	−0.3	0.3	0.228		
		Age	0.02	0.01	0.088		
		Sex	0.1	0.2	0.489		
		(B) MAAS-D2[2] ON:					
	$\beta 35$	SF12M-D2*	0.005	0.002	0.012*	$\beta 35$-$\beta 13 = -0.001$ (−0.04, 0.004)	N/A
	$\gamma 31$	Group1*	0.3	0.1	0.016*	$\gamma 31$-$\beta 13 = -0.09$ (−0.2, 0.03)	N/A

Table 2: Continued.

Health indicator	Graphic symbol	Variables	Estimated coefficient	S.E.	P value	Sobel test single mediation coefficient (95% CI)	Sobel test compound mediation coefficient (95% CI)
	$\gamma 32$	Group2*	0.3	0.1	0.015*	$\gamma 32$-$\beta 13 = -0.1$ $(-0.2, 0.03)$	N/A
		SF12M-D2 ON:					
	$\gamma 42$	Group1	−1.3	6.4	0.843	N/A	N/A
	$\gamma 52$	Group2	4.3	5.4	0.426	N/A	N/A

Variables included: the MAAS score change at D1 (9 weeks) and D2 (3 months), health indicator score change at D1 or D2, group status, age, and gender. Results presented only for the models that suggested presence of potential mediation.
*$P < 0.05$.
[1]Potential mediator ($P < 0.05$ for both β and γ pathways).
[2]Trend toward being a potential mediator ($P = 0.056$ for $\beta 13$, and $P < 0.05$ for γ pathways).

on ARI outcomes. In general, change in the MAAS score was identified as the primary mediator underlying intervention efficacy in both exercise and mindfulness groups. This was not an expected result. It may be an incidental finding; however, another possible explanation is that changes in mindfulness may interact with or support the effects of exercise. Mindfulness scores rose ($P < 0.05$) in both intervention groups at 3 months [14], thus, suggesting that exercising may contribute to improved mindfulness which, in turn, can be a driving force behind the positive change in cold outcomes. This hypothesis may be supported by the fact that, while both meditation and exercise groups experienced fewer ARI illness days than controls, only the meditation group displayed a statistically significant reduction in overall ARI illness severity [14]. This interpretation does not speak against exercise, which is proven to support health, but, rather, highlights one of the possible mechanisms through which exercise exerts benefits.

Consistent with the existing literature [53–55], mediational analysis also showed that older individuals with ARI illness tended to experience longer cold duration (Stage 1 model for perceived stress and Stage 2 models for optimism, social support, and perceived stress (details of the latter analysis not presented)) and women were more likely than men to report more severe illness (Stage 2 exercise model).

Logistic regression portion of mediational analysis evaluated factors that could differentiate between those who developed a cold versus those who did not. It indicated that older age, male gender, and being in the exercise group were the predictors of "no cold" status, findings which were also noted by others [55]. The "no-cold" participants were also more optimistic at 9 weeks, a finding consistent with the existing literature suggesting that optimism and other positive emotions may protect against infectious respiratory illness [9, 29].

Strengths and limitations of this RCT were described in detail elsewhere [14]. Of note, this was the first trial to evaluate effects of meditation and exercise on ARI illness outcomes in the settings of a comparative effectiveness RCT. The sample size may have been too small to draw firm conclusions from mediational analyses. Inability to blind participants and intervention instructors to the study arm could have introduced bias. We did not track meditation practice minutes during the study and so evaluation of "dose-response" relationship between meditation training and outcomes was not possible. There is diversity of opinion among researchers how best to evaluate the change in "mindfulness" resulting from a mindfulness training [56]; choosing a different questionnaire than the MAAS could have yielded different findings. Generalizability of results may also be limited by the fact that our sample was relatively healthy. At baseline, our participants reported less perceived stress (mean PSS-10 score: 11.9) and a higher degree of mindfulness (mean MAAS score: 4.6) than is usual [41, 57]. Over time, these scores further increased in the two experimental groups but remained unchanged in the control group. It is unclear who may benefit most from these interventions. It is possible that sicker, more stressed, and less mindful people could have gained more ("more room" for improvement). But the opposite may also be true, with early evidence suggesting that, compared to those with lower level of pretreatment mindfulness, individuals with higher pretreatment levels may experience larger increases in mindfulness and larger benefits from a mindfulness intervention [58]. In such a case, mindfulness "booster sessions" or even "retreatment" could facilitate additional gains. Due to the exploratory nature of this study, we elected to use unadjusted P values in our mediational models; although this approach allows for a more liberal investigation of possible mediational pathways which can be beneficial in exploratory investigations, it also accepts more "alpha error;" these results should be interpreted with caution. Future research, utilizing a larger sample size of less-healthy participants and controlling for dose-response effects of both meditation and exercise practices, can help corroborate the main findings and clarify mechanisms underlying efficacy.

5. Conclusions

This randomized trial suggests that positive effects of meditation and exercise on ARI illness burden may be explained by improved mindfulness scores over time. Given that apart from hand washing and exposure avoidance, no ARI-prevention strategies have before been proven, these findings, while tentative, are especially noteworthy. Future studies with a larger sample size are needed to confirm these promising preliminary findings. If improved mindfulness is the "key ingredient" for ARI illness prevention and treatment, it would have important implications for health care practice and policy.

Disclosure

Beyond normal scientific review process, the NIH did not contribute to design or conduct of the study, RCT data collection, management, analysis, interpretation of the data, preparation, review, or approval of the paper.

Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

All coauthors contributed substantially and approved the final paper. They all had full access to the study data and take full responsibility for the integrity of the data, the accuracy of the data analysis, and result interpretation. Aleksandra Zgierska was the lead author for this study and a coinvestigator on the clinical trial. She designed and contributed to the analyses and wrote the paper. Bruce Barrett was the principal investigator and Daniel Muller was a coinvestigator of the clinical trial that resulted in data for the present study; they both contributed to the paper writing. Roger Brown, Chidi N. Obasi, and Tola Ewers provided data analysis; Roger Brown and Chidi N. Obasi contributed to data interpretation. Tola Ewers, Shari Barlow, and Michele Gassman were research staff for the trial who participated in data collection, entry, database management, and paper preparation.

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Research Article

Developing and Testing the Effectiveness of a Novel Health Qigong for Frail Elders in Hong Kong: A Preliminary Study

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Eight-Section Brocades and Yijin Jing consist of some routine movements that are too difficult for frail elders. A novel health qigong protocol was developed and its effectiveness for frail elders was examined using a randomized clinical trial (RCT). An expert panel performed functional anatomy analysis and safety field test prior to the RCT. The experimental group ($n = 61$, 83 ± 6 yr) was given a 12-week qigong exercise program, while the comparison group ($n = 55$, 84 ± 6 yr) participated in a newspaper reading program with the same duration and frequency. Pre-, mid-, post-, and follow-up assessments were conducted. At 12 weeks, the qigong group had significant improvements in thinking operations ($F = 4.05$, $P = .02$) and significant reduction of resting heart rate ($F = 3.14$, $P = .045$) as compared to the newspaper reading group. A trend of improvements in grip strength and a decreasing trend of depression levels were observed among the qigong group. Significant perceived improvements in physical health ($F = 13.01$, $P = .001$), activities of daily living ($F = 5.32$, $P = .03$), and overall health status ($F = 15.26$, $P = .0001$) were found. There are improvements in some aspects of psychosocial, cognitive, physical, and physiological domains. Clinical applications and possibilities for further research are discussed.

1. Introduction

The aging population around the globe will soar from 37.3 years in 2000 to 45.5 years in 2050 [1] which will be accompanied by various levels of frailty and eventually increase utilization of health care services [2, 3]. Frail elders are at higher risk of physical and cognitive decline, disability, and finally death [4, 5]. Physical therapy and cognitive training programs are mainstream interventions to prevention of functional decline in frail elders [6–8]. Previous studies however focused only on either the physical or cognitive aspect of the frail elders. To date, no studies have been found to address both aspects at the same time with one treatment program. Studies have shown that compliance was low among physically frail elders on convention programs [6]. Because of these limitations, there is an enormous need to explore alternative and complementary ways of reducing frailty and the related disabilities which would then minimize burden on the health care system.

Health qigong, a form of mind-body intervention, is demonstrated to improve physical and psychosocial functions. Eight-Section Brocades is the most widely practiced qigong protocol among older adults which may help elders adapt stress, improve neurohormonal regulation, and strengthen their cardiovascular functions [9]. Similarly, Yijin Jing has received consistent and compelling scientific evidence of health benefits on homeostasis of internal organs and enhancement of physiologic capacity of individuals [9].

Clinical experiences suggest however that both Eight-Section Brocades and Yijin Jing have limitations as these protocols have some routine movements that are too difficult for the frail elderly. To address this concern, we developed a novel health qigong protocol, the "Yan Chai Yi Jin Ten-Section Brocades," putting together the easier and more suitable routines of these two well-known qigong protocols.

This paper reported the development of this new qigong protocol and adopted a randomized clinical trial (RCT) to examine its effectiveness for frail elders in the aspects of psychosocial, cognitive, physical, and physiological functioning.

2. Methods

2.1. Development of the Yan Chai Yi Jin Ten-Section Brocades. A core group involving the first author, a TCM practitioner, and an occupational therapist (OT) was formed to develop initial protocols for both sitting and standing positions. Ten easier routines suitable for frail elders covering movement of major joints all over the body were selected from the Eight-Section Brocades and Yijin Jing. The ten sequential movements were from upper limbs to lower limbs with five easier routines selected from each of the two established protocols (Table 1). An expert panel consisting of six researchers and practitioners with diverse expertise was then formed. The panel consisted of a qigong researcher, two OTs, a social worker, a physiotherapist, a psychologist, and a TCM practitioner. The members were invited to assess the therapeutic effects of the new protocols from various health and safety aspects [10]. All panel members evaluated 17 potential health effect statements for both positions using content validation ratios (CVRs). The CVRs of 0.75 or above were indicated as significant agreement among six experts. Fourteen out of 17 statements received CVR ranging from 0.83 to 1.00 which suggested that the new protocols could facilitate relaxation, relieve unpleasant feelings, arouse cultural interests, enforce "deep and slow" breathing, enhance coordination between respiration and movements, promote good health through reciprocal movements, promote physical and psychological health, and prevent potential harms (Table 2). Two experts in OT and physiotherapy were selected to perform a functional anatomy analysis for both positions. With the concordance rate ranging from 85.05% to 92.13%, both experts confirmed that all major joints including neck, shoulder, elbows, fingers, wrist, spine, hip, and knee were involved to provide health benefits for frail elders. A field test was arranged to assess the physiological responses of the new protocols against the standard safety criteria [11]. A total of 11 elders were referred by the residential homes to take part in the field test for both standing and sitting positions at separate sessions. Both sessions were led by a certified health qigong instructor and each session lasted for an hour. The referred elders were females aged between 77 to 95 years (mean = 86 years, SD = 5 years). Physiological responses were assessed individually before and after the practice. One elder from the sitting group was excluded from the field test because hypertensive response (SBP > 200) was detected prior to the practice. A compliance rate to safe practice was 100% for six criteria which included no chest pain nor dizziness, no signs of insufficient blood circulation, oxyhemoglobin saturation by pulse oximetry (SpO_2) above 90%, no palpitation together with irregular heart rate pattern, rise in heart rate within 70% of heart rate reserve, and rating of perceived exertion below level 7 on the 10-point Borg Scale. One elder from each of the standing group and sitting group showed hypertensive response after the practice. No other adverse events or maladaptive responses were observed during the field test. It was therefore concluded that the developed health qigong protocol "Yan Chai Yi Jin Ten-Section Brocades" was safe and suitable for frail elders including those who were wheelchair bound.

2.2. Study Design. An RCT was conducted to examine the effectiveness of the Yan Chai Yi Jin Ten-Section Brocades for the frail elders in terms of its beneficial effects on the psychosocial, cognitive, and physical functioning.

2.3. Sample Size Justification. The psychosocial functioning outcome on Geriatric Depression Scale (GDS) was used for sample size estimation. Using Cohen's method [12] effect sizes of these outcome measures are found to range from .25 to .29. The effect size of .25 was used for the calculation, as it is a commonly accepted principle to adopt smaller effect size for sample size estimation. With the help of power analysis and sample size (PASS), assuming power = .80, type I error = .05, and a 10% drop-out rate, at least 70 participants for each group making a total of 140 participants should be recruited from the Elderly Division of YCHSSD. A subsample of participants would receive physiological measures on their stress responses and cardiopulmonary functions. According to previous studies [13, 14] and practical concerns, it is estimated that approximately 40 to 50 participants should be engaged in more comprehensive physiological measures using polygraph, ultrasonoscope, and microspirometer.

2.4. Participants and Settings. A total of 182 elders aged 60 and over were recruited from the Elderly Service Unit from the Yan Chai Hospital Social Services Department in Hong Kong. The selection criteria included those who (1) aged 60 and over and (2) obtained a score of 8 or higher in 62-item frailty index. A total of 134 eligible participants (36 males, 98 females) from an original sample of 182 participants were eventually included in this study from March 2012 to July 2012. They were then randomly assigned to either the intervention group or the control group. 18 out of 134 eligible participants (13%) dropped out from the study because of returning home, hospitalization, or moving to other centers. A total of 116 participants were eventually involved in the study. Figure 2 reports the CONSORT diagram for the recruitment and randomization process.

2.5. Measurements

2.5.1. Psychosocial Functioning. The 15-item Geriatric Depression Scale (GDS) [15] was used to assess depressed mood of participants. A score of 8 or above indicated

Table 1: Yan Chai Yi Jin Ten Section Brocades protocol.

New protocol content	Established qigong protocol reference
Routine 1: Wei Tuo presents a Club 1 韋馱獻杵第一勢	Yi Jin Jing 易筋經
Routine 2: Wei Tuo presents a Club 2 韋馱獻杵第二勢	Yi Jin Jing 易筋經
Routine 3: prop up the sky with both hands to regulate the triple warmer 兩手托天理三焦	Eight-Section Brocades 八段錦
Routine 4: look back to treat five strains and seven impairments 五勞七傷往後瞧	Eight-Section Brocades 八段錦
Routine 5: show claws and flash wings 出爪亮翅	Yi Jin Jing 易筋經
Routine 6: pull toes with both hands to reinforce kidney and waist 兩手攀足固腎腰	Eight-Section Brocades 八段錦
Routine 7: three plates drop to the ground 三盤落地	Yi Jin Jing 易筋經
Routine 8: Clench fists and look with eyes wide open to build up strength and stamina 攢拳怒目增氣力	Eight-Section Brocades 八段錦
Routine 9: green dragon extends claws 青龍探爪	Yi Jin Jing 易筋經
Routine 10: rise and fall on tiptoes to dispel all diseases 背後七顛百病消	Eight-Section Brocades 八段錦

Table 2: Content validation ratios (CVRs) for potential therapeutic value of the Yan Chai Yi Jing Ten Section Brocades among six experts.

On therapeutic values: the Yan Chai Yi Jing Ten-Section Brocades protocol	CVR	
	Standing	Sitting
Psychosocial		
Facilitates relaxation	1.00*	1.00*
Relieves unpleasant feeling	1.00*	1.00*
Develops confidence to deal with disabilities and medical conditions	0.50	0.67
Culturally relevant activity and arouses interest	1.00*	1.00*
Promotes social contact	0.83*	0.83*
Physical and physiological aspects		
Enforces "deep and slow" breathing	1.00*	1.00*
Enforces coordination between respiration and movements	1.00*	1.00*
Enforces trunk, neck and upper limbs stretch	0.83*	0.83*
Promotes functional mobility and balance	1.00*	0.67
Movements can be easily picked up by elders	0.50	0.50
Easy to learn as routine exercise	0.83*	0.83*
General health		
From TCM perspective, it promotes good health through practice of reciprocal movements	1.00*	1.00*
From TCM perspective, it stimulates acupressure points and enforces the flow of "Qi"	0.67	0.67
Promotes physical and psychological health	1.00*	1.00*
Safety		
Can be adapted to activity tolerance of each individual	0.83*	0.83*
Can be practiced in old age home	0.83*	0.83*
Adequate precautions to prevent potential harm	1.00*	1.00*

*Indicating statements with consensus agreement among the experts, that is, CVR within 0.75–1.00.

presentation of clinical depression symptoms. This scale was reported to have good reliability in a validation study conducted in Hong Kong [16].

The 21-item Perceived Benefit Questionnaire (PBQ) [17] was adopted to measure the perceived improvement in physical health, activities of daily living, psychological health, social relationship, and health in general of participants for the qigong practice group. The coefficient alpha and test retest reliability for this questionnaire were .88 and .91, respectively.

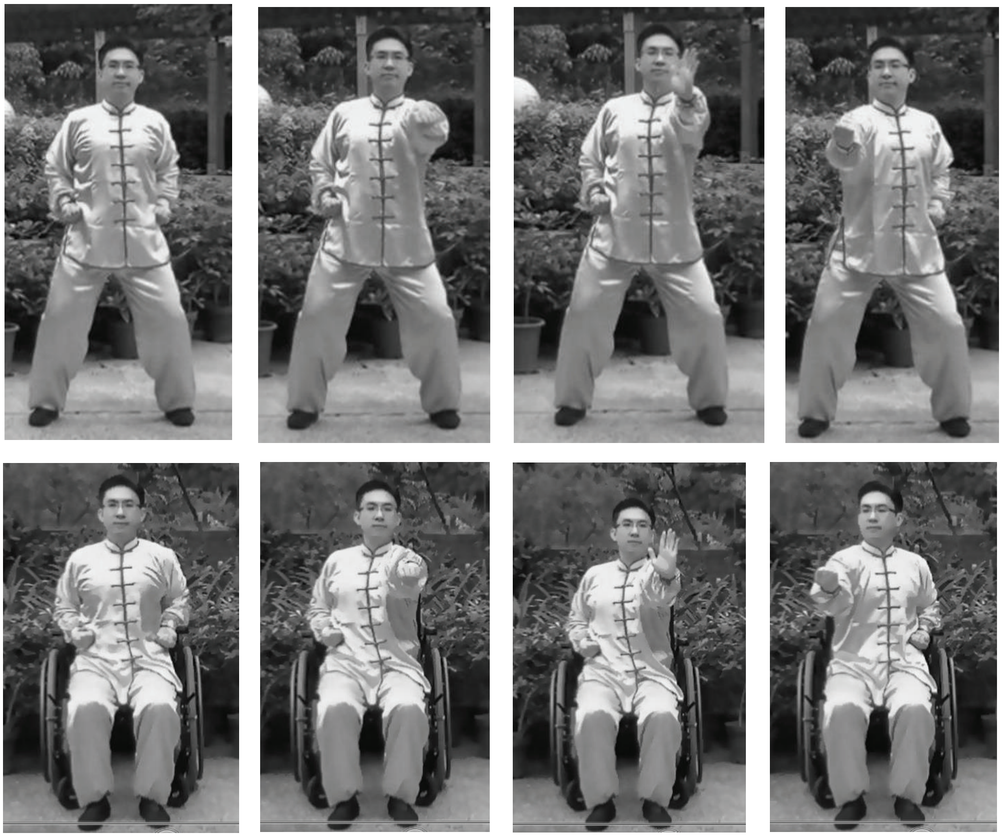
2.5.2. Cognitive Functioning. Lowenstein Occupational Therapy Cognitive Assessment-Geriatric (LOTCA-G) [18] was used to assess cognitive functioning of the participants. It consisted of 23 subsets on orientation, visual and spatial perception, praxis, visuomotor organization, and so forth, of the elders. LOTCA-G was reported to be a sound cognitive assessment tool among elders with good concurrent validity [19].

2.5.3. Physical Functioning. Handgrip strength provided an objective assessment of the subjects' general level of muscle strength [20]. The Jamar hydraulic dynamometer (Bolingbrook, IL) was used to test the maximum handgrip strength of both hands of each subject [21].

The Timed Up and Go test was used as a sensitive and valid measure for identifying older adults at risk of falls [22]. Three trials were timed for each subject and the mean value is calculated for comparison.

2.5.4. Physiological Parameters. Heart rate and systolic and diastolic blood pressure were measured by the OMRON electronics blood pressure monitor (model: BP724). Pulmonary function was assessed by lung capacity and circulation ability by a microspirometer. Lung capacity was measured by the maximum forced vital capacity (FVC). Circulation ability was evaluated by the forced expiratory volume in one second (FEV1).

2.6. Intervention Program. A 12-week intervention program was given to the participants at the corresponding day centers and residential care homes. Twenty-four intervention



Movement 8: Clench fists and look with eyes wide open to build up strength and stamina

Movement 9: Green dragon extends claws

FIGURE 1: Yan Chai Yi Jin Ten-Section Brocade with selected illustrations for standing and sitting positions.

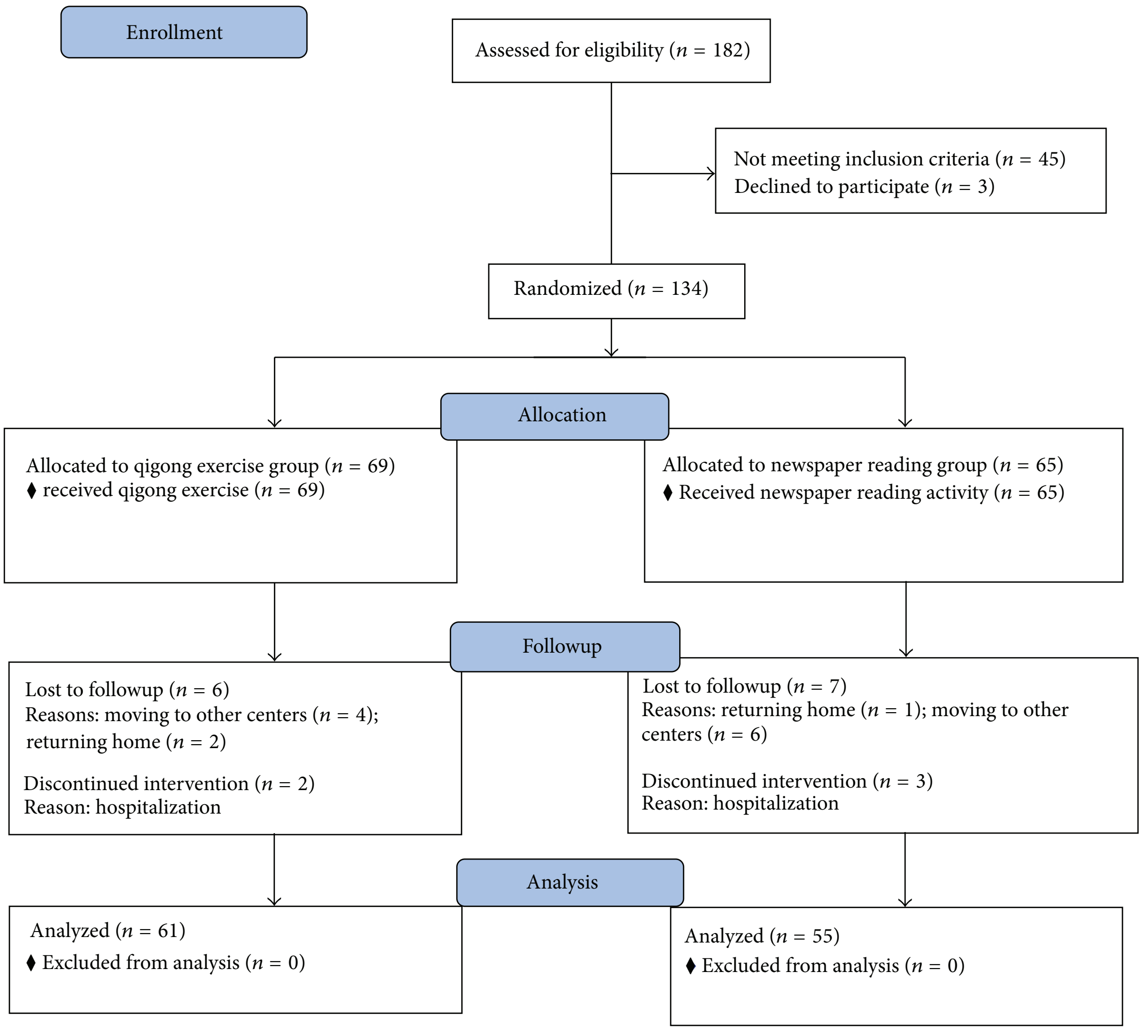


Figure 2: Consort flow diagram.

sessions were offered to the participants with two supervised 60-minute sessions per week. Participants assigned to the intervention group were provided with the Yan Chai Yi Jin Ten-Section Brocades in group format led by five qualified qigong instructors. Participants in the comparison group were assigned to a newspaper reading activity led by staff from elderly residential homes and day care center that had experience in leading rehabilitation activities.

2.6.1. Qigong Exercise Group. The Yan Chai Yi Jin Ten-Section Brocades protocol consisted of ten sequential forms of movements which was either practiced in both standing and sitting styles depending on the participants' abilities (see Figure 1). A complete cycle of the Yan Chai Yi Jin Ten-Section Brocades took 10 to 15 minutes. Each training session lasted for 60 minutes. Participants were led by certified qigong instructor to practice each of the movements of the qigong protocol 2-3 times with guided practice on mindfulness and rhythmic breathing at the beginning and short breaks between successive cycles. Participants were encouraged to practice qigong daily after the intervention program throughout the project period.

2.6.2. Newspaper Reading Group. Each session lasted for 60 minutes. The instructor read aloud the newspaper articles chosen from the news headlines during the week. The participants were asked to answer brief questions about the article and express their views. The newspaper reading and discussion activity was chosen as a comparison group activity because it was a basic rehabilitation activity that was often provided in geriatric settings and was able to neutralize the attention given by therapist compared with the experimental group. It was considered by international experts to be a good comparison activity in previous studies [23, 24]. The duration and frequency were identical to the intervention group.

2.7. Data Collection. Informed written consent was obtained from participants following policies of the institutional review board of the facilities. All participants completed the psychosocial, cognitive, and physical functioning assessments, with 57 (49.1%) participants taking part in the clinical assessments of physiological functioning (i.e., pulmonary function). All assessors were blinded as to the group assignment of the participants. The psychosocial functioning measures were collected by trained independent assessors via face-to-face interview before commencement of the intervention program (preassessment), after the 6th week of the program (mid-assessment), immediately after the end of the program (postassessment), and eight weeks after the completion of the program (follow-up assessment). The physiological measures were obtained before the commencement (preassessment) and immediately after the end of the program (postassessment). The assessment procedures were approved by the ethics committee of the authors' affiliated university and the institutional review board of the facilities.

2.8. Data Analysis. Predictive Analytics Software (PASW) 20 was used for data analysis. The outcome measures of this study included psychosocial, cognitive, physical, and physiological functioning. The intervention effects were examined by group × time interaction effects with repeated measures ANOVA/ANCOVAs followed by post hoc analyses where appropriate. The baseline scores were treated as covariates if significant group differences were detected by independent t-tests. Partial eta-squared (η_p^2) was adopted for the estimation of unbiased effect size of the intervention [25]. A two-stage analysis was adopted to compare differences between the two groups in terms of the acute intervention effects (from baseline to postassessment) and the maintenance effects (from post- to follow-up assessment). The outcome measures with significant acute intervention effects at the postassessment were included for the examination of the maintenance effects. All analyses followed the principle of "intent-to-treat" analysis. Missing data in mid- and postassessment were replaced using the "Last-Observation-Carried-Forward (LOCF)" method. Significant levels were set at $P < .05$ for all analyses. Using the median score obtained in a large-scale local study in 2,032 elders aged 70 or above [26], only participants with a frailty index score of eight or above were included in the analysis.

3. Results

3.1. Demographics Characteristics. The demographic information of the participants is summarized in Table 3. Comparison of the two groups did not reveal significant differences in demographic characteristics (Ps = .052 to .93). The mean age of experimental group participants ($N = 61$) was 83.3 (SD = 6.30), and that of the comparison group participants ($N = 55$) was 84.9 (SD = 6.03). The mean rating for the minimental state examination (MMSE) score of experimental group participants was 23.69 (SD = 3.52) and that of the comparison group participants was 23.58 (SD = 3.61), which suggested that the participants ranged from mild cognitive impairment to normal cognitive functioning subject to their educational levels [27]. The mean rating for the Clifton assessment procedures for the elderly (CAPE) score of experimental group was 9.21 (SD = 2.08) and that of the comparison group was 9 (SD = 1.98), meaning no mental impairment and no significant behavioral disability. Sixty-one (52.6%) experimental group participants and fifty-five (47.4%) comparison group participants scored eight or above in the frailty index, meaning the frailty level was higher than 50% of the elderly population. There were no reports of adverse events on both groups of participants during the implementation of interventions and assessments throughout the study.

3.2. Acute Intervention and Maintenance Effects on Psychosocial Measures. Repeated measures ANOVA within the experimental group in the acute intervention stage (Table 4) revealed significant across time effects on self-perceived benefits on physical health [$F(1,54) = 13.01$, $P = .001$, $\eta_p^2 = .19$], activities of daily living [$F(1,43) = 5.32$, $P = .03$, $\eta_p^2 = .11$] and overall health status [$F(1,57) = 15.26$, $P = .0001$, $\eta_p^2 = .21$]. From mid-assessment to postassessment, post hoc analyses found that the experimental participants had significantly higher level of self-perceived benefits on physical health (17.09 versus 18.05, resp.), activities of daily living (12.98 versus 13.48, resp.), and overall health status (6.95 versus 7.43, resp.). The self-perceived benefits on physical health were increased by 5.7%, activities of daily living was increased by 3.9%, and overall health status was increased by 6.9%. No significant across time effects on GDS [$F(2,228) = 1.16$, $P = .32$, $\eta_p^2 = .01$], self-perceived benefits on psychological [$F(1,57) = .05$, $P = .82$, $\eta_p^2 = .00$], and social relationship [$F(1,57) = .32$, $P = .58$, $\eta_p^2 = .01$] were found. A decreasing trend of levels of GDS was however observed among the experimental participants from mid-assessment to postassessment (from 4.61 to 4.31), whereas an increasing trend was observed in the comparison group participants (from 4.24 to 4.76). As to the maintenance effect, there were no significant across time effects on the perceived benefits on physical health [$F(1,53) = 2.82$, $P = .10$, $\eta_p^2 = .05$], activities of daily living [$F(1,45) = .15$, $P = .70$, $\eta_p^2 = .00$], and overall health status [$F(1,59) = .67$, $P = .42$, $\eta_p^2 = .01$].

3.3. Acute Intervention and Maintenance Effects on Cognitive Measures. A significant group by time interaction effect was indicated for thinking operations [$F(2,228) = 4.05$, $P = .02$, $\eta_p^2 = .03$], with an average increase of 8.6% (i.e., from 4.41 in preassessment to 4.79 in postassessment) observed among the experimental participants compared to an average decrease of 7.5% (i.e., from 4.56 in preassessment to 4.22 in postassessment) observed among the comparison participants (Table 5). Post hoc analyses found that experimental participants had significantly better thinking operations ($F = 7.87$, $P < 0.025$ with Bonferroni adjustment, $\eta_p^2 = .07$) in the mid-assessment. Repeated measures ANOVAs revealed no overall significant group by time interaction effects on measurements of orientation, perception, praxis, visuomotor organization, memory and attention (Ps > .05). However, from preassessment to postassessment, experimental participants were remarkably improved in perception than in

Table 3: Demographic characteristics of experimental and comparison groups.

Demographic (score range)	Mean (SD) or count (%) Experimental (N = 61)	Control (N = 55)	t or χ^2	df	P value
Age	83.33 (6.30)	84.85 (6.03)	$t = -1.31$	112	0.19
MMSE score	23.69 (3.52)	23.58 (3.61)	$t = 0.16$	114	0.87
CAPE score	9.21 (2.08)	9 (1.98)	$t = 0.56$	114	0.57
GDS score	4.07 (3.11)	4.36 (3.26)	$t = -0.50$	114	0.61
Frailty index	17.75 (6.03)	19.85 (5.43)	$t = -1.96$	114	0.052
Center			$\chi^2 = 0.25$	1	0.61
Residential care homes	51 (83.6%)	44 (80%)			
Day care center	10 (16.4%)	11 (20%)			
Gender			$\chi^2 = -0.50$	1	0.61
Male	14 (23%)	15 (27.3%)			
Female	47 (77%)	40 (72.7%)			
Marital status			$\chi^2 = 0.85$	2	0.66
Single	3 (4.9%)	5 (9.1%)			
Widowed	42 (68.9%)	35 (63.6%)			
Married, spouse alive	16 (26.2%)	14 (25.5%)			
Education level			$\chi^2 = 1.28$	2	0.53
No school completed	15 (24.6%)	17 (30.9%)			
Primary	38 (62.3%)	28 (50.9%)			
Secondary	8 (13.1%)	9 (16.4%)			
Walking ability			$\chi^2 = 0.87$	4	0.93
Walk independently	10 (16.4%)	10 (18.2%)			
Walk with stick	19 (31.1%)	15 (27.3%)			
Walk with frame	7 (11.5%)	4 (7.3%)			
Walk with rollator	7 (11.5%)	7 (12.7%)			
Wheelchair bounded	18 (29.5%)	18 (32.7%)			

Notes: MMSE: Mini-Mental State Examination; CAPE: Clifton Assessment Procedures for the Elderly; GDS: Geriatric Depression Scale.

Table 4: Acute intervention effects on psychosocial measures.

Outcome (Score range)	Means and SDs (in brackets) Pre-Ax Exp	Pre-Ax Com	Mid-Ax Exp	Mid-Ax Com	Post-Ax Exp	Post-Ax Com	Repeated measures ANOVA F	df	P-value (Group by time interaction)	P-value (Time interaction)	η_p^2	Power
GDS (0–15) (Exp: n = 61; Com: n = 55)	4.07 (3.11)	4.36 (3.26)	4.61 (2.91)	4.24 (3.23)	4.31 (3.33)	4.76 (3.52)	1.16	2,228	0.32	—	0.01	0.25
Perceived benefits												
Physical health (Exp: n = 55)	—	—	17.09 (1.97)	—	18.05 (2.37)	—	13.01	1,54	—	0.001**	0.19	0.94
Activities of daily living (Exp: n = 44)	—	—	12.98 (1.58)	—	13.48 (1.69)	—	5.32	1,43	—	0.026*	0.11	0.62
Psychological (Exp: n = 58)	—	—	25.22 (4.49)	—	25.36 (3.08)	—	0.05	1,57	—	0.82	0.00	0.06
Social relationship (Exp: n = 58)	—	—	9.84 (1.09)	—	9.91 (1.05)	—	0.32	1,57	—	0.58	0.01	0.09
Overall health status (Exp: n = 58)	—	—	6.95 (1.08)	—	7.43 (1.22)	—	15.26	1,57	—	0.0001***	0.21	0.97

Notes: Com: comparison group; Exp: experimental group; $^*P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$. GDS: Geriatric Depression Scale; only experimental group is required to complete the 21-item Perceived Benefit Questionnaire.

comparison participants. The experimental participants had an average increase of 1.7% in perception domain, while comparison participants had an average increase of 0.5% only. As the maintenance effect, repeated measures ANOVAs revealed a nonsignificant effect on the thinking operations $[F(1, 113) = 3.57, P = .06, \eta_p^2 = .03]$.

3.4. Acute Intervention and Maintenance Effects on Physical and Physiological Measures. A comparison of intervention effects between groups in the acute intervention stage showed significant group by time interaction effects on resting heart rate (RHR) $[F(2, 228) = 3.14, P = .045, \eta_p^2 = .03]$. Experimental participants had an average reduction of 2.9% in RHR after 12-week qigong practice (i.e., from 76.39 bpm in preassessment to 73.51 bpm in postassessment), while RHR of comparison group remains unchanged after the 12-week intervention period (Table 6). Although not statistically significant ($P = 0.58$), there was a trend of improvement in right handgrip strength among the experimental group participants by 1.43% on average (i.e., from 16.79 kg in preassessment to 17.03 kg in postassessment). For the comparison group, the participants had 2.47% of decrease on average from 15.37 kg in preassessment to 15 kg in postassessment (i.e., from 15.37 kg in preassessment to 15 kg in postassessment). Repeated measures ANOVAs did not reveal significant maintenance effect on the resting heart rate $[F(1, 114) = 0.22, P = .64, \eta_p^2 = .22]$.

4. Discussion

The present study demonstrated the impact of the novel health qigong on psychosocial, cognitive, physical, and physiological domains in a sample of frail elders in Hong Kong. Positive intervention effects were found in some aspects of psychosocial, cognitive, physical, and physiological domains which provided preliminary support to its potential benefits as a therapeutic activity for frail elders.

Studies on cognitive benefits of mind-body exercises are limited. Most studies reported only self-perceived benefits of qigong on cognitive functioning [28–30]. While earlier studies showed that Tai Chi and Shaolin Dan Tian Breathing reduced cognitive impairment and induce attentive state of mind [31, 32], the present study went further to explore the impact of qigong exercises on cognitive functioning using objective assessment. We showed that after a 12-week qigong intervention, the experimental group participants had significant improvement in thinking operations as measured by LOTCA-G, an assessment tool that assessed neurological deficits and mental health problems of our participants. Thinking operations refer to the ability of participants to categorize and perform sequencing of pictures. Based on our observation, the improvement in thinking operations is likely to be due to the qigong learning process. Some qigong routines required the participants to translate metaphorical imagery to movements. Frail elders were required to simulate and formulate movements according to the metaphorical hints from the routine names. For example, routine 5 and routine 9 of Yan Chai Yi Jin Ten-Section Brocade are movements that resemble bird and dragon. The learning and practice process might have trained frail elders' thinking operations. Improvement in categorization can help frail elders simplify and structure perception process and thus enhance their ability to deal with the complex and demanding social environment [33]. Sequencing ability is one of the fundamental abilities for instrumental activities of daily living (ADL) such as managing home and medications [34]. This is in line with the result that the participants had perceived improvement in their ADL. However, further studies using more objective assessment of ADL have to be conducted in order to explore if this qigong protocol improves instrumental activities of daily living of elders. Consistent with previous research efforts [31, 32], other dimensions in cognitive functioning such as memory and attention did not show significant changes after qigong practice. The present findings provided preliminary support to the hypothesis that practicing health qigong could bring positive benefits in specific aspect of cognitive functioning in frail elders. More research needed to be done in this area to investigate the mechanism behind such an effect.

In psychological aspect, the results are similar to our earlier studies [17, 23]. Participants perceived significant improvement in physical health, ADL, and overall health status as measured by the Perceived Benefits Questionnaire after the 12-week qigong practice. Given that most participants (i.e., 86%) did not show clinical depressive symptoms (GDS < 8) at the beginning of our study, it makes sense that no significant impact of health qigong exercise on the level of depression was found in this study. However, a decreasing trend of depression levels was still observed among experimental group participants from mid-assessment to postassessment, whereas an increasing trend was observed in the comparison group participants. This aligns well with our previous findings that qigong could relieve depressive symptoms [23, 24].

Significant reduction in RHR and a trend of improvement in right handgrip strength were found in physical and physiological aspects in the present study. Reduction in RHR was consistently found to be significantly reduced after qigong training [10]. RHR is associated with cardiovascular disease mortality [35]. Its drop will lower one's risk in having all-cause and cardiovascular disease mortality. This suggests that practice of this qigong protocol may have positive effects on heart health of the participants. Further studies using more sophisticated cardiovascular measurements should be conducted to explore this potential therapeutic effect. The trend of improvement in right handgrip was consistent with our earlier RCTs [24]. Less obvious physical and physiological effects observed in the present study might be due to the less physically demanding nature of the current qigong protocol tailor-made for frail elders.

There are a number of limitations that deserve our attention. First, our actual number of participants in each group did not reach the figure suggested by power analysis. This may be the reasons why some outcome measures were found to be not significant. Second, gender bias constituted a major limitation of the current study. Given that the elderly residential care center and day care center were female

Table 5: Acute intervention effects on cognitive measures.

Outcome (Score range)	Means and SDs (in brackets) Pre-Ax Exp	Pre-Ax Com	Mid-Ax Exp	Mid-Ax Com	Post-Ax Exp	Post-Ax Com	Repeated measures ANOVA (group by time interaction) F	df	P-value	η_p^2	Power
LOTCA-G (Exp: $n = 61$; Com: $n = 55$)											
Orientation (0–16)	14.13 (1.98)	13.87 (2.10)	14.31 (2.15)	13.91 (1.86)	14.11 (1.73)	13.38 (2.19)	0.94	1.9,216.10	0.39	0.01	0.21
Perception (0–28)	25.87 (2.00)	25.76 (2.34)	25.67 (2.07)	25.49 (2.40)	26.20 (2.00)	25.91 (2.44)	0.13	2,228	0.88	0.00	0.07
Praxis (0–12)	9.57 (1.28)	9.75 (1.06)	9.23 (1.04)	9.35 (1.27)	9.54 (1.15)	9.64 (1.32)	0.04	2,228	0.96	0.00	0.06
Visuomotor organization (0–24)	16.75 (3.58)	17.45 (4.03)	16.59 (3.34)	16.87 (3.62)	16.90 (3.65)	16.78 (4.35)	1.58	2,228	0.21	0.01	0.33
Thinking operations (0–8)	4.41 (1.80)	4.56 (1.69)	4.49 (1.84)	4.22 (1.64)	4.79 (1.83)	4.22 (1.70)	4.05	2,228	0.02*	0.03	0.72
Memory (12)	10.54 (1.48)	10.15 (1.88)	10.52 (1.97)	10.55 (2.18)	10.89 (1.83)	10.84 (1.57)	0.96	2,228	0.39	0.01	0.22
Attention (4)	3.84 (0.45)	3.76 (0.47)	3.77 (0.59)	3.87 (0.43)	3.74 (0.48)	3.73 (0.49)	1.26	2,228	0.29	0.01	0.27

Notes: Com: comparison group; Exp: experimental group; * $P < 0.05$.
LOTCA-G: Lowenstein Occupational Therapy Cognitive Assessment-Geriatric.

Table 6: Acute intervention effects on physical and physiological measures.

Outcome (Score range)	Means and SDs (in brackets) Pre-Ax Exp	Pre-Ax Com	Mid-Ax Exp	Mid-Ax Com	Post-Ax Exp	Post-Ax Com	Repeated measures ANOVA (group by time interaction) F	df	P-value	η_p^2	Power
Right handgrip strength (Exp: $n = 58$; Com: $n = 54$)	16.79 (6.24)	15.37 (5.70)	16.50 (6.59)	14.63 (4.93)	17.03 (6.74)	15.00 (5.18)	0.51	1.72,188.93	0.58	0.01	0.13
Left handgrip strength (Exp: $n = 54$; Com: $n = 51$)	13.70 (5.57)	13.90 (5.46)	14.02 (5.23)	13.63 (4.74)	14.24 (5.76)	14.24 (4.64)	0.36	2,206	0.70	0.004	0.11
Timed Up & Go (Exp: $n = 42$; Com: $n = 35$)	23.28 (12.75)	21.91 (13.05)	22.33 (11.91)	21.55 (12.12)	22.18 (12.71)	22.17 (11.72)	0.54	1.59,119.13	0.54	0.01	0.13
Systolic blood pressure (Exp: $n = 61$; Com: $n = 55$)	143.78 (22.20)	148.42 (18.45)	138.03 (20.04)	147.28 (18.74)	136.20 (20.94)	139.78 (16.72)	1.54	2,228	0.22	0.01	0.33
Diastolic blood pressure (Exp: $n = 61$; Com: $n = 55$)	76.55 (13.59)	80.13 (12.54)	74.03 (10.68)	77.62 (11.11)	72.82 (11.21)	75.52 (10.11)	0.12	1.89,215.53	0.88	0.00	0.07
Resting heart rate (Exp: $n = 61$; Com: $n = 55$)	76.39 (14.80)	75.07 (9.47)	75.47 (14.45)	73.95 (9.26)	73.51 (13.00)	75.04 (10.93)	3.14	2,228	0.045*	0.03	0.60
Forced vital capacity (max) (Exp: $n = 27$; Com: $n = 26$)	1.80 (0.62)	1.40 (0.45)	—	—	1.64 (0.62)	1.38 (0.47)	0.79	1,54	0.38	0.01	0.14
Forced expiratory volume in 1s (Exp: $n = 27$; Com: $n = 26$)	1.12 (0.38)	0.91 (0.36)	—	—	1.10 (0.39)	1.04 (0.37)	2.75	1,54	0.10	0.05	0.37
Forced expiratory volume in 1s % (Exp: $n = 27$; Com: $n = 26$)	64.61 (19.34)	65.93 (19.39)	—	—	70.40 (18.16)	76.00 (12.44)	0.86	1,54	0.36	0.02	0.15

Notes: Com: comparison group; Exp: experimental group; * $P < 0.05$.

dominant, we were unable to recruit male participants during the field test. Nonetheless, no adverse effects were reported during the RCT study. Third, the therapeutic effects in psychological, cognitive, physical, and physiological domains were not maintained in the follow-up period, which is in line with our previous findings [23]. This might be due to a lack of practice after the intervention period. Unfortunately, we did not have records on participants' practice pattern that has limited us to further understand the relationship between continuing practice and maintenance effects of qigong exercise.

5. Conclusions

It may be concluded that the new qigong protocol is safe and easy to learn among frail elders. It brings health benefits to frail elders in cognitive, psychosocial, physical, and physiological aspects. Finally, it may be advocated as an activity therapy program to help prevent health-related deterioration in clinical, residential, and community settings.

Conflict of Interests

There is no conflict of interests between authors.

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Research Article

Effects of Qigong Exercise on Fatigue, Anxiety, and Depressive Symptoms of Patients with Chronic Fatigue Syndrome-Like Illness: A Randomized Controlled Trial

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Background. Anxiety/depressive symptoms are common in patients with chronic fatigue syndrome- (CFS-) like illness. Qigong as a modality of complementary and alternative therapy has been increasingly applied by patients with chronic illnesses, but little is known about the effect of Qigong on anxiety/depressive symptoms of the patients with CFS-like illness. *Purpose*. To investigate the effects of Qigong on fatigue, anxiety, and depressive symptoms in patients with CFS-illness. *Methods*. One hundred and thirty-seven participants who met the diagnostic criteria for CFS-like illness were randomly assigned to either an intervention group or a waitlist control group. Participants in the intervention group received 10 sessions of Qigong training twice a week for 5 consecutive weeks, followed by home-based practice for 12 weeks. Fatigue, anxiety, and depressive symptoms were assessed at baseline and postintervention. *Results*. Total fatigue score [$F(1, 135) = 13.888$, $P < 0.001$], physical fatigue score [$F(1, 135) = 20.852$, $P < 0.001$] and depression score [$F(1, 135) = 9.918$, $P = 0.002$] were significantly improved and mental fatigue score [$F(1, 135) = 3.902$, $P = 0.050$] was marginally significantly improved in the Qigong group compared to controls. The anxiety score was not significantly improved in the Qigong group. *Conclusion*. Qigong may not only reduce the fatigue symptoms, but also has antidepressive effect for patients with CFS-like illness. Trial registration HKCTR-1200.

1. Introduction

CFS is characterized by unexplained persistent fatigue of at least 6 months with no definite effective treatment yet [1]. As a large part of the patients with CFS in the community remain unrecognized by general practitioners [2], CFS-like illness is defined based on self-reported fatigue symptoms and medical history with similar criteria for CFS, but no confirmed clinical examination [3–5]. Current and lifetime psychiatric disorders were common among the patients with CFS-like illness [6–9], with particularly strong association between unexplained fatigue and depression [10, 11]. A study with a multinational primary care sample from 14 countries suggested that over 80% of patients with CFS-like illness had a lifetime psychiatric disorder such as depression or generalized anxiety disorder [7, 12]. Most of the patients with CFS-like illness are undertreated for psychiatric illness [6]. Unexplained chronic fatigue is also a common disabling condition in the general population and is strongly associated with psychiatric morbidity [13]. In Hong Kong, the lifetime prevalence of anxiety and depressive disorders was 54% among the primary care patients with chronic fatigue (CF) [14]. The patients with CFS-like illness reported poorer mental health (higher levels of anxiety and depression) than their non-CFS-like illness counterparts [15].

To date, no curative treatment that is effective exists for the patients with CFS-like illness [16]. The use of complementary and alternative medicine (CAM) is increasing among the patients with CFS-like illness. A recent systematic review of 26 randomized clinical trials (RCTs) has suggested beneficial effects of CAM including Qigong, massage, and tuina for patients with CFS [17]. Qigong is an ancient self-healing mind-body exercise, which includes meditation, breathing, body posture, and gentle movement. It focuses to promote the circulation of vital energy, which is called "Qi" in the meridian system (Qi vital energy channel) of the human body to facilitate the harmony of the mind, body, and breathing [18].

A number of empirical studies reported that Qigong had beneficial effects on fatigue symptoms [19, 20] and other outcomes related with CFS such as sleep, pain, mental attitude, and general mobility [21]. Our prior study demonstrated that Qigong exercise was effective in reducing the severity of fatigue symptoms, improving health-related quality of life [22], and increasing telomerase activity for the patients with CFS-like illness [23]. RCTs of Qigong exercise also suggested a beneficial effect of Qigong for older people with depressive symptoms secondary to chronic illnesses [24, 25]. However, a recent systematic review and meta-analysis of the effect of Qigong exercise on depressive and anxiety symptoms suggested that scientific evidence in the field was still limited, and that further rigorously designed RCTs were warranted [26]. To date, to our knowledge, no study has examined the effect of Qigong exercise on depressive and anxiety symptoms in patients with CFS-like illness. Thus, the purpose of this large-scale study was to investigate the effectiveness of Qigong exercise as a modality of complementary and alternative therapy in reducing fatigue, anxiety, and depressive symptoms of patients with CFS-like illness.

2. Methods

2.1. Study Participants. One thousand four hundred and forty-one Chinese adults who claimed to have fatigue symptoms volunteered to fill in an online questionnaire after the study was advertised in the media. The screening questionnaire was set according to the US Centers for Disease Control and Prevention (CDC) Diagnosis criteria for CFS [1], which is widely used in the field. As it was rare that patients with persistent fatigue symptoms alone stayed in public hospitals, the participants were recruited from local community.

The diagnosis of CFS-like illness [3–5] was made based on subjective chronic symptoms and their medical history self-reported in the online questionnaire without further clinical confirmation by medical examination. A participant was diagnosed as having CFS-like illness if he or she had unexplained, persistent fatigue over 6 months which was of new onset (not lifelong) with presence of four or more of the following eight symptoms: impaired memory or concentration, postexertion malaise, unrefreshing sleep, muscle pain, multijoint pain, new headaches, sore throat, and tender lymph nodes [1]. To minimize the impact of other chronic illness as much as possible, those with any medical conditions that may explain the presence of chronic fatigue were excluded.

Two hundred and thirty-six participants met the inclusion criteria, of which 82 participants were excluded because they could not be contacted or were unavailable for the Qigong training. One hundred and fifty-four participants with CFS-like illness were recruited into the study and were randomly assigned to the intervention group ($n = 77$) and control group ($n = 77$), respectively. Among these 154 participants, 5 subjects in the intervention group and 12 subjects in the control group dropped out before the Qigong class. Only 137 subjects (72 for intervention group and 65 for control group) were included as the final sample for the data analysis. A flow chart of the selection of participants is presented in Figure 1.

2.2. Study Design and Procedure. This was a prospective randomized wait list-controlled trial. Each potential participant was required to complete an online screening questionnaire and was evaluated for eligibility by a pair of investigators with any discrepancies being resolved by discussion. Eligible participants were required to complete an additional questionnaire to measure the severity of their chronic fatigue symptoms and depressive and anxiety symptoms before intervention (T0) after having signed the written informed consent form. They were then randomly assigned to either an intervention group or a waitlist control group. Randomization was done using computer-generated random numbers. Blinding the participants to the allocation was not possible due to the nature of intervention. The intervention program lasted 4 months, with group Qigong training for 5 weeks followed by home-based Qigong exercise for 12 weeks in the intervention group. The primary outcome was fatigue symptoms and the secondary outcomes were anxiety and depressive symptoms. Data for the outcome measures were also collected at postintervention (T1) from each subject in the intervention group and control group. Ethical approval was obtained from the local review board.

Sample size was calculated according to power and estimated effect size. In order to achieve statistical power of 80% at a significance level of 0.05 (assuming treatment effect = 3 and standard deviation = 5 according to a previous local study on CFS [27]), 53 participants were required in each group. Assuming 30% dropout rate, at least 76 subjects were required in each group (the intervention group and the waitlist control group).

2.3. Intervention. Participants in the intervention group attended 10 sessions of Qigong exercise training (Wu Xing Ping Heng Gong, 五行平衡功) twice a week for 5 consecutive weeks, followed by home-based Qigong self-practice for 12 weeks. Each session of Qigong exercise training lasted 2 hours, with a brief introduction of the basic theories of traditional Chinese medicine (such as the concepts of Qi, yin-yang, five elements, and meridian system) or the precautions in doing Qigong exercise including answering any questions or concerns raised by the participants about Qigong practice (45 min), followed by mindful meditation for relaxation and then gentle movement or body stretching in standing postures to facilitate a harmonious flow of Qi along the energy channels (15 min) and a 1 h session of Qigong exercise training, which was delivered by an experienced Taoist Qigong master (Yuen L. P.) with more than 20 years

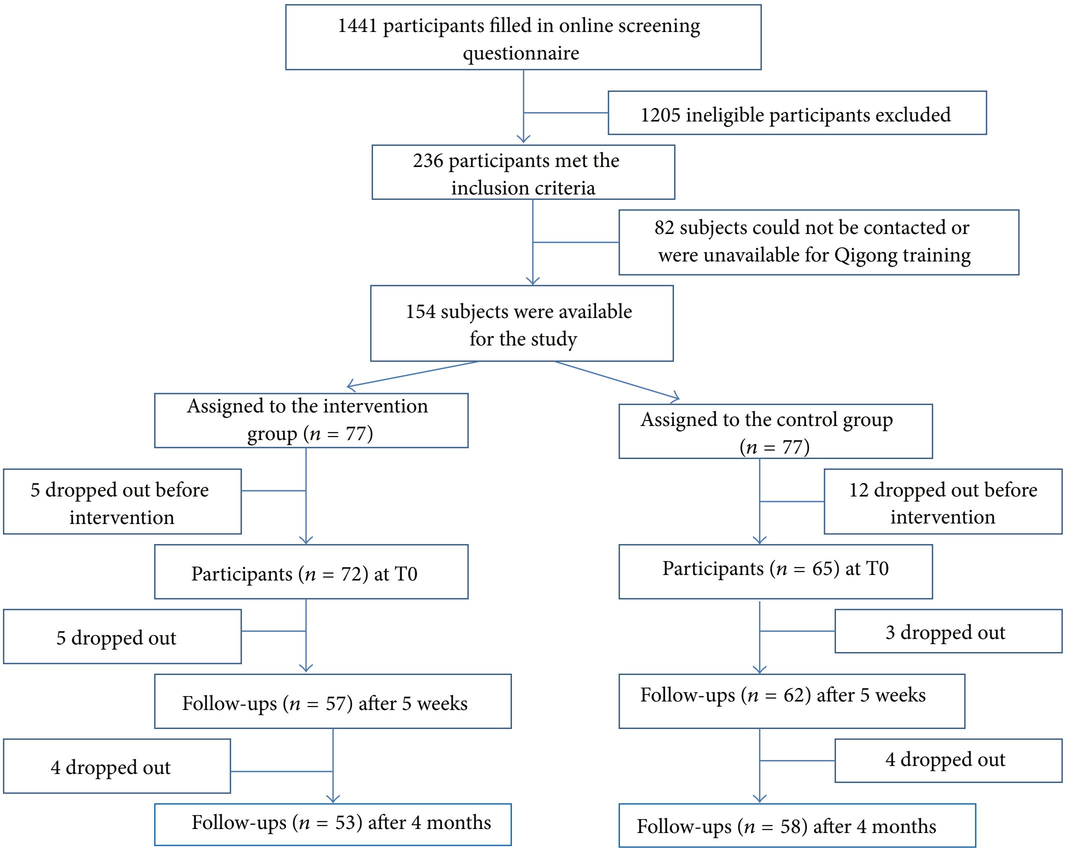

Figure 1: Flow chart of the selection of participants in the study.

of experience in Qigong practice and also a background in traditional Chinese Medicine.

Apart from mindful meditation, rhythmic breathing and concentrated relaxation, Xu Xing Ping Heng Gong, was applied in this study including 10 forms of movement which aims at enhancing the smooth flow of Qi along the various meridians of the body and meditation for relaxation and mind concentration. The movements involve stretching of arms and legs, turning of torso, relaxing, and deep breathing with the objectives of fostering harmonious energy flow of Qi along the various meridians of the body. A description of the Xu Xing Ping Heng Gong is presented in Appendix.

All participants in the intervention group were also required to do Qigong self-practice for at least 30 minutes every day at home during the 4-month intervention period. To assess home exercise, they were required to report the frequency and duration as well as adverse effects of the self-practice at home at the end of the program. The participants in control group were advised to keep their lifestyle as usual and to refrain from joining any outside Qigong exercise class during the study period. No participants in the control group joined any outside Qigong class as they were provided the Qigong training after the final outcome measurements were collected.

2.4. Measurements

2.4.1. Screening Measures. The potential participants were screened by online questionnaire including (1) whether or not the fatigue symptoms persisted or relapsed for six or more months; (2) a list of eight chronic fatigue symptoms of CDC diagnostic inclusion criteria for CFS [1]; (3) a list of medical diseases based on the CDC diagnostic exclusion criteria for CFS [1] according to their self-reported medical history without further medical examination; (4) basic demographic data such as age, gender, employment status, education level, marital status, religion, and monthly income; (5) lifestyle including exercise habits, smoking, alcohol drinking, and sleep time.

2.4.2. Chalder Fatigue Scale. The severity of fatigue symptoms was measured by the Chalder Fatigue Scale, which is a 14-item self-rating scale to measure the severity of both physical fatigue symptoms (8 items) and mental fatigue symptoms (6 items). The response pattern for each item is a five-point Likert scale (none, better than usual, no more than usual, worse than usual, much worse than usual), which is scored from 0 to 4. The subscale scores are equal to the summed scores of all items in the subscale and the total fatigue score was obtained by adding up all of the 14 items (the higher, the worse) [28]. The Chinese version of the Chalder Fatigue Scale has shown acceptable psychometric properties [29].

2.4.3. Hospital Anxiety and Depression Scale (HADS). Depressive and anxiety symptoms were measured by the HADS [30], which is a 14-item instrument with two subscales measuring anxiety symptoms (7 items) and depressive symptoms (7 items) separately. Each item is scored on a 0–3 scale and the total score of each subscale is scored on a 0–21 scale, with a higher score indicating a higher level of anxiety and depressive symptoms. Internal consistency for HADS Chinese version was revealed to be satisfactory, with Cronbach's alpha coefficients of 0.77 for anxiety subscale and 0.82 for depression subscale, respectively [31, 32].

2.5. Statistical Analyses. Means and standard deviations were used to summarize continuous data and frequency was used to summarize categorical data. Differences at baseline for the demographic information, lifestyles, and reported fatigue, anxiety, and depressive symptoms between the two groups were compared using a t-test for continuous data and a Chi-squared test for categorical data. The within group effects of outcome measures were compared between pre- and postintervention using pairwise t-test for each group. The effect size was determined by Cohen's d statistics for each outcome. The repeated measures analyses of variance (ANOVA) were then conducted to assess the interaction effect of group and time for each outcome. Intention to treat analysis was applied in this study and the missing data were substituted by the last observed values. The correlation analysis of the changes in all outcomes between pre- and postintervention and the linear regression analysis using the change of depression score as a dependent variable and changes of other outcomes as independent variables were also conducted. All data analysis was conducted with Statistical Package for the Social Sciences (SPSS version 18.0, SPSS Inc., Chicago, IL, USA). A P value of less than 0.05 was considered as statistically significant.

3. Results

3.1. The Demographic Characteristics and Lifestyles at Baseline. The data on demographic characteristics and lifestyles of the two groups are shown in Table 1. The mean ages were 42.4 (SD = 6.7) in the intervention group and 42.5 (SD = 6.4) in the control group, respectively. More than 70% of the participants were female (72% and 82% in the intervention and control groups, resp.). As shown in the table, baseline characteristics were well balanced between the two groups. The average number of reported fatigue symptoms was 6.3 (SD = 1.4) in both groups. Among eight chronic fatigue symptoms (last at least 6 months), the most common symptoms (n = 129, 94.2%) was sleep disturbance followed by muscle pain (n = 128, 93.4%) and impaired memory/concentration (n = 126, 92.0%). There was no significant difference in fatigue symptoms between the two groups. Overall, the participants had a moderate level of anxiety symptoms (mean scores for the anxiety subscale were 11.0 for the intervention group and 10.9 for the control group resp.) and a mild level of depressive symptoms (mean scores for the depression subscale were 9.1 and 9.4 for the intervention and control groups resp.) at baseline.

3.2. The Efficacy of Intervention. Table 2 shows the within-group and between-group differences of fatigue symptoms as measured by the Chalder Fatigue Scale and anxiety and depressive symptoms as measured by the HADS for the two groups. At baseline (T0), two groups were comparable in terms of total fatigue score, physical fatigue score, mental fatigue score, anxiety score, and depression score ($P > 0.05$ for all variables). Compared with baseline values, the total fatigue score ($d = -1.2$, $P < 0.001$), physical fatigue score ($d = -1.4$, $P < 0.001$), mental fatigue score ($d = -0.9$, $P < 0.001$), anxiety score ($d = -1.1$, $P < 0.001$), and depression score ($d = -0.5$, $P < 0.001$) were significantly improved in the intervention group after 4 months of Qigong intervention, while the total fatigue score, physical fatigue score, mental fatigue score and anxiety score in the control group were also significantly improved 4 months after ($d = -0.8$, $P < 0.001$; $d = -0.8$, $P < 0.001$; $d = -0.6$, $P < 0.001$; $d = -0.6$, $P = 0.006$, resp.). However, the change of the depression score in the control group was not significant ($d = 0.1$, $P = 0.365$).

The between-group difference in the change of each outcome measure was then examined by interaction effect of time and group. Compared with controls, the total fatigue score [$F(1, 135) = 13.888$, $P < 0.001$], physical fatigue score [$F(1, 135) = 20.852$, $P < 0.001$], and depression score [$F(1, 135) = 9.918$, $P = 0.002$] were significantly improved, and the mental fatigue score [$F(1, 135) = 3.902$, $P = 0.050$] was marginally significantly improved in the intervention group, whereas the change in the anxiety score in the intervention group was not significant after adjusting for control [$F(1, 135) = 0.302$, $P = 0.584$]. No adverse effects were reported in both groups during the implementation of intervention and self-practice at home throughout the study.

3.3. Predictors of Changes in Depressive Symptoms. In correlation analysis, change in the depression score was significantly correlated with changes in the total fatigue score ($r = 0.331$, $P < 0.001$) and anxiety score ($r = 0.579$, $P < 0.001$). Linear regression analysis further revealed that the change in the total fatigue score ($\beta = 0.182$, $P = 0.013$) and anxiety score ($\beta = 0.528$, $P < 0.001$) significantly explained the change in the level of depressive symptoms (adjusted $R^2 = 0.356$).

4. Discussion

To the best of our knowledge, this study is the first large-scale randomized control trial to investigate the anti-depressive effect of Qigong exercise for the patients with CFS-like illness. The findings of this study showed that Qigong exercise could improve depressive symptoms and fatigue symptoms among the patients with CFS-like illness, which provided additional evidence to support the conclusive statement of a recent systematic review [26] that Qigong exercise may have beneficial effect on depressive symptoms. An earlier study [33] showed that depressive symptoms were not significantly improved after Qigong intervention in elderly with chronic illnesses, probably due to the small sample size (n = 50) and short intervention period (12 weeks). The current study with a larger sample suggested that Qigong exercise could reduce depressive symptoms for persons with CFS-like illness. Our

Table 1: Patients' demographic information and lifestyles at baseline (n = 137).

Demographic	Intervention (n = 72)		Control (n = 65)		P^*
	Mean (SD)	N (%)	Mean (SD)	N (%)	
Age (years)	42.4 (6.7)		42.5 (6.4)		.979
Gender					.198
Female		52 (72.2%)		53 (81.5%)	
Employment					.629
Full-time		55 (76.4%)		52 (80.0%)	
Part-time		3 (4.2%)		1 (1.5%)	
Housewife		9 (12.5%)		10 (15.4%)	
Unemployed		4 (5.6%)		1 (1.5%)	
Other		1 (1.4%)		1 (1.5%)	
Education					.366
Secondary school		31 (43.1%)		33 (50.8%)	
Tertiary or above		41 (56.9%)		32 (49.2%)	
Marital status					.738
Single		21 (29.2%)		23 (35.4%)	
Married/cohabiting		46 (63.9%)		38 (58.5%)	
Divorced/separated/widowed		5 (6.9%)		4 (6.2%)	
Have religion					.334
Yes		21 (29.2%)		24 (36.9%)	
Monthly income					.824
<10,000		11 (15.3%)		6 (9.2%)	
10,000–19,999		20 (27.8%)		18 (27.7%)	
20,000–29,999		9 (12.5%)		8 (12.3%)	
≥30,000		9 (12.5%)		10 (15.4%)	
No income/not available		10 (13.9%)		7 (10.8%)	
Not want to answer		13 (18.1%)		16 (24.6%)	
Lifestyles					
Do exercise regularly		19 (26.4%)		17 (26.2%)	.975
Smoking		6 (8.3%)		2 (3.1%)	.190
Alcohol drinking		31 (43.1%)		22 (33.8%)	.269
Sleep time (hours)	5.0 (1.8)		4.7 (2.2)		.434
Average number of reported fatigue symptoms	6.3 (1.4)		6.3 (1.4)		.864

*Chi-squared test for categorical variable and t-test for continuous variable.

findings coincided with the results reported in other studies that Qigong exercise might have a beneficial effect on depressive symptoms in depressed elderly with chronic illness [24, 25], mild essential hypertension [34], subhealth [35], and female college students [36].

In this study, participants' anxiety symptoms were significantly improved in both groups compared with baseline values, but there was no significant difference in the change of anxiety symptoms between the intervention group and the control group. To date, only a very few studies [34–37] have examined the effect of Qigong exercise on anxiety symptoms but the findings were inconsistent, probably due to diversity of participants or sample size, variability in the severity of comorbidities or anxiety symptoms, and heterogeneity in outcome measures. Our results supported the conclusive statement of a recent systematic review that the limited existing evidence did not support the effect of Qigong exercise on anxiety symptoms [26]. Further well-designed RCTs were still warranted to test the effect of Qigong on anxiety disorders.

Interestingly, we found that the total fatigue, physical fatigue, mental fatigue, and anxiety symptoms in the waitlist control group were also significantly improved four months after. These results may be explained by two schools of mechanism. The first one may be that the results were due to the effects of self-care or other self-applied treatments. Generally, efforts to manage their symptoms are always under way for patients with chronic illnesses. In our study, most participants reported that they had tried other numerous therapies to manage their symptoms or treat their illnesses before joining this study, even though those therapies were ineffective. The second possible reason may be related to a beneficial effect of hope on physical health and psychological or emotional wellbeing [38]. In our study, all participants in the control group were told that they could join the Qigong training after completing the study, so they might have

Table 2: Within-group and between-group comparisons for Chalder Fatigue Scale, anxiety, and depression at T0 and T1 ($n = 137$) using repeated measures ANOVA.

	Within-group effects				Between-group effects		
	Baseline (T0) [a]	Post-intervention (T1)[b]			T1-T0	Time × group	
	Mean (SD)	Mean (SD)	P^b	Effect Size (d)	Mean (SD)	$F(1, 135)$	P
Total fatigue score						13.888	.000
Intervention group ($n = 72$)	39.7 (6.6)	26.6 (13.6)	<0.001	−1.2	−13.1 (11.7)		
Control group ($n = 65$)	39.8 (6.3)	33.2 (9.6)	<0.001	−0.8	−6.6 (8.3)		
Physical fatigue score						20.852	.000
Intervention group ($n = 72$)	24.7 (4.0)	15.9 (8.0)	<0.001	−1.4	−8.8 (7.3)		
Control group ($n = 65$)	24.6 (3.7)	20.8 (5.7)	<0.001	−0.8	−3.8 (5.0)		
Mental fatigue score						3.902	.050
Intervention group ($n = 72$)	15.0 (3.8)	10.6 (6.1)	<0.001	−0.9	−4.3 (5.3)		
Control group ($n = 65$)	15.2 (3.9)	12.4 (4.9)	<0.001	−0.6	−2.7 (3.9)		
Anxiety score						0.302	.584
Intervention group ($n = 72$)	11.0 (2.1)	8.7 (3.2)	<0.001	−1.1	−2.3 (3.9)		
Control group ($n = 65$)	10.9 (2.4)	9.0 (4.0)	0.006	−0.6	−1.9 (5.4)		
Depression score						9.918	.002
Intervention group ($n = 72$)	9.1 (2.0)	7.7 (3.2)	<0.001	−0.5	−1.3 (2.7)		
Control group ($n = 65$)	9.4 (2.2)	9.8 (4.1)	0.365	0.1	0.4 (3.7)		

[a]Compared with control group using independent t-test, [b]Compared with baseline using pairwise t-test.

a desirable expectation that might exert a beneficial effect on their psychological wellbeing and physical symptoms. Previous studies have shown that hope is inversely associated with total fatigue, mental fatigue and level of anxiety and depression [39–41].

Our study also showed a significant correlation between alleviation of depression and fatigue reduction, as well as reduced anxiety following Qigong exercise. Regression analyses further revealed that the improvements of fatigue and anxiety symptoms significantly predicted the alleviation of depressive symptoms after Qigong intervention. The results confirmed an established association between fatigue symptoms and psychiatric disorders [8, 9, 11].

Qigong as a mind-body integrative exercise is distinguished from conventional forms of exercise [42]. The underlying physiological mechanism of mind-body intervention may be of interest. Tsang and Fung [43] have hypothesized three possible neurobiological pathways of the antidepressive effect of Qigong exercise including monoamine neurotransmitters in the brain, the hypothalamic-pituitary-adrenal (HPA) axis, and the brain-derived neurotropic factors (BDNF), but these hypotheses need to be further tested.

Although the results of our study are promising, some limitations of this study should be noted. First, the participants with CFS-like illness were recruited from local community, who did not receive medical examinations conducted by clinicians. Thus, some of them may not fully meet the CDC criteria for CFS. Although around three-quarters of the participants were female, it is similar to the proportion of females with CFS in other earlier studies [16]. Second, this study was a waitlist controlled trial, so social interaction effects might have been existed in the intervention group. It is recommended that active controls should be applied in future studies to avoid possible placebo effect. Third, the dosage and quality of home-based Qigong exercise were not adjusted for in our data analysis. Given that some studies have suggested a relationship between amount of Qigong practice and health outcomes [44], it should be measured and taken into account in data analysis in future studies. Finally, some other factors such as diet, physical activities, social interaction, body weight, and comorbidities may affect the outcomes, which should be adjusted in further trials. Despite these limitations, this study was the first RCT to examine the effect of Qigong exercise on anxiety and depressive symptoms among patients with CFS-like illness, which may provide complementary evidence to the body of knowledge in this field.

5. Conclusion

In conclusion, the results of this study show that Qigong exercise may be effective in reducing fatigue symptoms and alleviating depressive symptoms for patients with CFS-like illness and that the improvement of fatigue symptoms may predict the alleviation of depressive symptoms after Qigong intervention. The findings suggest that Qigong exercise may be used as an alternative and complementary therapy or rehabilitation program for patients with CFS-like illness.

Appendix

Description of the Movements in Wu Xing Ping Heng Gong

Warm-up Movement. Swinging of arms by turning the torso with relaxed shoulders (preferably to be practiced in a relaxing outdoor space with trees).

Movement 1. Standing on toes with hand movements to the front and to the side.
Movement 2. Circular movements of hands, wrists, hips; stretching by arching backwards of neck and torso.
Movement 3. Movement of fingers, wrists, elbow and shoulders; stretching of arms.
Movement 4. Movement of wrists; stretching shoulder muscles; twisting movements of shoulders.
Movement 5. Massage of ears.
Movement 6. Swinging of hands to gently hit the chest and back; standing on one foot and hitting back of the standing foot's calf by the dorsum of other foot.
Movement 7. Stretching of trunk and hip joints by stepping forward and backward.
Movement 8. Swinging movements of lower body; squatting and bending forward to stretch the back of the torso.
Movement 9. Movement of legs with hands in cupping pose; turning of torso in kneeling position.
Sitting meditation. Sitting meditation with deep breathing can be conducted for 20–30 minutes after the movement exercises if possible. If not, move directly to the concluding movement. Sitting meditation is recommended in the evening, before going to bed.
Concluding movement. Hands in cupping pose in front of the lower abdomen for about 20 seconds; rub hands and then use palms to massage face (upward movement like washing face), followed by the use of fingertips to massage the scalp in combing movement.

Conflict of Interests

The authors declare that they have no conflict of interests.

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