



A Prospective, Single-arm, Interventional Study to Evaluate the Effects of Kriya Yoga and 6-step Nirmal Dhyana on Neurocardiac Physiology and Quality of Life

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Abstract—Kriya Yoga involves sequential breathing practices followed by meditation. Few studies have systematically studied the short- and long-term physiological effects of Kriya Yoga on respiratory and cardiovascular systems. A prospective, single-arm study was conducted in 53 adult healthy participants to evaluate potential effects of Kriya Yoga (49 Healing Breaths Nirmal Kriya followed by 6-step Nirmal Dhyana) for 48 days on neurocardiac outcomes. Primary objective was to evaluate change in coherence of heart rate variability (HRV) in participants pre- and postintervention. Secondary objectives included evaluation of short- and long-term effects of the intervention on coherence, low frequency to high frequency ratio, and mid-frequency peak of HRV and on cortical function (cingulate, pre-frontal and insular areas) using standardized low resolution brain electromagnetic tomography. Also, the long-term effect of the intervention on quality of life (QoL) using World Health Organization Quality of Life-Brief version (WHO QOL-BREF) scores and on anxiety and depression using Hospital Anxiety and Depression Scale (HADS). There was no statistically significant short-term or long-term effect of the intervention on HRV in the 53 participants. In 32 participants, statistically significant reduction was seen for the theta band frequency at Broadman area 23 (cingulate gyrus, limbic area) on Day 48 preintervention compared with Day 1 preintervention ($p=0.046$) and on Day 48 60-minutes postintervention as compared with Day 1 60-minutes postintervention ($p=0.026$). Mean anxiety score and depression score of HADS significantly declined on Day 48 from Day 1. WHO QOL-BREF scores for all domains, except social relationship, had

increased significantly over 48 days. No intervention-related adverse event was reported. Forty-nine Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyana has the potential to improve cortical function as well anxiety and depression symptoms and QoL in the general population.

Index Terms—6-Step Nirmal Dhyana, 49 Healing Breaths Nirmal Kriya, electroencephalogram, Kriya Yoga, heart rate variability, meditation, sLORETA

INTRODUCTION

In lieu of the role of breathing in our life, significant research has been carried out to understand the respiratory and cardiovascular systems and their physiology, pathophysiology, and the effect of relevant interventions [1,2,3]. Though a major contribution from a physical perspective, most of these are observational studies or studies that have focused on applications of breathing practices and breathing control; they have seldom attempted to understand the subtler aspects of breath and its impact on the body and mind [4,5,6,7].

Evidence suggests that yogic practices like Iyengar Yoga [8], Pranayama [9,10], Sudarshan Kriya [11,12], Transcendental meditation® [13,14] are beneficial in relieving psychological disorders like depression, stress, and melancholia [8,10,11], and are also useful in improving respiratory and cardiovascular functioning [9,13]. Kriya Yoga



is a type of yoga that involves a sequence of precisely designed breaths followed by meditation for maintaining harmony in the body-mind system. Despite its potential benefits and widespread popularity, only few studies [15,16] have systematically evaluated and documented its short-term and long-term physiological effects. A single, 2-hour session of Kriya Yoga has been shown to considerably increase the alpha and theta activity on EEG in most regions of the brain indicating that the brain is deeply relaxed and focused following Kriya Yoga [15]. Three-month yoga and meditation has also shown beneficial effects on cardiovascular risk factors including body-mass index, total serum and low-density lipoprotein cholesterol, fibrinogen, and blood pressure [16]. Understanding neurocardiac effects and defining functional brain activity change after Kriya Yoga practice in Kriya Yoga-naïve individuals can be an initial step towards understanding its effects on the body-mind continuum.

The study was undertaken with the hypothesis that Kriya Yoga may decrease the resting heart-rate variability (HRV) when practiced regularly for 48 days. Accordingly, we conducted a prospective, single-arm study to evaluate the short- and long-term effects of Kriya Yoga (49 Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyān) on neurocardiac physiology. The primary objective of this study was to evaluate change in coherence of HRV in participants before and after practicing the intervention. The secondary objectives of the study were to evaluate short- and long-term effects of the intervention on coherence, low frequency to high frequency (LFHF) ratio, and mid-frequency peak (MFP) of HRV and on cortical function (cingulate, prefrontal and insular areas). Additionally, we also evaluated the long-term effect of the intervention on quality of life (QoL) and on depression and anxiety scores. Safety of the intervention was evaluated by noting all the adverse events (AEs) during the study period.

METHODOLOGY

A. Ethics

All study-related procedures began after obtaining ethics approval from the Clinical Ethics Forum, India (CEF/12-13/029).

B. Study Design

This was a prospective, single-arm, interventional study conducted at the TAO Anand Spiritual Center and International Institute of Sleep Sciences (IISS), Mumbai, India.

C. Study Population

Healthy men and women, 18 to 60 years of age, not practicing meditation or yoga since at least 1 month were screened for eligibility to participate in the study. To facilitate logistics and investigations, healthy volunteers residing in Maharashtra, India who could communicate in English and/or Hindi languages were screened. All volunteers were required to sign the informed consent form before any study-related

procedure was performed. Women who were pregnant or unwilling to use an acceptable method of contraception during the study period and men and women with cardiac pacemakers or history of cardiac disorders, respiratory disorders, seizures, vertigo, bipolar disorder, moderate to severe untreated depression (score of ≥ 11 for anxiety or depression when measured with Hospital Anxiety And Depression Scale [HADS]), as well as those currently receiving antipsychotic/antidepressant drugs or drugs that could influence cardiac rhythm (e.g. β -blockers) and those suffering from sleep-related disorders were not allowed to participate in the study. All participants could continue with their routine physical exercises provided they followed the same exercise schedule and exercise intensity throughout the study period.

D. Intervention

The participants were trained and were expected to follow the study intervention once a day in the morning for 48 days. The details of the conduct of training of participants for the study intervention are provided in section on Study Implementation. The Kriya Yoga intervention included:

1) 49 Healing Breaths Nirmal Kriya [9,17,18]

a) Anuloma Viloma (Nadishuddhi) Pranayama

This breathing practice involved 21 cycles of breathing where each cycle consisted of inhalation through left nostril and exhalation through right nostril followed by inhalation through right nostril and exhalation through left nostril. The inhalation and exhalation ratio was to be kept 3:2 during the breathing practice.

b) 49 Healing Breaths Nirmal Kriya

This breathing practice involved 7 continuous cycles of rhythmic breathing. Each cycle had 7 breaths in all. The initial 4 breaths were short breaths followed by 1 medium breath and finally 2 long breaths. The inhalation and exhalation ratio was to be kept 3:2 during the breathing practice.

2) 6-steps Nirmal Dhyān (meditation)

The 6 steps of Nirmal Dhyān were to be practiced sequentially, each for a period of 5 minutes, except Steps 5 and 6, which could be practiced for up to 10 minutes.

Step 1: Breath awareness

Participants were asked to close their eyes and observe their natural inhalation and exhalation process without any alteration in the breathing pattern and be aware of the process of breathing.

Step 2: Body awareness

Participants were asked to observe their body sensations in tandem with the breath awareness. They were asked to be aware of their heart beat, experience the sensations on their skin and in different body parts.

Step 3: Thought awareness

While being aware of the breath and body, participants were then asked to observe their thoughts. They were asked to witness the thoughts without analysing or getting involved in the thoughts.



Step 4: Refreshing awareness

Participants were then asked to continuously be aware of each breath throughout the inhalation and exhalation process and maintain unbroken continuous awareness.

Step 5: Gap awareness

For each breath, participants were asked to observe the gap between the end of inhalation and before the beginning of exhalation and the gap between the end of exhalation and before the beginning of next inhalation. Next they were instructed to observe the gap between two thoughts.

Step 6: Expanding awareness

Participants were requested to attain to and be aware of all the sounds simultaneously. While maintaining the awareness of sounds within the body they were also expected to remain simultaneously aware of all far-off sounds to expand their awareness.

E. Study implementation

Potential volunteers were invited to participate in the study using advertisements in electronic and social media. Eligible participants were oriented and received intervention-training in a group session at TAO Anand Spiritual Center, Thane, India. A simple 10-item questionnaire was used to evaluate whether the participants were appropriately trained and that they were clear and confident to implement the intervention for 48 days. The study assessments were carried out at IISS, Mumbai, India. Neurocardiac responses were evaluated using HRV (coherence, LFHF ratio, and MFP). Cortical function was evaluated using standardized low resolution electromagnetic tomography (sLORETA) and calibrated Quantitative Electroencephalography (EEG) devices. Neurocardiac responses were measured preintervention, immediately postintervention and 60 minutes postintervention on Day 1 and Day 48 of the study. Quality of life and psychological (depression and anxiety) outcomes were measured using the World Health Organization Quality of Life-Brief version (WHO QoL-BREF) and HADS, respectively at the start of the intervention on Day 1 and postintervention on Day 48 of the study. All participants were asked to maintain a diary record of their regular practice. This served as a method to check compliance to the intervention. They were also asked to maintain a diary record of their experiences and AEs.

F. Endpoints

The primary endpoint of the study was to evaluate the effect of the intervention on coherence of HRV in participants before practicing the intervention on Day 1 and 60 minutes after practicing the intervention on Day 48 of the study.

The secondary endpoints of the study were:

to evaluate short- and long-term effects of the intervention on coherence, LFHF ratio, and MFP of HRV on Day 1 and Day 48;

to evaluate short- and long-term effects of the intervention on cortical function (cingulate, prefrontal and insular areas) from the start of the intervention on Day 1 to

start of the intervention on Day 48 and from 60 minutes after the intervention on Day 1 to 60 minutes after the intervention on Day 48.

Other endpoints included:

Evaluation of long-term effect of the intervention on QoL using the WHO QoL-BREF;

Evaluation of long-term effect of the intervention on depression and anxiety scores using the HADS.

Evaluation of safety of the intervention by noting all the AEs during the study period.

G. Assessments

1) Heart rate variability

Heart rate variability (coherence, LFHF ratio, and MFP) is a measure of the beat-to-beat changes in heart rate. The normal variability in heart rate is due to the synergistic action of the sympathetic and parasympathetic nervous systems, both of which together constitute the autonomous nervous system (ANS). Many factors affect the activity of the ANS and therefore, influence HRV. These include the breathing patterns, physical exercise, and even the thoughts [19,20,21]. Heart rate variability was used for evaluation of neurocardiac responses.

2) Standardized low resolution brain electromagnetic tomography

As opposed to EEG activity, which represents the 'volume conducted' activity from multiple spatially dispersed sources of the brain, sLORETA spatially represents the local effects of the brain sources responsible for the recorded scalp potentials, thereby providing differential topographic patterns of cortical activations that can be used to potentially correlate or serve as biomarkers for a particular neural disorder. Thus, it was our method of choice as it broadly demonstrates zero error under ideal conditions. However, the drawback of the method is that it has a very low spatial resolution which decreases with depth and if fed noisy measurements it gives noisy images. [22,23,24,25,26].

Discovery™ amplifier from BrainMaster Technologies INC, USA was used for acquisition of 24-lead EEG. All data was manually inspected for artefact rejection.

3) Subject-reported outcomes

a) WHO QoL-BREF

The WHO QoL-BREF is a 26-item, self-administered, cross-culturally validated questionnaire in which items are rated on a 5-point scale [27]. The 26 items measure the following broad domains: physical health, psychological health, social relationships, and environment. We used the English [28] and Hindi [29] versions of the scale in our study.

b) HADS

The HADS is a 14-item cross-culturally validated scale with 7 items each in 2 subscales for evaluation of symptoms of anxiety (HADS-A) and depression (HADS-D) [30,31,32,33]. It detects symptoms of anxiety and depression, rather than making a diagnosis of the syndrome and excludes symptoms that may arise from physical illness, insomnia, or fatigue. Each



item is scored (0 to 3) according to severity, with a maximum possible score of 21 for each subscale. A score of 0 to 7 indicates no anxiety or depression, a score of 8 to 10 indicates a borderline case, and a score of ≥ 11 indicates presence of anxiety and/or depression. We used the English [33] and Hindi versions of the scale in our study.

H. Statistical methodology

The sample size of the study was determined to estimate the mean change in coherence of HRV at the end of 48 days of intervention with desired precision. Thus, the study was conducted with 53 participants to achieve the two-sided 95% confidence interval (CI) of width of ± 10.0 assuming standard deviation (SD) of the change in coherence of HRV as 35, and a drop-out rate of 10.0%. The assumptions were based on a feasibility pilot study conducted in the same population.

All analyses were performed on the intent-to-treat (ITT) population, defined as all participants who were trained for the intervention satisfactorily and provided Day 48 visit assessments. All outcomes (except EEG analysis) were evaluated using mean change, with corresponding 95% CI, at postbaseline visit from the baseline visit using the paired t-test. The 24-lead EEG analysis was done per frequency bands suggested by sLORETA/eLORETA software package- delta band: 0.5 to 3.5 Hertz (Hz); theta band: 4 to 7 Hz; alpha band: 8 to 12 Hz; beta-1 band: 12 to 18 Hz; beta-2 band: 19 to 30 Hz; and beta-3 band: 30 to 45 Hz. The methodology used was nonparametric. It was based on estimating, via randomization, the empirical probability distribution for the max-statistic (e.g. the maximum of a t- or an F-statistic), under the null hypothesis. This methodology corrected for multiple testing i.e. for the collection of tests performed for all electrodes and discrete frequencies. Due to the nonparametric nature of the method, its validity did not rely on any assumption of Gaussianity [34].

RESULTS

The study enrolled 53 participants. All participants completed at least 33 days of the study intervention and assessment data were available for both Day 1 and Day 48 study visits. Data from all participants was included in the analysis. The majority of participants were men (57.0%) and the mean age was 39 years. Thirty-six participants (68.0%) were married. All were non-smokers. Demographic characteristics of the participants are summarized in Table 1.

The changes in accumulated coherence, LFHF ratio, and MFP over time for the ITT populations are summarized in Table 2. The mean accumulated coherence of HRV postintervention on Day 48 had decreased by 6.7 points (95% CI: -20.9 to 7.4) from preintervention on same day. However, the preintervention mean on Day 48 had increased by 7.7 points from that on Day 1 (95% CI: -7.1 to 22.4). The mean LFHF ratio and MFP had increased by 0.3 (95% CI: -2.9 to 6.8) and 4.0 (95% CI: -41.8 to 49.8), respectively postintervention on Day 48 from that of preintervention on

same day. Similar results were observed for the long-term effects.

TABLE 1: DEMOGRAPHIC AND BASELINE CHARACTERISTICS- ITT POPULATION

Characteristics	
Male, n (%)	30 (56.6)
Age (years), mean (SD)	38.5 (10.5)
Married, n (%)	36 (67.9)
Smoker, n (%)	0.0
Body mass index (kg/m ²), mean (SD)	24.9 (4.4)
Systolic blood pressure (mm Hg), mean (SD)	120.9 (15.6)
Diastolic blood pressure (mm Hg), mean (SD)	79.9 (11.0)
ITT=intention-to-treat; n=number of subjects; SD=standard deviation	

sLORETA analysis was performed on a total of 32 subjects; the postbaseline data from 19 subjects had to be excluded from analysis due to presence of artefacts in EEG data from 1 or more sessions. Baseline EEG data and demographic data of subjects included and excluded in the sLORETA analysis were similar.

In the 32 subjects included in the analysis, statistically significant reduction in theta band activity was observed at preintervention Day 48 as compared to that on preintervention Day 1 ($p=0.046$). Exceedance proportion test with intensity value of -0.98 showed that change was seen at Broadman Area 23 (cingulate gyrus, limbic area) (Figure 1). Similarly, statistically significant reduction was found in theta activity at Broadman area 23 ($p=0.026$) at 60 minutes postintervention on Day 48 as compared to 60 minutes postintervention on Day 1. The results of the exceedance proportion tests can be made available separately for review.

Table 3 summarizes the results for change in HADS and WHO QoL-BREF from Day 1 to Day 48 for the ITT population. Results from the evaluation of HADS ($n=46$) on Day 1 preintervention and 60 minutes postintervention on Day 48 showed statistically significant reduction in anxiety score (mean difference= -1.5 [95% CI: -2.3 to -0.7]) and depression score (mean difference= -1.2 [95% CI: -1.9 to -0.5]). The WHO QoL-BREF scores showed improvement in physical health (mean difference= 4.1 [95% CI: 0.4 to 7.7]), psychological (mean difference= 6.4 [95% CI: 2.6 to 10.2]), social relationship (mean difference= 3.0 [95% CI: -0.2 to 6.1]), and environment (mean difference= 4.0 [95% CI: 1.5 to 6.5]) domains.

Three AEs were reported in the study: glossitis, rhinitis, and diarrhea (3-4 episodes) in 1 participant, each. None of the AEs were related to the study intervention.



TABLE 2: HEART-RATE VARIABILITY AT DAY 1 AND DAY 48

Statistic	Day 1 (n=53)			Day 48 (n=53)		
	Pre-intervention	Immediate post-intervention	60 minutes post-intervention	Pre-intervention	Immediate post-intervention	60 minutes post-intervention
<i>Accumulated coherence</i>						
Mean (SD)	38.4 (32.5)	30.8 (27.9)	40.4 (36.9)	46.1 (52.6)	50.3 (41.8)	39.3 (37.4)
Mean change from Day 1 (pre-intervention) (95% CI)	-	-7.6 (-15.5, 0.4)	2.0 (-8.9, 12.9)	7.7 (-7.1, 22.4)	-	-
Mean change from Day 48 (pre-intervention) (95% CI)	-	-	-	-	4.2 (-10.2, 18.6)	-6.7 (-20.9, 7.4)
<i>Ratio between low frequency and high frequency band powers</i>						
Mean (SD)	5.0 (4.3)	7.0 (8.7)	7.0 (8.7)	6.8 (10.4)	5.3 (4.7)	8.8 (14.9)
Mean change from Day 1 (pre-intervention) (95% CI)	-	2.0 (-0.3, 4.3)	2.0 (0.3, 3.7)	1.8 (-1.1, 4.8)	-	-
Mean change from Day 48 (pre-intervention) (95% CI)	-	-	-	-	-1.5 (-4.2, 1.1)	0.3 (-2.9, 6.8)
<i>Mid frequency power</i>						
Mean (SD)	121.5 (108.4)	135.6 (108.4)	158.5 (156.1)	137.0 (133.4)	147.9 (156.9)	141.0 (134.8)
Mean change from Day 1 (pre-intervention) (95% CI)	-	14.1 (-16.8, 45.1)	37.0 (-2.0, 76.0)	15.5 (-22.3, 53.3)	-	-
Mean change from Day 48 (pre-intervention) (95% CI)	-	-	-	-	-10.9 (-34.6, 56.4)	4.0 (-41.8, 49.8)

CI=confidence interval; ITT=intention-to-treat; n=number of participants included for analysis; SD=standard deviation

(a)

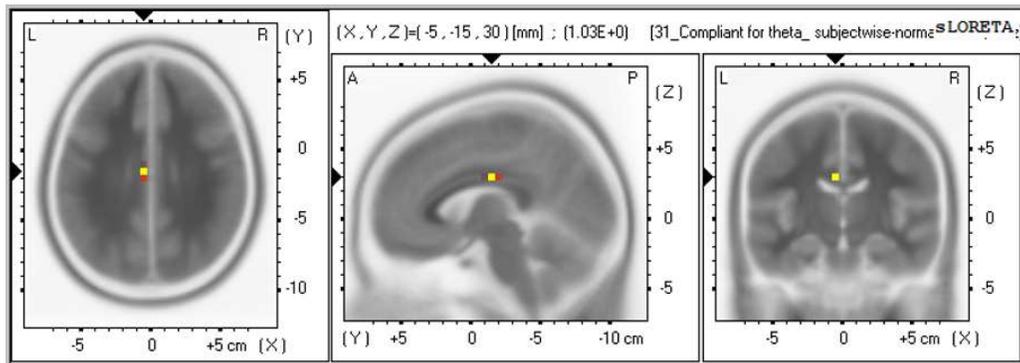


FIGURE 1: SLORETA IMAGING

(a) Source density localization is a method to quantify the electrical activity that produces the EEG waves of particular frequency. Thus, reduction in the electrical activity between pre-and postintervention (over the study duration of 48 days) is shown in “yellow colour”. Only Brodmann area 23 (posterior cingulate gyrus) shows statistically significant reduction in electrical activity that cause theta band (4 hz to 7 hz) production.



DISCUSSION

This was a prospective, single-arm study to evaluate the short- and long-term effects of Kriya Yoga (49 Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyana) on neurocardiac physiology.

The study found no significant short-term or long-term impact of the intervention for 48 days on neurocardiac responses in terms of accumulated coherence, LFHF ratio and MFP of HRV. Heart-rate variability could be affected by many variables including circadian rhythms, sleep duration and sleep quality, stress-inducing factors, intake of caffeine or any other stimulants. This was a pilot study where the intervention was not supported by consistent lifestyle modifications or changes in physical activity, and therefore, may not have affected the HRV over 48 days of practice.

Standardized LORETA analysis showed a significant reduction in current density for theta frequency at Broadman Area 23 (posterior cingulate gyrus). This is a first study to show reduction in theta activity in a specific area (Broadman area 23). Majority of the studies have focused on other frequency bands, including alpha- and gamma-bands. Awareness is a part of consciousness which itself is an emergent property of neural networks in cerebral cortex. Vegetative state (VS) is defined as a disorder of consciousness in which awareness is completely abolished. In VS, Broadman Area 23 (posterior cingulate cortex) is shown to have lesser connection with prefrontal areas and persistent theta (low frequency) activity over the scalp region [35]. This will imply that current density source for theta frequency will show increased intensity in VS. On the contrary, after the intervention, Broadman Area 23 showed significant decrease in current density generation for theta activity, suggesting activation of that area. Broadman Area 23 is associated with “self-awareness” as well as judgement and memory. This implies greater awareness about the self and greater retrieval of self-relevant information.

Besides awareness, posterior cingulate gyrus is also involved in episodic as well as self-referential memory [36]. Additionally, it is also involved in the evaluation of retrieved information (e.g. evaluation of personal-relevance, meaning, accuracy of information) [37]. This is consistent with empirical evidence suggesting that the degree of posterior cingulate gyrus activation during retrieval is directly related to depth of processing at encoding [38] as well as a subjective sense of detailed, conscious reexperiencing of items during retrieval [39]. Patients with mild cognitive impairment show attenuated posterior cingulate gyrus activation during both episodic recognition and self-appraisal tasks [37]. Activation of posterior cingulate gyrus due to Kriya Yoga practice may have benefit in thwarting Alzheimer’s disease progression which is shown to affect this region at the early stages leading to mild cognitive impairment.

Feeling of happiness is shown to be associated with activation of posterior cingulate gyrus [40]. Our study showed significant improvement in WHO QoL-BREF as well as HADS reflecting increase in sense of wellbeing. These findings suggest that the changes observed in posterior cingulate gyrus might be the neurobiological correlate of subjective happiness.

The subjects showed statistically significant decline in the depression score and anxiety score according to HADS at the end of the study compared to the baseline. Reductions in the anxiety and depression scores were about 0.5 times their baseline SDs. This is equivalent to a medium effect size as per Cohen’s suggestion [41] and could be clinically meaningful. The baseline values of the scores were consistent with the normative values reported elsewhere in literature [42, 43]. Quite a few studies have been carried out investigating the effect of yoga exercises and/or meditation on anxiety and depression in normal subjects as well as patients affected with clinical depression. A study carried out by Kjelgren (2007) investigating Sudarshan Kriya and related practices in healthy volunteers reported a decrease of 1.73 units in anxiety scores and 1.38 units in depression scores after 6 weeks of intervention when calculated using HADS [44]. Another study carried out in breast cancer outpatients undergoing adjuvant radiotherapy showed that 6 weeks of yoga intervention involving breathing and postural exercises and meditation decreased HADS anxiety scores by 3.17 and depression scores by 3.43 [45]. Another study investigating effect of a 20-week contemplative self-healing program in breast and gynaecologic cancer survivors showed no significant change in HADS anxiety score and only 0.1 decrease in depression scores [46].

Similar to the HADS, the WHO QoL-BREF scores also showed statistically significant improvement in the majority of domains at the end of study compared to the baseline. The improvement was of small-to-medium effect size (0.2 to 0.5 SD) in each of the domains [41]. The benefits of various yoga techniques for improving the QoL in patients with various diseases like hypertension [47], back pain [48], and epilepsy [49] have already been demonstrated in literature. While the current study results show a similar trend, it is noteworthy that the increased values were reported in normal, healthy volunteers with values similar to those reported in literature [50]. This highlights the capacity of 49 Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyana to induce positive changes in QoL in healthy, normal subjects, making it not just a tool for helping patients but also as an overall instrument for improving the QoL.

CONCLUSION

The intervention- 49 Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyana- showed positive effects on cortical function and on symptoms of anxiety and depression, as well as QoL. However, it did not appear to have a meaningful



effect on HRV. This might be due to the sensitive and variable nature of HRV itself. Changes were observed in cortical functions especially reduced theta band activity at Broadman area 23 (posterior cingulate cortex). This suggests a potential of the intervention to change cortical function and bring about neuroplastic changes that can lead to greater awareness about the self and greater retrieval of self-relevant information. The positive findings in neurophysiological as well as subjective criteria suggest that this intervention can be used as an instrument to improve QoL in healthy subjects. Further investigations may be needed to assess potential applications of 49 Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyana in clinical settings for psychological disorders. Also the prominent differences between endpoint values for HRV in compliant subjects suggest that the intervention has potential to show observable physiological changes in individuals showing compliance and regular practice. Future studies ensuring adequate compliance and assessing more robust endpoints will allow unambiguous measurements. Here we would like to position 49 Healing Breaths Nirmal Kriya and 6-step Nirmal Dhyana practice as a noninvasive tool capable of enhancing and modulating cognition by causing neuroplastic changes at a specific area (Broadman Area 23) with correlated subjective improvement in QoL.

TABLE 3: SUMMARY OF HADS AND WHO QoL-BREF AT DAY 1 PREINTERVENTION AND DAY 48 60-MINUTES POSTINTERVENTION

Participant-reported outcomes		Day 1 pre-intervention (n=53)	Day 48 60-minutes post-intervention (n=53)
HADS			
Anxiety score	Mean (SD)	4.3 (3.0)	2.8 (2.6)
	Mean difference (95% CI)	-1.5 (-2.3, -0.7)	
Depression score	Mean (SD)	2.3 (2.6)	1.1 (1.5)
	Mean difference (95% CI)	-1.2 (-1.9, -0.5)	
WHO QoL-BREF			
Physical health	Mean (SD)	77.0 (14.5)	81.1 (12.6)
	Mean difference (95% CI)	4.1 (0.4, 7.7)	
Psychological	Mean (SD)	69.6 (14.3)	75.9 (11.1)
	Mean difference (95% CI)	6.4 (2.6, 10.2)	
Social relationship	Mean (SD)	63.9 (19.2)	66.9 (19.8)
	Mean difference (95% CI)	3.0 (-0.2, 6.1)	
Environment	Mean (SD)	74.6 (12.8)	78.6 (11.8)
	Mean difference (95% CI)	4.0 (1.5, 6.5)	
CI=confidence interval; HADS=hospital anxiety and depression scale; ITT=intention-to-treat; n=number of participants analyzed; QoL BREF=quality of life, brief version; SD=standard deviation; WHO=World Health Organization			

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REFERENCES

1. Krogh M. The diffusion of gases through the lungs of man. *J Physiol.* 1915;49(4): 271–300.
2. Barnes PJ. The third nervous system in the lung: physiology and clinical perspectives. *Thorax* 1984;39(8):561–7.
3. Nadel JA, Barnes PJ. Autonomic regulation of the airways. *Annu Rev Med.* 1984;35(1):451–67.
4. Vermeire P, Butler J. Effect of respiration on pulmonary capillary blood flow in man. *Cir Res.* 1968;22(2):299–308.
5. Laude D, Goldman M, Escourrou P, Elghozi, JL. Effect of breathing pattern on blood pressure and heart rate oscillations in humans. *Clin Exp Pharmacol Physiol.* 1993;20(10):619–26.
6. Kunik ME, Roundy K, Veazey C, Soucek J, Richardson P, Wray NP, et al. Surprisingly high prevalence of anxiety and depression in chronic breathing disorders *Chest* 2005;127(4):1205–11.
7. van Dixhoorn J. Cardiorespiratory effects of breathing and relaxation instruction in myocardial infarction patients. *Biol Psycho.* 1998;49(1–2):123–35.
8. Shapiro D, Cook IA., Davydov DM, Ottaviani C, Leuchter AF, Abrams M. Yoga as a complementary treatment of depression: effects of traits and moods on treatment outcome. *Evid Based Complement Alternat Med.* 2007;4(4):493–502.
9. Telles S, Nagarathna R, Nagendra HR. Breathing through a particular nostril can alter metabolism and autonomic activities. *Indian Journal Physiol Pharmacol.* 1994 Apr;38(2): 133–7.
10. Bhimani NT, Kulkarni NB, Kowale A, Salvi S. Effect of pranayama on stress and cardiovascular autonomic tone & reactivity. *Nat J Integ Res Med.* 2011;2:48–54.
11. Janakiramaiah N, Gangadhar BN, Naga Venkatesha Murthy PJ, Harish MG, Subbakrishna DK, Vedamurthachar A. Antidepressant efficacy of Sudarshan Kriya Yoga (SKY) in melancholia: a randomized comparison with electroconvulsive therapy (ECT) and imipramine. *J Affect Disord.* 2000;57(1):255–9.
12. Kjellgren A, Bood SA, Axelsson K, Norlander T, Saatcioglu F. Wellness through a comprehensive yogic breathing program – a controlled pilot trial. *BMC Complement Altern Med.* 2007 Dec;7(1):43.
13. Barnes VA, Treiber FA, Davis H. Impact of Transcendental Meditation on cardiovascular function at rest and during acute stress in adolescents with high normal blood pressure. *J Psychosom Res.* 2001 Oct;51(4):597–605.



14. Paul-Labrador M, Polk D, Dwyer JH, Velasquez I, Nidich S, Rainforth M, et al. (2006). Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. *Arch Intern Med.* 2006 Jun 12;166(11):1218-24.
15. Hoffman, E. Mapping the brain's activity after Kriya Yoga. In. *Scandinavian Yoga and Meditation School. HAA International Retreat Center* 1998. <https://www.yogameditation.com/reading-room/mapping-the-brains-activity-after-kriya-yoga/>. Accessed 08 Jan 2017.
16. Schmidt T, Wijga A, Von Zur Mühlen A, Brabant G, Wagner TO. Changes in cardiovascular risk factors and hormones during a comprehensive residential three month kriya yoga training and vegetarian nutrition. *Acta Physiol Scand Suppl.* 1997;640:158-62.
17. Telles S, Nagarathna R, Nagendra HR. Physiological measures of right nostril breathing. *J Altern Complement Med.* 1996 Winter;2(4):479-84.
18. Naveen KV, Nagarathna R, Nagendra HR, Telles S. Yoga breathing through a particular nostril increases spatial memory scores without lateralized effects. *Psychol Rep.* 1997 Oct;81(2):555-61.
19. The Science Behind the emWave® and Inner Balance™ Technologies. Accessed 08 Jan 2017. <http://www.heartmath.com/personal-use/emwave-science-behind.html>
20. Stein PK, Bosner MS., Kleiger RE, Conger BM. Heart rate variability: a measure of cardiac autonomic tone. *American heart journal* 1994 May;127(5):1376–81.
21. McCraty R, Atkinson M, Tomasino D, Bradley RT. (2009). The coherent heart: heart-brain interactions, psychophysiological coherence, and the emergence of system-wide order. *Integral Review* 2009 Dec;5(2):10–115.
22. Pascual-Marqui RD. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. *Methods Find Exp Clin Pharmacol.* 2002;24 Suppl D:5-12.
23. Fuchs M, Kastner J, Wagner M, Hawes S, Ebersole JS. A standardized boundary element method volume conductor model. *Clin Neurophysiol.* 2002 May;113(5):702-12.
24. Jurcak V, Tsuzuki D, Dan I. 10/20, 10/10, and 10/5 systems revisited: their validity as relative head-surface-based positioning systems. *Neuroimage.* 2007 Feb 15;34(4):1600-11.
25. Sekihara K, Sahani M, Nagarajan SS. Localization bias and spatial resolution of adaptive and non-adaptive spatial filters for MEG source reconstruction. *Neuroimage.* 2005 May 1;25(4):1056-67.
26. Greenblatt RE, Ossadtchi A, Pflieger ME. Local linear estimators for the bioelectromagnetic inverse problem. *IEEE Transactions on Signal Processing* 2005;53(9):3403–12.
27. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. *Psychol Med.* 1998 May;28(3):551-8. <http://bib.irb.hr/mzos/prikazi-rad?rad=18150>
28. WHO Quality of Life-BREF (WHOQOL-BREF). *WHO.* Accessed 08 Jan 2017. http://www.who.int/substance_abuse/research_tools/who_qolbref/en/
29. Saxena S, Chandiramani K, Bhargava R. WHOQOL-Hindi: a questionnaire for assessing quality of life in health care settings in India. *World Health Organization Quality of Life. Natl Med J India.* 1998 Jul-Aug;11(4):160-5. <http://www.nmji.in/archives/Volume-11/issue-4/original-articles-1.pdf>
30. White D, Leach C, Sims R, Atkinson M, Cottrell D. Validation of the Hospital Anxiety and Depression Scale for use with adolescents. *Br J Psychiatry.* 1999 Nov;175:452-4.
31. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res.* 1997 Jan;42(1):17-41.
32. Snaith RP. The Hospital Anxiety And Depression Scale. *Health and Quality of Life Outcomes.* 2003;1:29.
33. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983 Jun;67(6):361-70.
34. Nichols TE, Holmes AP. Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Human Brain Mapping.* 2002 Jan;15 (1):1-25.
35. Laureys S, Goldman S, Phillips C, Van Bogaert P, Aerts J, Luxen A, Franck G, Maquet P. Impaired effective cortical connectivity in vegetative state: preliminary investigation using PET. *Neuroimage.* 1999 Apr;9(4):377-82.
36. Maddock RJ, Garrett AS, Buonocore MH. Remembering familiar people: the posterior cingulate cortex and autobiographical memory retrieval. *Neuroscience.* 2001;104(3):667-76.
37. Ries ML, Schmitz TW, Kawahara-Baccus TN, Torgerson BM, Trivedi MA, Johnson SC. Task-dependent posterior cingulate activation in mild cognitive impairment. *NeuroImage.* 2006;29(2):485-492.
38. Shannon BJ, Buckner RL. Functional-anatomic correlates of memory retrieval that suggest nontraditional processing roles for multiple distinct regions within posterior parietal cortex. *J Neurosci.* 2004 Nov 10;24(45):10084-92.
39. Wheeler ME, Buckner RL. Functional-anatomic correlates of remembering and knowing. *Neuroimage.* 2004 Apr;21(4):1337-49.
40. Damasio AR, Grabowski TJ, Bechara A, Damasio H, Ponto LL, Parvizi J, Hichwa RD. Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nat Neurosci.* 2000 Oct;3(10):1049-56.
41. Cohen J. *Statistical Power Analysis for the Behavioral Sciences.* 2nd ed. New Jersey: Lawrence Erlbaum Associates;1988.
42. Crawford JR, Henry JD, Crombie C, Taylor EP. Normative data for the HADS from a large non-clinical sample. *Br J Clin Psychol.* 2001 Nov;40(Pt 4):429-34.
43. Hinz A, Brähler E. Normative values for the hospital anxiety and depression scale (HADS) in the general German population. *J Psychosom Res.* 2011 Aug;71(2):74-8.
44. Kjellgren A, Bood SA, Axelsson K, Norlander T, Saatcioglu F. Wellness through a comprehensive yogic breathing program - a controlled pilot trial. *BMC Complement Altern Med.* 2007 Dec 19;7:43.
45. Vadiraja HS, Raghavendra RM, Nagarathna R, Nagendra HR, Rekha M, Vanitha N, Gopinath KS, Srinath BS, Vishweshwara



- MS, Madhavi YS, Ajaikumar BS, Ramesh BS, Nalini R, Kumar V. Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial. *Integr Cancer Ther.* 2009 Mar;8(1):37-46.
46. Loizzo JJ, Peterson JC, Charlson ME, Wolf EJ, Altemus M, Briggs WM, Vahdat LT, Caputo TA. The effect of a contemplative self-healing program on quality of life in women with breast and gynecologic cancers. *Altern Ther Health Med.* 2010 May-Jun;16(3):30-7.
47. Wolff M, Sundquist K, Larsson Lönn S, Midlöv P. Impact of yoga on blood pressure and quality of life in patients with hypertension—a controlled trial in primary care, matched for systolic blood pressure. *BMC Cardiovasc Disord.* 2013 Dec 7;13:111.
48. Tekur P, Chametcha S, Hongasandra RN, Raghuram N. Effect of yoga on quality of life of CLBP patients: A randomized control study. *Int Journal Yoga* 2010 Jan;3(1): 10-7.
49. Lundgren T, Dahl J, Yardi N, Melin L. Acceptance and Commitment Therapy and yoga for drug-refractory epilepsy: a randomized controlled trial. *Epilepsy Behav.* 2008 Jul;13(1):102-8.
50. Skevington SM, McCrate FM. Expecting a good quality of life in health: assessing people with diverse diseases and conditions using the WHOQOL-BREF. *Health Expect.* 2012 Mar;15(1):49-62.